Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care

Hemanshu Prabhakar
Shobana Rajan
Indu Kapoor
Charu Mahajan
Editors

Springer

Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care

Hemanshu Prabhakar • Shobana Rajan
Indu Kapoor • Charu Mahajan
Editors

Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care

Springer

Editors
Hemanshu Prabhakar
Department of Neuroanesthesiology & Critical Care
All India Institute of Medical Sciences
New Delhi, Delhi
India

Shobana Rajan
Vice chair for education & Associate Director of Neuroanesthesiology
Allegheny Health Network
Pittsburgh, Pennsylvania
USA

Indu Kapoor
Department of Neuroanesthesiology & Critical Care
All India Institute of Medical Sciences
New Delhi, Delhi
India

Charu Mahajan
Department of Neuroanesthesiology & Critical Care
All India Institute of Medical Sciences
New Delhi, Delhi
India

ISBN 978-981-15-0457-0 ISBN 978-981-15-0458-7 (eBook)
https://doi.org/10.1007/978-981-15-0458-7

© Springer Nature Singapore Pte Ltd. 2020, corrected publication 2020
This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.
The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.
The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

To Anavi and Amyra, my precious angels and gifts from heaven
—Hemanshu Prabhakar

To my mother, Saraswathy Nagarajan, who has been a great source of enthusiasm, encouragement, and support for my academic endeavors, someone I could always turn to and the best part is that she leads by example.
—Shobana Rajan

To Namyah and Nyra, who mean all the world to me.
—Charu Mahajan

To Ansh, my bundle of joy, who made my life more beautiful.
—Indu Kapoor

Foreword

The Authors of this book, dedicated to clinical practice of *Neuroanesthesia and Neurocritical Care*, have adopted an innovative approach based on "case scenario" discussion. I am extremely pleased and honored to contribute to these forewords to present the result of a long-lasting effort in international networking aimed to fulfill educational need of our subspecialty. In time, I have met and had the opportunity to cooperate with several of the contributors of this book, and this makes it easy for me to witness their quality as scientists and clinicians.

The first notion of neuroanesthesia—the practice of anesthesia for brain or spinal surgery—dates back to the late 1940s. Since then, this subspecialty has experienced significant improvements in terms of quality of delivered care, complexity of treated patients and performed procedures, and the number of treated cases. Specific education path are now available, and this is a substantial contribution to reach high level of quality in patients care along with personal experience and case load. This book provides a substantial contribution within these three important aspects to obtain better short- and long-term outcomes in patients undergoing neurosurgical procedures and to better define the competences necessary for an accredited subspecialty practice.

According to a contemporary approach, clinical workup should take into account principles of "evidence-based medicine" that are derived by clinical experience and research results. In everyday neuroanesthesia, it is important to achieve a dedicated clinical training—that begins in general anesthesiology—and a full understanding of the unique features of the neurosurgical or neurologically injured patients. Education in neuroanesthesia and neurocritical care should also include simulation training and research activity so that residents and fellows could learn specific tasks and build confidence with essential features in order to provide excellent ability. In clinical practice, neuroanesthesiology requires also nonprofessional competencies such as effective communication and interdisciplinary interactions among all the members of the clinical team. Specific knowledge and competences required make neuroanesthesia and neurocritical care a unique medical field.

This book entitled *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care* edited by Hemanshu Prabhakar and colleagues includes four major chapters: neurosurgical procedures; neurological patients; neuroradiology procedures; and "other" procedures and specific circumstances such as pregnant or HIV patients with brain tumor, or geriatric

patients with intraparenchymal bleed. The chapter on neurosurgical procedures is dedicated to clinical management of intracranial A-V malformation, brachial plexus injury, brain abscess, cerebellopontine angle tumor, subarachnoid hemorrhage, cervical spine injury, craniosynostosis, craniopharyngioma, acromegaly, craniovertebral junction anomaly, hydrocephalus, lumbar PIVD, Moyamoya disease, meningomyelocele, pituitary tumor-Cushing's disease, posterior fossa tumor, supratentorial tumor, traumatic brain injury—EDH, traumatic brain injury—SDH, motor strip gliomas—awake craniotomy and trigeminal neuralgia. The chapter on neurological patients is dedicated to clinical management of scoliosis, Guillain–Barre syndrome, myasthenia gravis, Parkinson's disease, stroke, and polyneuropathy. The chapter on neuroradiology procedures is dedicated to clinical management of embolization-aneurysm, carotid stenting, and vein of Galen malformation.

I strongly recommend for those that approach the clinical practice of *Neuroanesthesia and Neurocritical Care* to go through this book in a systematic way and to use it to get ready for "best clinical management." I also suggest this book to colleagues that are routinely involved in our discipline and to read the dedicated chapters when they will face one of the clinical scenario presented in this book; I am positive that it will be of great help in setting up a rationale workup for the daily practice.

Federico Bilotta
Department of Anesthesiology,
Critical Care and Pain Medicine,
University of Rome "La Sapienza",
Rome, Italy

Preface

There have been some great textbooks in neuroanesthesiology. However, as editors of this book, we felt the need to bring out a book that would interest the millennial generation of anesthesiologists and trainees. They are not just interested in clinical facts but would like to know how things work out and why it works out. It is important to communicate the foundations of neuroanesthesiology to the next generation effectively. Hence, the idea of writing a book in a case-based, problem-oriented format was born.

Our highly qualified experienced team of editors then set to work to determine common yet challenging neuroanesthesia scenarios one would encounter during their practice. Due to advancements in the field of neurosurgery, there have been several new surgical procedures. Monitoring the brain has also taken a giant leap with the technology boom. "Time is brain" and we hope that reading this book will give all the insight and skills necessary to deal with these complex situations posed to the clinician practicing neuroanesthesia.

Each chapter begins with a case, and this is followed by pre-operative evaluation, intra-operative management, and post-operative complications in a question format with answers and references for these answers. Multiple choice questions at the end of each chapter serve as a test to assess the reader's comprehension of the chapter.

As editors, we sought out neuroanesthesia experts throughout the world. Our authors have a high degree of expertise in their field, have been extremely willing and encouraging with this educational endeavor, and have shared their knowledge and experience with us.

Our team consisting of Hemanshu Prabhakar, Indu Kapoor, Charu Mahajan, and myself are happy to present you with this unique book. We think this would be of great benefit and we hope that you will enjoy reading every bit.

Happy reading,

Cleveland, OH, Pittsburgh, PA, USA — Shobana Rajan

Acknowledgements

We wish to acknowledge the support of the administration of the All India Institute of Medical Sciences (AIIMS), New Delhi, in allowing us to conduct this academic task.

Words are not enough to express our gratitude for the constant support and encouragement from the faculty and staff of the department of Neuroanesthesiology and Critical Care.

Special thanks are due to the production team of Springer—Dr. Naren Aggarwal, Dr. Eti Dinesh, Gaurav Singh, and Saanthi Shankhararaman.

Hemanshu Prabhakar
Charu Mahajan
Indu Kapoor

I would like to acknowledge the Society of Neuroscience in Anesthesiology and Critical Care (SNACC), where I have found inspiring mentorship and guidance. I would like to acknowledge the insight and support I have received from Dr. Rafi Avitsian who has always had time for me as a mentor from the early stages of my career in the United States.

It has been a great pleasure working with this wonderful team, Hemanshu, Indu, and Charu, and I thank them sincerely for their teamwork.

Shobana Rajan

Contents

About the Editors

Hemanshu Prabhakar is a Professor in Department of Neuroanesthesiology and Critical Care at the All India Institute of Medical Sciences (AIIMS), New Delhi, India. He received his training in neuroanesthesia and completed his PhD at the same institute. He is the first Indian to be admitted to the degree of PhD in Neuroanesthesia in the country. He is recipient of the AIIMS Excellence award for notable contribution in academics and has more than 250 publications in peer-reviewed national and international journals to his credit. Dr. Prabhakar is a reviewer for various national and international journals. He is also a review author for the Cochrane Collaboration and has a special interest in evidence-based practice of neuroanesthesia. Dr. Prabhakar is a member of various national and international neuroanesthesia societies and is past secretary of the Indian Society of Neuroanesthesiology and Critical Care. He is an invited faculty for various national and international conferences. He is on the editorial board of the Indian Journal of Palliative Care and is the past Executive Editor of the Journal of Neuroanesthesiology and Critical Care. He has published many international books in the specialty of neuroanesthesia and neurocritical care. He is an active member of the Education Committee and Membership Committee of the SNACC (Society for Neuroscience in Anesthesiology and Critical Care). He is the present Secretary of the Society of Neurocritical Care (SNCC) a global partner of Neurocritical Care Society (NCS). He was featured in Limca Book of Records 2019 as the 'most prolific writer' on Neuroanesthesiology.

Shobana Rajan is an anesthesiologist at the Allegheny General Hospital, Pittsburgh. She is also vice chair for education and associate director for neuroanesthesiology at the Allegheny Health Network. After residency at Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, she practiced anesthesia in some of the top hospitals in India like Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGI), Lucknow, Sri Ramachandra Medical College, Chennai, and Apollo Specialty Hospital, Chennai, for 10 years. She moved to the United States in 2006 and went on to do a residency and fellowship in neuroanesthesia at the Cleveland Clinic, where she served as associate program director for the neuroanesthesia fellowship. She has a number of peer-reviewed publications, book chapters, and national and international presentations to her credit. She is a board

member for the SNACC (Society for Neuroscience in Anesthesiology and Critical Care). She also currently leads the trainee engagement sub-committee of the SNACC. She is a member of the committee for "Technology for Advancement of Education in Anesthesia" which is a part of the Society for Education in Anesthesia (SEA). Her areas of interest in research are enhanced recovery pathways in neuroanesthesia and multimodal analgesia for spine surgery.

Indu Kapoor is an Associate Professor in the Department of Neuroanesthesiology and Critical Care at All India Institute of Medical Sciences (AIIMS), New Delhi, India. She received her training in neuroanesthesia at the same institute. She is the recipient of the prestigious Dr. T N JHA Memorial Award in 2009, by the Indian Society of Anesthesiologists (ISA). She has also received the SMT Chandra and SH Narayan Wadhwani Memorial Award for best outgoing postgraduate in anesthesia at the University College of Medical Sciences, Delhi, in 2010. She has many publications in national and international journals to her credit. She is also a reviewer of national and international journals and a review author for the Cochrane Collaboration. She has published international books in the specialty of neuroanesthesia and has contributed chapters in many books under renowned international publishers. Dr. Kapoor has a special interest in evidence-based practice in neuroanesthesia.

Charu Mahajan is an Associate Professor in the Department of Neuroanesthesiology and Critical Care at the All India Institute of Medical Sciences (AIIMS), New Delhi, India. After completing DM in Neuroanesthesiology at AIIMS, she later joined the department as a faculty member. She has authored several publications in peer-reviewed national and international journals. She has authored chapters in many books and has also received awards for scientific presentations. She is also a co-editor of three neuroanesthesia speciality books. She is member of the editorial board for Journal of Neuroanesthesiology and Critical Care and is a reviewer for several reputable scientific journals. Her areas of special interest are subarachnoid hemorrhage, awake craniotomy, and pediatric anesthesia.

Part I

Neurosurgery

Management of Patient with Intracranial A-V Malformation

1

Suparna Bharadwaj and K. N. Gopalakrishna

Stem Case Terminology

A 35-year-old male presented to your hospital with headache and vomiting for 5 months.

Question 1:
You are the neuroanesthesiologist on call and asked to assess this patient for future anesthetic and critical care management. How do you proceed?

Answer:
History taking and physical examination

Demographics: This patient is a 35-years-old gentle man hailing from Tamil Nadu. He is educated till twelfth grade and works as mason.

Chief complaints: Patient is a right-handed individual. He presented with episodic transient headache and vomiting since 5 months.

History of presenting illness: Patient was apparently normal 5 months back. That is when he was traveling in a bus and he had a sudden onset of headache. It was throbbing type and peaked over 10 min. Head ache was holocranial in location. It was so severe that the patient had to rush immediately to a regional hospital. After about 30 min, the patient had an episode of vomiting which relieved his headache.

Patient had four to five such episodes over the past 5 months with a frequency of one episode a month. Last two episodes were associated with giddiness.

There is no history of hypertension, seizures or weakness, visual loss, weakness in limbs, deviation of angle of mouth, loss of consciousness, and altered sensorium. There is no history of fever, alcoholism, vomiting, and diarrhea leading to dehydration. There is no history of fever and past history of tuberculosis. There are no signs of gait disturbances, difficulty in swallowing, or regurgitation of food particles and hoarseness of voice.

Treatment history: In the regional hospital, he was evaluated for migraine without any diagnostic success. Presently he is not on any medication.

Summarizing the history: This 35–year-old man is presenting with sudden onset of headache associated with features of raised intracranial pressure (ICP). His differential diagnosis would be causes of sudden onset head ache: (a) aneurysmal subarachnoid hemorrhage (b) cerebral arteriovenous malformation (cAVM) with bleed (c) intracranial tumor with bleed (d) cortical vein thrombosis (e) acute pyogenic meningitis.

S. Bharadwaj (✉) · K. N. Gopalakrishna
Department of Neuroanesthesia and Neurocritical care, National Institute of Mental Health and Neurosciences, Bangalore, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_1

General physical examination: Patient is middle aged, moderately built, and nourished. He does not have pallor, icterus, pedal edema, cyanosis, clubbing, and generalized lymphadenopathy.

Pulse is 82/min regular, blood pressure 126/80 mmHg in the right arm in supine position, and respiratory rate is 16/min regular.

1.1 Systemic Examination

1.1.1 Central Nervous System

Higher mental function: The patient is oriented with time, place, and person. Mini-mental state examination may be done for detailed assessment.

Cranial nerve examination: Clinical implications of cranial nerve examination to neuroanesthesiologist are given in Table 1.1.

Table 1.1 Clinical implications of cranial nerve examination to neuroanesthesiologist

Cranial nerve	Examination	Clinical implication to neuroanesthesiologist
1	smell	Not relevant
2	Visual acuity, afferent for pupillary reaction	Blurred vision in acute hydrocephalic attacks associated with headache and vomiting, pupillary asymmetry in cerebral herniation
3,4,6	Efferent for pupillary reaction Extraocular movement	Lateral rectus palsy-one of the signs of raised ICP Tumor in proximity to cavernous sinus may hamper Extraocular movements
5	Sensory and motor testing	Intraoperative monitoring of cranial nerve using electromyography (EMG) of masseter
7	Motor testing	Intraoperative facial nerve monitoring using EMG of frontalis, orbicularis occuli, and orbicularis oris
8	Sensory testing	Brain stem auditory evoked potentials to monitor hearing as well as brain stem integrity
9,10,12	Motor testing	Intraoperative cranial nerve monitoring, caution during extubation if preoperative gag and cough are impaired
11	Motor testing	Lower cranial nerve monitoring

1.1.2 Motor System Examination

Bulk and tone of muscles—normal, power is 5/5 in all four limbs. Superficial and deep tendon reflexes are normal. Plantar reflex is down-going

Sensory system examination: Touch, pain, and temperature are normal in all dermatomes.

Proprioception is normal, vibration sense is normal, Romberg's sign is negative

No cerebellar signs. Gait and stance are normal

Clinical implication: It is essential to study from surgical notes about the preexisting sensory and motor deficits. Somatosensory and motor-evoked potentials may be used intraoperatively to monitor sensory and motor tracts, respectively.

Cardiovascular system: Normal heart sound is heard and no added sounds on auscultation.

Respiratory system: Normal vascular breath sounds are heard.

Gastrointestinal system: Normal on palpation and auscultation.

Question 2:
What are the diagnostic tools that help to arrive at diagnosis in this patient

Answer:
Imaging of the brain is an useful modality to arrive at diagnosis (Fig. 1.1)

1. Non-contrast computed tomography (CT): to rule out space occupying lesion. CT brain of patient showed hyperdense lesion in right parieto-occipital region with enlarged draining veins. There is no mass effect or midline shift.
2. CT angiogram: Right parieto-occipital arteriovenous malformation (AVM) with specks of calcifications. Nidus is 2 × 2.2 cm. Feeders are from right middle cerebral artery (MCA) and right posterior cerebral artery (PCA).
3. Magnetic resonance angiogram: T2-weighted image shows flow voids in right parieto-occipital region. Feeders are from MCA branches. Nidus drains into transverse sinus.

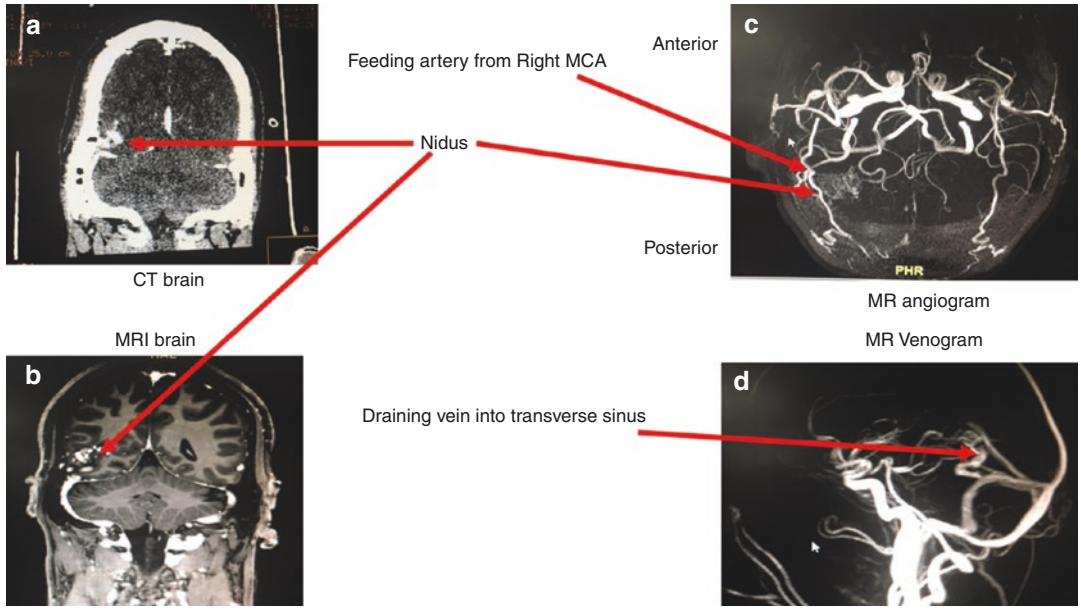


Fig. 1.1 Imaging modalities. (**a**) CT brain, (**b**) MRI brain, (**c**) MR angiogram, (**d**) MR venogram. *CT* computed tomography, *MRI* magnetic resonance imaging, *MR* magnetic resonance

4. Digital subtraction angiogram (DSA): shows nidus measuring $1.6 \times 2.2 \times 2.6\ cm^3$ (Fig. 1.2). Feeders are from posterior temporal branch of right MCA and right PCA. Nidus drains into transverse sinus.

Question 3:
What is cAVM? Discuss its epidemiology.

Answer:
cAVMs are anomalies of intracranial vessels where an abnormal connection exists between the arterial and venous systems, and they lack normal capillary angio-structure [2].

Epidemiology [2]**:** Incidence: 1.3 per 100,000 person-years. Prevalence: 10–18 per 100,000 adults.

Question 4:
What is the pathophysiology of cAVM?

Answer:
In cAVM, arteries are directly connected to veins without intervening capillary bed [3]. A tangle of abnormal dilated channels that are neither arterial nor venous shunt blood from arterial end to venous end. This tangle is called the nidus. Thus cAVM has a single or multiple feeding arteries and a single or multiple draining veins. Figure 1.1c shows the feeding artery, and Fig. 1.1d shows draining veins of cAVM in the pateint. Blood flow in both the feeding artery and draining vein is higher than normal, and there exists higher than normal pressure on the venous side. Long-standing high flow rates may cause shear stress, intranidal flow-related aneurysms, arterial steal in the surrounding region and venous outflow obstruction. Mutation in RASA 1 gene is associated with capillary malformation-arteriovenous malformation syndromes [4]. However, cAVM may be an acquired condition as well.

Question 5:
What is the natural history and symptomatology of cAVM?

Answer:
Natural history is poorly understood. Spontaneous obliteration may occur with small AVMs (<2.5 cm) that present with intracerebral hemor-

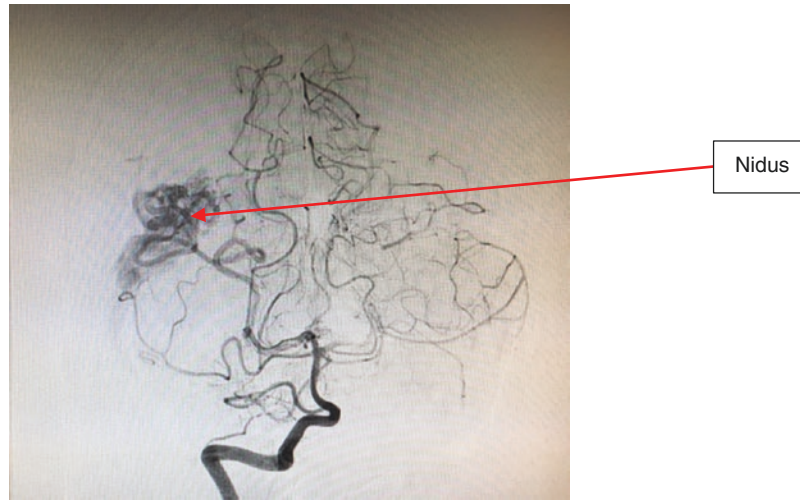


Fig. 1.2 Digital subtraction angiogram of cAVM

rhage (ICH). Favorable anatomic features for spontaneous obliteration are single draining vein, small AVM, and presenting with ICH. cAVMs may present with ICH, seizures, headache, and long-term disability [5]. Majority of cAVMs are superficial and supratentorial.

ICH: Annual incidence of hemorrhage of unruptured cAVM is 2–4%. About 38–71% of patients with cAVM present with ICH [6]. Age of presentation of ICH with cAVM is 20–40 years. Risk factors for hemorrhage include (1) deep venous drainage (periventricular, galenic, or cerebellar) (2) flow-related nidal aneurysm (3) deep seated AVM, and (4) infratentorial AVM. Patients presenting with ICH may undergo emergency decompressive craniectomy in the presence of raised ICP features. History of ICH guides the need for therapeutic intervention of cAVM.

Seizures [7]: 18–40% of patients with cAVM present with seizures. Most commonly associated seizures are generalized seizures (30%).

Headache: Headaches [8] occur in about 5–14% of patients. Headache can be unilateral and bilateral and can have migrainous features with or without aura.

Focal neurological deficits (FND): 1–40% of patients with cAVM manifest with FNDs [9]. Pathophysiology of FNDs is multifactorial. They are (a) vascular steal phenomenon (b) venous hypertension. Vascular steal is centered around perinidal tissue. Venous dilatation may lead to mass effect and compression of brain tissue leading to FNDs. FNDs are independently associated with increasing age, female gender, deep brain location, and venous drainage pattern [10].

Question 6:
What are the diagnostic imaging modalities?

Answer:
Conventional DSA is the gold standard in the evaluation of cAVM angioarchitecture. Other initial modalities of imaging include—CT brain, CT angiography, MRI brain, MR angiography [11].

Question 7:
What are the treatment modalities available for cAVM?

Answer:
Important decision-making process in choosing the treatment modality for cAVM is to compare the risks of all treatment modalities against the natural history risks of cAVMs. Management of cAVM involves either single modality alone or multimodal treatment involving medical management [12], microsurgical resection [12], stereotactic radiotherapy [13], and endovascular embolization [14]. The factors that direct treatment modality are operator skill, cAVM size and

Table 1.2 Spetzler Martin (SM) Grading Scale for cAVMs (this table is reproduced from Google images)

Characteristic	Number of points assigned
Size of AVM	
Small (<3 cm)	1 point
Medium (3–6 cm)	2 points
Large (>6 cm)	3 points
Location	
Non-eloquent site	0 points
Eloquent site[a]	1 point
Pattern of venous drainage	
Superficial only	0 points
Deep component	1 point

[a]Sensorimotor, language, visual cortex, hypothalamus, thalamus, internal capsule, brain stem, cerebellar peduncles, or cerebellar nuclei

location, surgical or endovascular accessibility, venous drainage, and presence of nidal flow aneurysm. ARUBA (a randomized trial of unruptured brain arteriovenous malformations) was the randomized controlled trial to assess surgical intervention versus medical management for unruptured cAVM. Fallacy in study design, implementation, short length of follow-up, and insufficient information regarding the treatment arm and the recruitment process invalidated the authors' conclusions [15].

Question 8:
Which is the mostly used grading system of cAVM in the context of micro-surgical resection?

Answer:
In 1986, Spetzler and Martin established a grading system (Table 1.2) for cAVMs based on the size of the nidus, location with respect to eloquent cortex, and venous drainage system [16].

Question 9:
What is the Spetzler Martin (SM) grading of cAVM of the above patient and what is the most suitable modality of treatment for him?

Answer:
SM grading of cAVM of the patient is

Size of cAVM is 1.6 × 2.2 × 2.6 cm^3 SM score = 1, Location—non eloquent—SM score = 0, Pattern of venous drainage-superficial component only—SM score 0

SM grade of the cAVM is 1 since it is a low-grade AVM in a surgically resectable, non-eloquent right parieto-occipital area with a single feeding artery, and a superficial draining vein.

Question 10:
Discuss anesthetic consideration for a patient with cAVM planned for a surgical resection.

Answer:
Neuroanesthesiologist encounters patients with cAVM for preoperative investigation (CT/MRI or DSA), preoperative endovascular embolization, surgical resection, or stereotactic radiosurgery.

Anesthetic drugs and cerebral physiology: Intravenous anesthetics reduce cerebral metabolic rate (CMR). There is also increase in vascular resistance resulting in decrease in cerebral blood flow (CBF). But most of the inhalational anesthetics except nitrous oxide cause vasodilation, increased CBF, and decrease in the cerebral metabolic rate of oxygen ($CMRO_2$). With normal anesthetic doses of inhalational agents, flow metabolism coupling is maintained [17]. Barbiturates, etomidate, and propofol may be used for brain protection during AVM embolization and/or surgical resection, when the brain is at the risk of focal ischemia [18].

Although not proved for each anesthetic, those that produce vasodilation may cause the steal phenomenon, and the anesthetics that constrict the vessels have the opposite effect, resulting in inverse steal, and may protect the brain or enhance the damage [19]. Effects of opioids on CBF, $CMRO_2$, and ICP are variable, slow administration in titrated doses, with care to maintain mean blood pressure is recommended [20]. Muscle relaxants, with the exception of succinylcholine have least effects on CBF and $CMRO_2$ as long as normocapnia is maintained, whereas succinylcholine causes an increase in ICP because of fasciculations [21].

Anesthesia for preoperative investigations: If the patient is a child or an uncooperative adult, monitored anesthesia care (MAC) or/and general

anesthesia is required for preoperative imaging (CT/MRI/DSA). In our institution, MAC with intravenous midazolam 0.02–0.05 mg/kg is followed by intravenous infusion of propofol at the rate of 75 μg to 100 μg/kg/min. Injection midazolam followed by intravenous dexmedetomidine infusion at the rate of 0.02 μg to 1 μg/kg/h is also administered to patients for whom injection propofol is deemed unsuitable. Normoxia/normocarbia and ward blood pressures are maintained during MAC. General anesthesia with airway intervention is administered to cases in which MAC is failed or to cases requiring preoperative nidus embolization to occlude surgically inaccessible arterial feeder or to decrease the size of the nidus preoperatively. Imaging is done either electively or on an emergency basis. During preoperative assessment, neurological status of the patient including clinical assessment of ICP, CBF, cerebral oxygenation, airway, fasting status, and cardiovascular stability should be evaluated. Choice of anesthetic and technique of anesthesia is dictated by the clinical status of the patient at presentation.

Question 11:
What are the surgical considerations of cAVM?

Answer:
Standard surgical resection of cAVM involves microsurgical technique. The arterial feeders are tackled first, followed by excision of the nidus and finally resection of the draining veins. Veins are preserved till the very end of surgery [21]. Completeness of resection can be confirmed by intraoperative ultrasonography, intraoperative MRI, or DSA. If there is residual nidus, resection should be considered to avoid subsequent hemorrhage [21]. Stereotactic radiosurgery may also be considered for residual cAVM [22].

Question 12:
Discuss anesthetic management of surgical resection of cAVM

Answer:
Use of microsurgical technique combined with preoperative embolization and advanced neuroanesthesia techniques has enabled the total resection of cAVM, previously considered inoperable. General anesthesia is usually administered to patients undergoing surgical resection of cAVM. However, awake craniotomy may be required to resect cAVM in eloquent areas of brain.

Preoperative evaluation and premedication: Resection of cAVM is rarely performed as an emergency procedure [23]. Hence thorough preoperative evaluation is feasible. Preexisting comorbidities should be optimally treated and controlled prior to surgery. Existence of neurological dysfunction secondary to ICH due to ruptured cAVM, oligemic stroke, or mass effect due to cAVM itself should guide the choice of anesthetics and perioperative monitoring techniques to optimize postoperative neurological outcome [24]. An important consideration throughout the operation is the potential for rapid and massive blood loss [25]. Since most of the resection surgeries are elective, we counsel and explain the patient in detail of the perioperative management, and hence, we reserve anxiolytic medication like midazolam to apprehensive adults and to pediatric patients. Patients who have undergone preoperative embolization may have new onset neurological deficits [26], renal dysfunction [27] due to contrast used for angiography, and dehydration secondary to contrast agents. Accurate patient history and examination, optimization of fluid balance, renal parameters, and preparedness with blood and blood products prior to anesthetic induction are absolutely necessary.

Anesthetic technique: Choice of anesthetic agents is mainly guided by the coexistent morbidity. ICP is not a major concern as most of the cAVMs are operated on an elective basis [28]. Anesthetic agents whether intravenous or inhalational are titrated to maintain normoxia, normocapnia, and preoperative hemodynamics. Smooth and rapid emergence from anesthesia is also crucial for postoperative neurological assessment and avoidance of hemodynamic upheavals. The major differences between embolization and surgery are the presence of noxious surgical stimula-

tion and possibility of sudden and profuse blood loss. Thiopentone, etomidate, and propofol are used as induction agents, and in children, we use sevoflurane for induction. Hemodynamic response to laryngoscopy, application of may field clamp to head, skin incision, periosteal elevation, and craniotomy should be anticipated and appropriate drugs like analgesics, local anesthetics (scalp block or pin site infiltration), thiopentone, propofol, and antihypertensives may be used. Careful patient positioning is essential to avoid nerve injury (padding pressure points), damage to eyes (eye padding and doughnut-shaped headrest), obstructed venous drainage (avoid excessive neck flexion and rotation), high airway pressure (avoid excessive neck flexion and rotation), and brain swelling (provide head end elevation). For awake craniotomy, we use MAC with injection dexmedetomidine. A bolus dose of 1 μg/kg/h is followed by an infusion of 0.2–1 μg/kg/h. Once the patient is asleep scalp block with 0.25% bupivacaine and 1% lignocaine with adrenaline calculated as per patient's body weight. After the craniotomy is completed, dexmedetomidine infusion is either stopped or lowered to keep the patient awake and cooperative for neurological assessment during cAVM resection. Post resection, dexmedetomidine infusion is resumed to keep the patient sedated during craniotomy wound closure.

Cerebral injury: Cerebral injury is caused by either surgical or anesthetic causes. Neurosurgeon-induced injury includes brain retraction, direct vascular injury (ischemia, thrombosis, and venous occlusion), and mechanical disruption of neuronal tissue or white matter tracts [24]. Anesthesia-induced injury may result in physiological trespass. Management goals should include ensuring brain relaxation and optimal systemic and cerebral hemodynamics, avoiding hypotonicity, maintenance of euglycemia, and a smooth emergence from anesthesia [24].

Cerebral protection: Pharmacological: Intraoperative brain swelling is the most common indication for pharmacological cerebral protection [29]. We use injection propofol or thiopentone titrated to burst suppression guided by scalp electroencephalogram (EEG). Avoid inhalational agents above mean alveolar concentration of 1. Use of appropriate vasopressors/inotropes and or intravenous fluids to maintain optimal cerebral perfusion pressure (CPP) is recommended [30]. Intraoperatively we assess volume responsiveness guided by pulse pressure variation (PPV). After optimizing the PPV values and hemoglobin values, we use intravenous noradrenaline infusion at the rate of 0.05–0.1 μg/kg/min when indicated. If the systemic blood pressure is suboptimal at the end of surgery, we assess cardiac function by transthoracic echocardiography (TTE) at the earliest opportunity and add appropriate inotropes to improve cardiac function. We continue to follow improvements in cardiac function and fluid status periodically by assessing inferior vena cava (IVC) diameter and TTE.

Non-pharmacological interventions: Head end elevation, avoidance of extreme neck flexion to avoid kinking of neck veins which facilitates venous drainage. Hyperventilation for a shorter duration taking care to avoid fall in $PaCO_2$ below 30 mmHg. Hyperventilation may be guided by cerebral oxygenation monitors like near infrared spectroscope (NIRS) or jugular venous oximetry [31].

Question 13:
What are the perioperative complications of surgical resection of cAVM and how are they managed?

Answer:
Intraoperative bleeding: Neuroanesthesiologist should be prepared for rapid and torrential bleeding with blood and blood products.

Intraoperative brain swelling due to ICH may be tackled by techniques of pharmacological and non-pharmacological cerebral protection.

Intraoperative and postoperative brain edema and hemorrhage: Two propositions for the development of brain edema and hemorrhage during and after surgery are normal pressure perfusion breakthrough (NPPB) and occlusive hyperemia. The NPPB hypothesis proposes that postoperative hemorrhage and edema are caused by a preexistent deranged autoregulation in the isch-

emic brain around the AVM. Chronic oligemia in brain surrounding cAVM may produce maximal chronic vasodilation, which results in failed or insufficient vasoconstriction in response to the reinstitution of normal perfusion pressure after the AVM has been resected. According to this hypothesis, the key to avoid postoperative hemorrhage and edema is staged reduction of blood supply to the malformation. However, a number of observations suggest that the details of this theory are not applicable to most cases of malignant postoperative hemorrhage and edema. Some studies showed preserved autoregulation in the region surrounding a cAVM both before and immediately after its resection, and such cases went on to develop edema and hemorrhage. This observation argues against the theory of impaired autoregulation leading to NPPB. It has also led to the proposal of an alternative hypothesis termed "occlusive hyperemia." This proposal postulates that malignant postoperative hemorrhage and edema are caused by either arterial stasis and obstruction or venous outflow obstruction, secondary to resection of cAVM. Consequences of NPPB like cerebral edema and hemorrhage are diagnosed by brain imaging, whereas occlusive hyperemia is diagnosed by DSA. NPPB requires lowering of MAP and antiedema measures. In our institute, MAP is maintained at 70–80 mmHg with labetalol infusion at the rate of 1–2 mg/min. We use clinical examination and NIRS to monitor cerebral oxygenation during labetalol infusion. When occlusive hyperemia is established, patient is hydrated to euvolemia, and MAP is maintained at 90–100 mmHg. Fluid infusion is guided by periodic TTE and/or IVC diameter assessments. Vasopressors and or inotropes are used to maintain desired MAP as and when needed.

Question 14:
How do you use bedside multimodality monitoring in the management of a case of cAVM?

Answer:
Perioperative bediside multimodality monitoring includes.

Preoperative monitoring: CBF velocities in feeding arteries are higher than in normal arteries remote from cAVM, and their pulsatality indices are lower than normal arteries [32]. Autoregulation may or may not be intact in the feeding arteries [33]. Jugular venous oximetry of the dominant jugular bulb demonstrates higher than normal (usually >70) jugular venous oxygen saturation as a result of shunting of arterial and venous blood without gas exchange occurring at nidus [34]. NIRS in the frontal region may display $rSO_2 > 70$ when the NIRS sensor picks up signals from shunted blood which is rich in oxyhemoglobin [35]. NIRS may display $rSO_2 < 40$ if it picks up signals from surrounding oligemic brain.

Intraoperative monitoring: We monitor cerebral oxygenation using jugular oximetry or NIRS. EEG, somatosensory-evoked potentials and motor-evoked potentials are monitored for the detection of ischemia. We titrate hemodynamics when global suppression of cerebral oximetry and neurophysiological parameters occur. In the event of regional variation of cerebral oxygenation, EEG, and evoked potentials, neurosurgeon is warned about the changes, and appropriate measures of cerebral protection are executed. Intraoperative ultrasonography [36] (Fig. 1.3) or neuronavigation is gaining popularity because of their ability to localize the cAVM and also help to determine the extent of final resection. Intraoperative indocyanine green injection and examination under microscope also helps to determine the extent of resection of cAVM. Intraoperative DSA is the gold standard technique both for localization and to detect the presence of residual nidus.

Postoperative monitoring: Substantial fall in cerebral oximetry and jugular oximetry from baseline indicates significant shunt fraction reduction of cAVM [35]. Shunt fraction reduction is a reliable predictor of postoperative NPPB [37]. Increased CBF velocities demonstrated by TCD also indicates hyperemia.

Multiple Choice Questions:

1. Which of the following is not a component of cAVM?
   (a) Feeding artery
   (b) Draining vein
   (c) Nidus connecting artery to vein
   (d) Capillary-plexus connecting artery to vein

   Answer: d

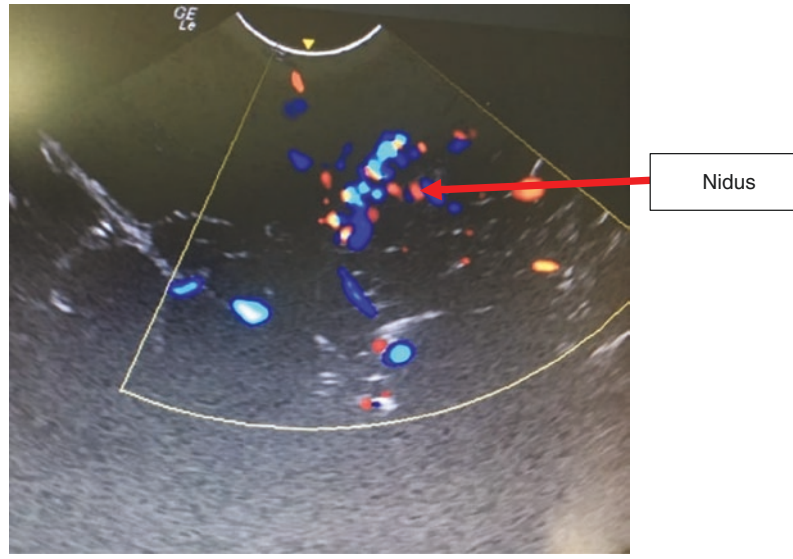


Fig. 1.3 Intraoperative ultrasonography showing nidus

Explanation: cAVMs are anomalies of intracranial vessels where an abnormal connection exists between the arterial and venous systems, and they lack normal capillary angio-structure. cAVM has a single or multiple feeding arteries and a single or multiple draining veins. In cAVM, arteries are directly connected to veins without intervening capillary bed.

2. Which of the following is the definitive curative modality of treatment for cAVM?
   (a) Microsurgical resection
   (b) Stereotactic radiosurgery
   (c) Embolization
   (d) Medical management
   Answer: a

   Explanation: Microsurgical resection involves excision of all components of cAVM, namely feeding artery, draining vein, and the nidus. Whereas other modalities of treatment decrease the shunt fraction, but new feeder arteries may recruit with time when residual nidus exists.
3. NPPB is a postoperative complication of
   (a) Cerebral aneurysm
   (b) cAVM
   (c) Moyamoya disease
   (d) Pituitary apoplexy
   Answer: b

   Explanation: Chronic oligemia in brain surrounding cAVM may produce maximal chronic vasodilation, which results in failed or insufficient vasoconstriction in response to the reinstitution of normal perfusion pressure after the AVM has been resected. Such a phenomenon is known as NPPB. It is not seen with conditions a, c, and d.
4. Which of the following regarding multimodality monitoring in a patient with cAVM is incorrect?
   (a) Increased CBF velocities as measured by transcranial Doppler in feeding artery
   (b) Jugular venous oximetry ($SjvO_2$) of <40
   (c) Oligemia surrounding nidus on DSA
   (d) Raised ICP in a longstanding cAVM
   Answer: b

   Explanation: Jugular venous oximetry of the dominant jugular bulb demonstrates higher than normal (usually >70) jugular venous oxygen saturation as a result of shunting of arterial and venous blood without gas exchange occurring at nidus

References

Question 1

1. Purkait R, Samanta T, Thakur S, Dhar S. Neurocutaneous syndrome: a prospective study. Indian J Dermatol. 2011;56(4):375–9.

Question 3

2. Ozpinar A, Mendez G, Abla AA. Epidemiology, genetics, pathophysiology, and prognostic classifications of cerebral arteriovenous malformations. Handb Clin Neurol. 2017;143:5–13.

Question 4

3. Martin NA, Vinters HV. Arteriovenous malformations. In: Carter LP, Spetzler RF, Hamilton MG, editors. Neurovascular surgery. New York: McGraw-Hill; 1995. p. 875–903.
4. Revencu N, Boon LM, Mulliken JB, Enjolras O, Cordisco M, et al. Parkes Weber syndrome, vein of Galen aneurysmal malformation, and other fast-flow vascular anomalies are caused by RASA1 mutations. Hum Mutat. 2008;29(7):959–65.

Question 5

5. Goldberg J, Raabe A, Bervini D. Natural history of brain arteriovenous malformations: systematic review. J Neurosurg Sci. 2018;62(4):437–43.
6. Mine S, Hirai S, Ono J, Yamaura A. Risk factors for poor outcome of untreated arteriovenous malformation. J Clin Neurosci. 2000;7:503–6.
7. Fults D, Kelly DL Jr. Natural history of arteriovenous malformations of the brain: a clinical study. Neurosurgery. 1984;15(5):658–62.
8. Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenousmalformations of the brain: a 24-year follow-up assessment. J Neurosurg. 1990;73(3):387–91.
9. Mast H, Mohr JP, Osipov A, et al. “Steal” is an unestablished mechanism for the clinical presentation of cerebral arteriovenous malformations. Stroke. 1995;26(7):1215–20.
10. Choi JH, Mast H, Sciacca RR, et al. Clinical outcome after first and recurrent hemorrhage in patients with untreated brain arteriovenous malformation. Stroke. 2006;37(5):1243–7.

Question 6

11. Geibprasert S, Pongpech S, Jiarakongmun P, Shroff MM, Armstrong DC, Krings T. Radiologic assessment of brain arteriovenous malformations: what clinicians need to know. Radiographics. 2010;30(2):483–501.

Question 7

12. Barr JC, Ogilvy CS. Selection of treatment modalities or observation of arteriovenous malformations. Neurosurg Clin N Am. 2012;23(1):63–75.
13. Sun DQ, Carson KA, Raza SM, Batra S, Kleinberg LR, et al. The radiosurgical treatment of arteriovenous malformations: obliteration,morbidities, and performance status. Int J Radiat Oncol Biol Phys. 2011;80(2):354–61.
14. Krings T, Hans FJ, Geibprasert S, Terbrugge K. Partial “targeted” embolization of brain arteriovenous malformations. Eur Radiol. 2010;20(11):2723–31.
15. Mohr JP, Parides MK, Stapf C, Moquete E, Moy CS, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet. 2014;383(9917):614–21.

Question 8

16. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg. 1986;65(4):476–83.

Question 10

17. Steen PA. Inhalational versus intravenous anesthesia: cerebral effects. Acta Anaesthesiol Scand Suppl. 1982;75:32–5.
18. Sinha PK, Neema PK, Rathod RC. Anesthesia and intracranial arteriovenous malformation. Neurol India. 2004;52(2):163–70.
19. Sakabe T, Nakakimura K. Effects of anesthetic agents and other drugs on cerebral blood flow, metabolism and intracranial protection. In: Cottrell JE, Smith DS, editors. Anaesthesia and neurosurgery. 4th ed. St. Louis: Mosby; 2002. p. 129–43.
20. Oddo M, Crippa IA, Mehta S, Menon D, Payen JF, Taccone FS, Citerio G. Optimizing sedation in patients with acute brain injury. Crit Care. 2016;20(1):128.

Question 11

21. Bhatoe HS. Operative nuances of surgery for cortical arteriovenous malformations: a safe solution and permanent cure. Neurol India. 2016;64(Suppl S1):101–9.
22. Moorthy RK, Rajshekhar V. Sterotactic radiosurgery for intracranial arteriovenous malformations: A review. Neurol India. 2015;63:841–51.

Question 12

23. Bhatoe HS. Operative nuances of surgery for cortical arteriovenous malformations: a safe solution and permanent cure. Neurol India. 2016;64(Suppl S1):101–9.

24. Sinha PK, Neema PK, Rathod RC. Anesthesia and intracranial arteriovenous malformation. Neurol India. 2004;52(2):163–70.
25. Conger A, Kulwin C, Lawton MT, Cohen-Gadol AA. Endovascular and microsurgical treatment of cerebral arteriovenous malformations: Current recommendations. Surg Neurol Int. 2015;6:39.
26. Jordan J, Llibre JC, Vazquez F. Predictors of neurological deficit after endovascular treatment of cerebral arteriovenous malformations and functional repercussions in prospective follow-up. Neuroradiol J. 2014;27(6):718–24.
27. Tao Y, Dong W, Li Z, Chen Y, Liang H, et al. Proteinuria as an independent risk factor for contrast-induced acute kidney injury and mortality in patients with stroke undergoing cerebral angiography. J Neurointerv Surg. 2017;9(5):445–8.
28. Sinha PK, Neema PK, Rathod RC. Anesthesia and intracranial arteriovenous malformation. Neurol India. 2004;52(2):163–70.
29. Jha SK. Cerebral edema and its management. Med J Armed Forces India. 2011;59(4):326–31.
30. Ling GS, Neal CJ. Maintaining cerebral perfusion pressure is a worthy clinical goal. Neurocrit Care. 2005;2(1):75–81.
31. Schell RM, Cole DJ. Cerebral monitoring: jugular venous oximetry. Anesth Analg. 2000;90(3):559–66.

Question 14

32. Shakur SF, Amin-Hanjani S, Mostafa H, Aletich VA, Charbel FT, et al. Relationship of pulsatility and resistance indices to cerebral arteriovenous malformation angioarchitectural features and hemorrhage. J Clin Neurosci. 2016;33:119–23.
33. Hacein-Bey L, Young WL. Hemodynamic perturbations in cerebral arteriovenous malformations and management implications. Interv Neuroradiol. 1999;5(Suppl 1):177–82.
34. Sharma D, Siriussawakul A, Dooney N, Hecker JG, Vavilala MS. Clinical experience with intraoperative jugular venous oximetry during pediatric intracranial neurosurgery. Paediatr Anaesth. 2013;23(1):84–90.
35. Asgari S, Röhrborn HJ, Engelhorn T, Fauser B, Stolke D. Intraoperative measurement of cortical oxygen saturation and blood volume adjacent to cerebral arteriovenous malformations using near-infrared spectroscopy. Neurosurgery. 2003;52(6):1298–304; discussion 1304–6.
36. Sinha PK, Neema PK, Rathod RC. Anesthesia and intracranial arteriovenous malformation. Neurol India. 2004;52(2):163–70.
37. Katayama Y, Tsubokawa T, Hirayama T, Himi K. Continuous monitoring of jugular bulb oxygen saturation as a measure of the shunt flow of cerebral arteriovenous malformations. J Neurosurg. 1994;80(5):826–33.

2 Management of Patient with Brachial Plexus Injury

Hossam El Beheiry

Stem Case

A nonobese 68-year-old female presented with left-sided hearing loss and vertigo. MRI study showed a left cerebellopontine angle tumor having features of a large vestibular schwannoma 3.5 cm in size. There was no evidence of obstructive hydrocephalus or trigeminal involvement. She has been a non-insulin-dependent diabetic for 20 years with the evidence of peripheral neuritis in the upper and lower limbs. The blood sugar was controlled with oral hypoglycemics and her latest HBA1C was 7.6%. Other laboratory tests were normal. She also had incidentally diagnosed left cervical rib. The patient consented for a left suboccipital craniotomy for tumor excision. After she was intubated with a 7.5 mm endotracheal tube, an arterial and central line were inserted in the left radial and right internal jugular vein, respectively. She was then placed in the right park-bench position. A three-point head fixation device was applied, the patient was turned on her side and the shoulder contralateral to the lesion supported by a roll in the axilla; the ipsilateral shoulder was rolled forward and pulled down with tape. The head was kept in a relatively neutral position. The dependent arm was suspended by a sling in the crook of the Mayfield attachment. All pressure points were carefully padded, and the patient head was slightly elevated with a reverse Trendelenburg position. The tumor was totally removed. The surgical duration was 14 h. The position of the patient was changed few times in a right or left tilt along the longitudinal axis of the body. The mean arterial blood pressure was maintained at 70–80 mmHg. She had about 6000 mL IV Ringer's lactate and maintained normal urine output. The estimated blood loss was 400 mL, and no blood transfusions were necessary. After removal of the drapes, the contralateral shoulder was found to be posteriorly displaced. The patient was kept intubated and transferred to the ICU where she was extubated the next day.

Few hours after extubation, the patient complained of weakness in her right hand. Physical examination showed weak grip 1/5 of the right hand. The right hand attained a claw-like position with hyperextension at the metacarpophalangeal joints and flexion at the interphalangeal joints. Additionally, there was a narrow zone of lost sensation along the ulnar border of the forearm and hand. Nerve conduction studies confirmed BPI on the right side involving C8 and T1 distribution. The studies also indicated that the type of injury is probably at the level of the trunks involving the lower trunk (Fig. 2.1). Neurosurgery was consulted, and conservative treatment was recommended. The patient

The original version of this chapter was revised. An erratum to this chapter can be found at https://doi.org/10.1007/978-981-15-0458-7_33

H. El Beheiry (✉)
Department of Anesthesia, University of Toronto, Toronto, ON, Canada
e-mail: h.el.beheiry@utoronto.ca

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_2

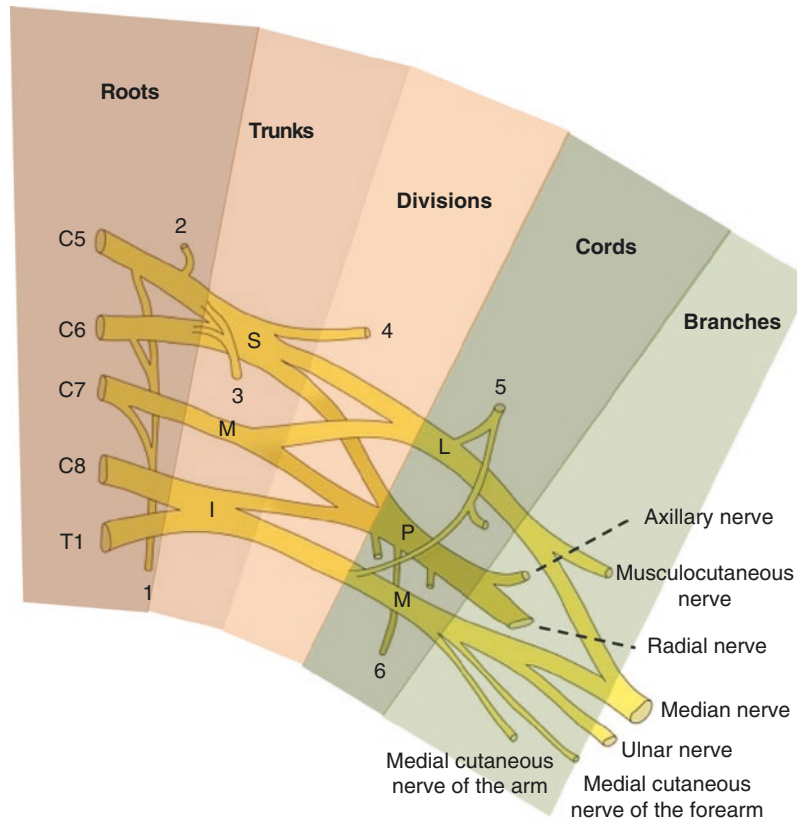


Fig. 2.1 Anatomy of the brachial plexus. The roots combine to form superior (S), middle (M), and inferior (I) trunks. Each trunk divides into anterior and posterior divisions. Posterior divisions unite to form the posterior cord (P). Anterior divisions of the superior and middle trunks unite to form the lateral cord (L). Anterior division of the inferior trunk continues to be the medial cord (M). The important nerves that originate proximal to the terminal branches include long thoracic nerve (*1*), dorsal scapular nerve (*2*), nerve to subclavius (*3*), subscapular nerve (*4*), pectoral nerve (*5*), and thoracodorsal nerve (*6*)

was discharged with weakness, paresthesia, and mild to moderate pain in the right hand. Extensive physiotherapy was performed. The patient's hand weakness improved slowly over 9 months and full motor power returned within 12 months with residual paresthesia.

2.1 Preoperative

Question 1:
What is the incidence of PNI?

Answer:
The incidence is not precisely known due to the absence of a reliable denominator and possible underreporting of PNI. Retrospective studies quoted 0.03–1.4% perioperative PNI [1]. It should be noted that some of these studies included patients who received neuraxial or peripheral plexus or single nerve blockade. Ulnar nerve, brachial plexus, and lumbosacral root injuries represent 28%, 20%, and 16%, respectively, of the total PNI events. Perioperative injuries to the sciatic, median, radial, and femoral nerves are less common. PNI in many cases have undetermined etiology or mechanism, e.g., 90% of ulnar nerve injuries [2].

Question 2:
What are the preoperative risk factors for PNI in this patient? Mention the risk factors for brachial plexus nerve injury during anesthesia and surgery.

Answer:
The preoperative risk factors for the brachial nerve injury in this case include preexisting diabetes and diabetic peripheral neuropathy, and the presence of cervical rib on the same side of injury. Other perioperative factors include park-bench position including abduction, posterior displacement of the shoulder, and increased surgical duration.

The perioperative risk factors are summarized in Table 2.1 [3].

Table 2.1 Perioperative risk factors for brachial plexus injury

Preoperative factors	Intraoperative factors
Preexisting diseases	Positioning
Diabetes	Shoulder/arm abduction >90°
Hypothyroidism	Steep Trendelenburg
Acromegaly	Posterior shoulder displacement
Neuropathy	External arm rotation
Polyarteritis nodosa	Rotation of head >20°
Herpes zoster	Anesthesia and surgery
Preexisting abnormal anatomy	Long duration
Anomalous nerve root origins	Sternotomy
Cervical rib	Hypotension
Shoulder deformity	Hypothermia

Question 3:
Mention the neurologic effects of the presence of cervical rib.

Answer:
A cervical rib represents a persistent ossification and elongation of the transverse process of C7. The long transverse process can develop into full-size extra rib or fuse with the T1 rib.

Cervical ribs can cause a neurogenic type of thoracic outlet syndrome due to compression of the lower trunk of the brachial plexus [4]. Compression of the lower trunk of the brachial plexus causes weakness (weak grip) and sometimes atrophy of the thenar and hypothenar muscles. Additionally, sharp, burning, or aching pain can be present in the ulnar aspect of the arm and hand and reduced sensation to light touch in the fourth and fifth fingers. Patients may have pain in the side of the neck, the infraclavicular area, the axilla, and the upper back. Discoloration and coldness of the ipsilateral hand are not uncommon. If the upper trunk of the brachial plexus is involved, pain and paresthesias are experienced on the neck, shoulder, and face. Paresthesias radiate into the lateral arm and simulate fifth or sixth cervical nerve root compression.

2.2 Intraoperative

Question 4:
Discuss the common BPIs related to intraoperative patient positioning.

Answer:
The brachial plexus and its terminal branches are vulnerable to injury because of intraoperative malpositioning. The most common intraoperative injuries include ulnar nerve, upper/middle trunk, and lower trunk injuries [5].

Ulnar nerve injury: The incidence of intraoperative positioning-related ulnar nerve injury is between 1:215 and 1:385. If the ulnar nerve is subjected to injury, pain, paraesthesia, and/or weakness in its distribution usually occur in the immediate or early postoperative period. Ulnar nerve function recovers within 6 weeks in 50% of cases; however, the remaining 50% usually recovers within 24 months. Patients typically complain of numbness and/or pain in the ulnar-side of the hand (small finger and ulnar aspect of the ring finger). Additionally, motor functional impairment can be present in the form of clumsiness and loss of dexterity due to weakness of the intrinsic muscles of the hand.

Upper/middle trunk injury (C5/6): Such injuries have an overall incidence of approximately 1:2000. They present with motor deficit in the C5/C6 myotomes, often without sensory deficits. There is weakness of shoulder abduction and elbow flexion. The upper trunk is most at risk of stretch during prolonged and excessive shoulder depression and can be exacerbated by contralateral neck flexion. Full recovery is expected in about 80% of patients.

Lower trunk injury (C8/T1): It can complicate up to 1:20 cases of median sternotomy in cardiac surgery due to traction of the first rib against the lower trunk. Also, the lower trunk can be vulnerable during prolonged and excessive shoulder abduction (>90°), contralateral head rotation >20°, and when the arms are

positioned below the height of the torso. Injury leads to numbness and may be pain in the distribution of the ulnar nerve. Motor impairment follows median and ulnar nerve distribution in the form of weak finger and thumb flexion as well as weakness in the small muscles of the hand.

Question 5:
Propose recommendations related to perioperative positioning to prevent BPIs?

Answer:
Several recommendations have been proposed for protecting the brachial plexus from injury during intraoperative positioning including [6, 7]:

- In the supine position, avoid extension and external rotation of the arm by limiting abduction to <90° and placing the arm supinated in the neutral position.
- In the prone position, avoid extreme arm abduction by tucking in and padding the arms by the patient's side, rather than abducting the arm above the head by more than 90°. Alternatively, the arms can be flexed at the elbow and the forearms placed on arm boards at a level lower than the torso and the upper arm placed almost vertical, and adducted without posterior displacement of the shoulder.
- In steep Trendelenburg position, tuck the arms in at the patient's side with draw sheets. Use "Butterfly Steep Trendelenburg Bean Bag Positioner" to support the patient and prevent the body from sliding cephalad. Using wrist suspensions or shoulder braces to prevent cephalad sliding increases the risk of BPI.
- In the lateral decubitus position, always use an axillary-chest roll and avoid suspension of the arm from an L-shaped bar or a sling.
- In any position, always keep the head in neutral position. Excessive rotation and lateral flexion of the neck can dangerously stretch the contralateral brachial plexus.

Question 6:
What are the anesthetic considerations and management if this patient had to undergo major brachial plexus exploration and repair?

Answer:
Major brachial plexus exploration and repair is a lengthy procedure. Hence, general anesthesia is usually preferred. Table 2.2 shows the anesthetic consideration and actions that can be done to provide safe anesthesia for those patients with prolonged surgery that may involve microvascular techniques [8, 9].

2.3 Postoperative

Question 7:
Discuss the clinical anatomy of the brachial plexus.

Answer:
The brachial plexus consists of a complex system of nerves [10]. It passes through the posterior triangle of the neck into the axilla. The brachial plexus is bounded anteriorly by the anterior scalene muscle, posteriorly by the mid scalene muscle, and inferiorly by the outer border of the first rib. It is a complex intercommunicating network of nerves formed in the neck by the anterior rami of the spinal nerve roots C5, C6, C7, C8, and T1. Figure 2.1 summarizes the structure of the brachial plexus including roots, trunks, divisions, cords, and terminal branches. Various branches of the subclavian artery supply the brachial plexus along its length, i.e., vertebral artery; spinal arteries supply the roots; ascending and deep cervical arteries and superior intercostal artery supply the trunks and divisions; and the axillary artery supplies the cords.

It supplies sensory innervation to the upper limb and most of the axilla except a small area in the medial upper arm and axilla (supplied by the intercostobrachial nerve).

It delivers motor innervation to the muscles of the upper limb and shoulder girdle except the trapezius muscle (supplied by the spinal accessory nerve).

Table 2.2 Anesthetic considerations for prolonged brachial plexus repair

Anesthetic consideration	Action
Pressure care	Use of thick foam (3–4″) on top of the OR table mattress
	All dependent areas such as the heels, elbows, and occiput should be additionally protected by fluid filled bags or pillows
	All sites, where nerves lie superficially over bone, should be inspected and protected
Temperature control	Falls in core temperature must be vigorously treated
	Avoiding a skin/core temperature gradient during grafting
	Use forced air warming systems
	Use fluid warmers for IV fluids
	Use warmed irrigation solution
Fluid therapy and avoid hypotension	Maintain euvolemia
	Urinary catheterization is necessary for bladder decompression and urine output monitoring
	Arterial line may be necessary for blood pressure control and blood sampling
Prolonged ventilation	Maintain normocapnia
	Use lung protective ventilation strategies
Metabolic changes	Control blood sugar
	Maintain normal acid–base balance
Neuromuscular junction monitoring	Maintain 2/4 twitches for possible EMG monitoring
DVT prophylaxis	Use of intermittent pneumatic compression devices
	Use of unfractionated heparin or low-molecular weight heparin per institutional protocols
Pain control	Intraoperative long-acting opioids
	Postoperative PCA in case of large incisions
Immune status	N_2O may be avoided to prevent granulocyte and B- and T-immune cells depression
Personnel staffing and vigilance	To prevent failure of care, work in a "shift" pattern
	Plan to provide adequate number of anesthetists

It also supplies autonomic innervation to the upper limb by receiving sympathetic fibers from the stellate ganglion. Such autonomic supply has vasomotor, pilomotor, and secretomotor functions.

Question 8:
Classify BPIs.

Answer:
BPI is classified into three lesions: preganglionic, postganglionic, and mixed pre- and postganglionic [11]. A preganglionic lesion signifies avulsion of nerve roots, whereas a postganglionic lesion involves the nerve structure distal to the sensory ganglion. Postganglionic lesions can be in the form of nerve rupture or nerve injury in continuity.

Preganglionic injuries: Because it results from avulsion proximal to dorsal root ganglion, it does not regenerate. There is little potential for motor function recovery. Signs suggesting preganglionic injury include Horner's syndrome (ptosis, meiosis, anhidrosis of the cheek, and enophthalmos) due to disruption of sympathetic chain, winged scapula medially due to loss of motor fibers to serratus anterior through the long thoracic nerve, and rhomboids through the dorsal scapular nerve, flail arm, absence of a Tinel sign or tenderness to percussion in the neck, normal histamine test, i.e., intact triple response (redness, wheel, and flare), and elevated hemidiaphragm (phrenic nerve palsy), and evaluation by EMG may show loss of innervation to cervical paraspinals.

Postganglionic injuries: Because it is distal to the dorsal root ganglion, it involves the peripheral nervous system. Hence regeneration and better prognosis are possible. It presents

Table 2.3 Brachial plexus injury syndromes

Syndrome	Mechanisms	Nerves injured	Features
Upper plexus injury[a] (C5/6 ± C7)	Excessive lateral neck flexion	Musculocutaneous	Loss of shoulder abduction, external rotation
	Excessive shoulder depression	Axillary	Loss of elbow flexion
		Suprascapular	Loss of wrist supination
		Nerve to subclavius	"Waiter's tip" position
		Radial	
Lower plexus injury[b] (C8/T1)	Excessive traction of abducted shoulder	Median	Loss of MCPJ flexion
		Ulnar	Loss of IPJ extension
			Loss of fingure abduction, adduction, and opposition
			Loss of wrist flexion
			"Claw hand" deformity
			Sensory loss of medial aspect forearm and hand
Total palsy (C5−T1)	Sever and complex traction injuries	Entire brachial plexus	Flaccid arm
			Paraesthesia of upper limb
Posterior cord injury	Direct injury	Subscapular nerves	Loss of arm extension
		Thoracodorsal	Loss of elbow extension
		Axillary	Loss of wrist extension
		Radial	

MCPI indicates metacarpal phalangeal joint, and IPJ indicates interphalangeal joint
[a]Upper plexus injury (Erb–Duchenne palsy syndrome) includes superior trunk (C5/6) ± middle trunk (C7)
[b]Lower plexus injury (Klumpke's palsy) includes the inferior trunk (C8/T1)

with both motor and sensory deficits according to the postganglionic fibers disrupted (Table 2.4), abnormal histamine test (only redness and wheal, but no flare), and evaluation with EMG shows maintained innervation to cervical paraspinals.

Question 9:
Discuss BPI syndromes.

Answer:
BPI syndromes can be described according to the anatomical part that sustained injury (Table 2.3). Upper BPI (Erb–Duchenne palsy) is caused by difficult child birth, Burner syndrome, motor biking accidents, reduction of shoulder dislocations, direct trauma, e.g., injury by fractured clavicle, gunshot wounds, or stabbing. Lower BPI (Klumpke's palsy) is caused by difficult child birth, falling person grabbing on a tree, motor biking accidents, and direct trauma, e.g., injury by fractured clavicle, gunshot wounds, or stabbing.

Table 2.4 Motor and sensory loss in brachial plexus injury

Injury	Gross motor loss	Sensory loss
C5/C6	Shoulder abduction	Thumb
	Shoulder lateral rotation	Index finger
	Elbow flexion	
	(± wrist extension)	
C5/6/7	As above	As above
	Elbow extension	Middle finger
	Wrist extension	
	Finger and thumb extension	
C8/T1	Loss of wrist flexion	Medial forearm
	Finger and thumb flexion	Little finger
		Middle finger
C5−T1	Flail upper limb	Multiple dermatomes

Also, injuries of the plexus can be described by the loss of motor function and sensations following dermatomal distributions (Table 2.4) [12].

Question 10:
What is Seddon's classification of nerve injury?

Answer:
Seddon in 1942 classified nerve injuries into three classes according to the extent of damage to axons and surrounding connective tissue layers. The classification has a prognostic significance and can help in planning treatment strategies [13]. In 1951, Sunderland expanded Seddon's classification to five degrees of PNI.

Neuropraxia (Sunderland type 1): There is no anatomical disruption. There is a localized transient electrophysiologic conduction block along the injured nerve without distal Wallerian degeneration. Clinical presentation is variable, but often it is associated with motor paralysis with residual sensory or autonomic function. Nerve conduction studies show a conduction block at the level of the injury. Good prognosis is expected with full recovery in 2–3 weeks. Conservative treatment is indicated.

Axonotmesis (Sunderland types 2, 3, and 4): There is anatomical disruption in the form of axonal damage within the nerve with axonal degeneration and myelin sheath, but endoneurial tubes and surrounding connective tissue elements remain intact. Distal Wallerian degeneration may occur in severe axonotmesis. Clinical presentation is in the form of complete muscle paralysis with progressive atrophy and complete sensory deficits. Nerve conduction studies show absent distal nerve conduction, absent motor unit action potential, and muscle fibrillation. Prognosis is fair with possible full recovery without surgery. Axons will grow by 1 mm/day; hence, full recovery may take weeks to months with possible residual deficits.

Neurotmesis (Sunderland type 5): There is complete anatomical disruption of the endoneurium, perineurium, and epineurium with complete nerve division. Wallerian degeneration occurs distal to the injury, usually caused by direct trauma to the nerve, i.e., open injuries and surgical transection. Prognosis is poor, and surgery is indicated. Full recovery is unlikely even with surgery.

Question 11:
Discuss brachial plexus neuritis syndrome.

Answer:
Acute brachial plexus neuritis syndrome is an uncommon disorder of unknown etiology that is easily confused with other neck and upper extremity abnormalities, such as cervical spondylosis and cervical radiculopathy [14]. Traumatic, viral, and inflammatory causes have been implicated. It also has idiopathic and inherited forms that can be triggered by injury to the plexus. It is characterized by severe shoulder and upper arm pain followed by marked upper arm weakness. Pain always precedes weakness. Magnetic resonance imaging of the shoulder and upper arm musculature may reveal denervation within days. EMG can localize the lesion within 2–4 weeks of the onset of symptoms. Supportive treatment is indicated including analgesics, physiotherapy, and corticosteroids. Symptoms usually resolve in 3–4 months.

Question 12:
What is Tinel sign?

Answer:
Tinel sign is a tingling sensation elicited by slight percussion of a nerve trunk following an injury. The sensation radiates into the cutaneous distribution of the specific nerve and signifies the presence of regenerating nerve fibers.

Brachial plexus tapping in the posterior triangle of the neck may evoke several different responses [15]:

(a) No response at all implies preganglionic injury of the root assessed.
(b) Pure local pain implies that there is an underlying recovering lesion.
(c) Pure Tinel sign means that the lesion is in anatomical continuity, and sequential recordings can demonstrate progression of recov-

Table 2.5 Simplified clinical scheme to identify injuries to major terminal branches of the brachial plexus

Terminal branch	Muscles affected	Main motor and sensory deficits
Musculocutaneous	Biceps, brachialis	Weakness of elbow flexion
Ulnar	Flexor carpi ulnaris	Weakness of wrist and fingers flexion
	Intrinsic hand muscles	Weakness of finger abduction/adduction
		Numbness over little and ring fingers
Median	Forearm pronators	Forearm kept in supination
	Flexors of wrist and fingers	Weakness of wrist flexion
		Weakness of thumb abduction
		Numbness of lateral three-and-half fingers
Radial	Supinator	Wrist drop
	Triceps brachii	Weakness of thumb and fingers extension
	Extensors of wrist and fingers	Numbness of posterior surface of forearm
Axillary	Deltoid, teres minor	Weakness of shoulder abduction

ery. Roots C5 and C6 are the most superficial, and hence, the test can be most easily applied to these. Roots C7, C8, and T1 can occasionally be difficult to assess. A Tinel sign elicited in one nerve distribution when tapping on another nerve should not give a misleading diagnosis as this is due to the regenerating axons growing down the wrong endoneurial tubes; this is a feature of traction lesions.

(d) Pain elicited in the distribution of the nerve when tapping. This is called the "neuroma sign" which indicates a disruption of the continuity of the whole nerve.

Question 13:
What are the symptoms and signs of perioperative BPI?

Answer:
Alarming symptoms include persistent weakness or heaviness of an arm. Additionally, neck pain, dysesthesias (an unpleasant, abnormal sense of touch), and paresthesia in the neck or arm should alert the anesthesiologist to possible BPI [16, 17].

An upper BPI involves C5 and C6. It causes of the shoulder muscles and biceps. When the damage extends to C7, it leads to weak wrist. A lower BPI involves C8 and T1. It causes weakness of the forearm flexor and the intrinsic muscles of the hand. Injuries to the cervical sympathetic trunk cause Horner syndrome. Clinical recognition of major terminal branches of BPI is summarized in Table 2.5 [16, 17].

Physical examination should also include palpation of Tinel sign testing (see answer to question 12), Erb's point palpation, and Spurling test [18]. Erb's point represents the fusion of C5 and C6. It is located 2–3 cm above the mid-clavicular point. Palpation of Erb's point elicits tenderness in cases of BPI. Spurling test is performed by extending the neck and rotating the head toward the affected arm. In this position, downward pressure applied to the head reproduces symptoms in the arm on the same side to which the head is rotated. Positive test may indicate cervical radiculopathy rather than BPI. This test has high specificity but low sensitivity.

Question 14:
Are there any clinical utility for electrophysiologic studies in the management of BPI?

Answer:
Electrophysiologic studies may confirm the diagnosis of BPI, identify the location of the lesions, and determine the severity of the nerve injury [12]. EMG and nerve conduction velocity (NCV) studies may be performed 3–4 weeks after the injury. Serial testing in conjunction with repeated physical examination for several weeks can document and quantify nerve recovery.

EMG tests muscles at rest and during activity. Denervation changes (fibrillation potentials) can be seen as early as 1–2 weeks after injury in proximal muscles and as late as 3–6 weeks in distal muscles. The presence of voluntary motor unit potentials with limited fibrillation potentials signifies better prognosis than the cases where there is absence of motor unit potentials and many fibrillation potentials.

NCV studies are performed along with EMG. In posttraumatic BPIs, the amplitude of compound muscle action potentials is generally low and is related to the total amount of functional muscle fibers. Sensory nerve action potentials (SNAPs) are very important in localizing a lesion as preganglionic or postganglionic. In preganglionic injuries, there are normal SNAPs in an anesthetized dermatome while muscle action potentials are absent. SNAPs will be absent in a postganglionic or combined pre- and postganglionic lesion.

Question 15:
Mention the indication for surgical exploration and repair in BPI.

Answer:
Any BPI which has not shown substantial spontaneous recovery in 3 months should be explored [19]. Timing is crucial due to the eventual loss of neuromuscular end plates at 20–24 months after denervation which makes the neuromuscular junction increasingly incapable of accepting reinnervation. The best time for surgery depends on the mechanism and type of injury. If there is an unequivocal evidence of preganglionic injury with spinal nerve root avulsions, there is no rationale in waiting, and surgery for nerve transfer is undertaken as soon as possible. However, if there is a postganglionic injury, it is prudent to wait for 3–4 months for spontaneous recovery.

Multiple Choice Questions

1. Middle trunk results in:
   (a) Radial nerve distribution problems
   (b) Erb's palsy
   (c) Klumpke's palsy
   (d) Brachial neuritis syndrome
   Answer: a
2. Which of the following describes the statement: the nerve fibers distal to the injury degenerate, but the bulk of the nerve is intact.
   (a) Neurapraxia
   (b) Axonotmesis
   (c) Neurotmesis
   (d) Sunderland type 5 nerve injury
   Answer: b
3. Patient presents with claw hand. What nerve has been affected?
   (a) Long thoracic nerve
   (b) Median nerve
   (c) Ulnar nerve
   (d) Musculocutaneous nerve
   Answer: c
4. Which of these nerves have been injured if the patient cannot abduct their arm?
   (a) Radial nerve
   (b) Ulnar nerve
   (c) Axillary nerve
   (d) Suprascapular nerve
   Answer: c
5. The posterior cord of the brachial plexus gives rise to the following nerves:
   (a) Thoracodorsal nerve
   (b) Axillary nerve
   (c) Radial nerve
   (d) All of the above
   Answer: d

References

1. Welch MB, Brummett CM, Welch TD, Tremper KK, Shanks AM, Guglani P, Mashour GA. Perioperative peripheral nerve injuries: a retrospective study of 380,680 cases during a 10-year period at a single institution. Anesthesiology. 2009;111(3):490–7.
2. Warner M, Warner D, Matsumoto J, Harper M, Schroeder D, Maxson P. Ulnar neuropathy in surgical patients. Anesthesiology. 1999;90:54–9.
3. Ben-David B, Stahl S. Prognosis of intraoperative brachial plexus injury: a review of 22 cases. Br J Anaesth. 1997;79(4):440–5.
4. Nichols AW. Diagnosis and management of thoracic outlet syndrome. Curr Sports Med Rep. 2009;8(5):240–9.
5. Hewson DW, Bedforth NM, Hardman JG. Peripheral nerve injury arising in anaesthesia practice. Anaesthesia. 2018;73(Suppl 1):51–60.

6. Cooper DE, Jenkins RS, Bready L, Rockwood CA. The prevention of injuries of the brachial plexus secondary to malposition of the patient during surgery. Clin Orthop. 1988;228:33–41.
7. Anonymous. Practice advisory for the prevention of perioperative peripheral neuropathies: a report by the American Society of Anesthesiologists Task Force on Prevention of Perioperative Peripheral Neuropathies. Anesthesiology. 2000;92:1168–82.
8. Bird TM, Strunin L. Anaesthetic considerations for microsurgical repair of limbs. Can Anaesth Soc J. 1984;31(1):51–60.
9. Dodds C. Prolonged anaesthesia for plastic and reconstructive surgery. Curr Anaesth Crit Care. 1996;7:20–4.
10. Netter FH. Atlas of human anatomy. 7th ed. North York: Elsevier; 2018.
11. Moran SL, Steinmann SP, Shin AY. Adult brachial plexus injuries: mechanism, patterns of injury, and physical diagnosis. Hand Clin. 2005;21(1):13–24.
12. Park HR, Lee GS, Kim IS, Chang J-C. Brachial plexus injury in adults. Nerve. 2017;3(1):1–11.
13. Chandler MH, Dimatteo L, Hasenboehler EA, Temple M. Intraoperative brachial plexus injury during emergence following movement with arms restrained: a preventable complication? Patient Saf Surg. 2007;1:8. (page 1–5).
14. Dillin L, Hoaglund FT, Scheck M. Brachial neuritis. J Bone Joint Surg Am. 1985;67:878–80.
15. Landi A, Copeland S. Value of the Tinel sign in brachial plexus lesions. Ann R Coll Surg Engl. 1979;61:470–1.
16. Sawyer RJ, Richmond MN, Hickey JD, Jarrratt JA. Peripheral nerve injuries associated with anaesthesia. Anaesthesia. 2000;55(10):980–91.
17. Yoshikawa T, Hayashi N, Yamamoto S, Tajiri Y, Yoshioka N, Masumoto T, Mori H, Abe O, Aoki S, Ohtomo K. Brachial plexus injury: clinical manifestations, conventional imaging findings, and the latest imaging techniques. Radiographics. 2006;26(Suppl 1):S133–43.
18. Shveiky D, Aseff JN, Iglesia CB. Brachial plexus injury after laparoscopic and robotic surgery. J Minim Invasive Gynecol. 2010;17(4):414–20.
19. Belzberg AJ, Dorsi MJ, Storm PB, Moriarity JL. Surgical repair of brachial plexus injury: a multinational survey of experienced peripheral nerve surgeons. J Neurosurg. 2004;101(3):365–76.

3 Management of Patient with Brain Abscess

Suman Rajagopalan

Stem Case Terminology

A 24-year-old female with chronic otitis media presents to the emergency department with fever, headache, and vomiting for 2 days and an episode of generalized tonic-clonic seizure an hour ago. Her examination showed normal consciousness, weight 54 kg, heart rate of 96 beats/min, blood pressure of 128/80 mmHg, respiratory rate of 20 breaths/min, and SpO_2 of 98% in room air. Computed tomography (CT) of the brain revealed a 3 cm × 2.6 cm space-occupying lesion in the frontal region of the brain that was consistent with brain abscess.

Question 1:
What is the etiology of brain abscess?

Answer:
Brain abscess is a localized collection of pus within the brain parenchyma. The incidence ranges from 0.4 to 0.9 cases per 100,000 populations. It constitutes about 8% of the intracranial masses in the developing countries and about 1–2% of the masses in the developed countries [1]. It is more common in the first three decades of life.

S. Rajagopalan (✉)
Trauma Anesthesia Division, Department of Anesthesiology, Baylor College of Medicine, Houston, TX, USA
e-mail: srajagop@bcm.edu

Organism causing the brain abscess can enter the brain by [2]

- Contiguous spread from the adjacent site of infection like the paranasal sinuses, mastoid, or teeth.
- Hematogenous seeding in patients with pulmonary infections, abdominal or pelvic infection, bacterial endocarditis, or congenital cyanotic heart disease (CHD).
- Direct inoculation as in trauma or as a complication of neurosurgical procedures.

In recent years, immunosuppression secondary to human immunodeficiency virus infection has become an important predisposing factor for brain abscess. However, in 20–40% of the patients, brain abscess has occurred without any predisposing factor or identifiable source.

Question 2:
Describe the pathogenesis of brain abscess?

Answer:
The organism is inoculated into the brain parenchyma in the area of devitalized brain tissue or in the region of poor microcirculation. Abscess usually occurs in the white matter or at the junction of grey and white matter. The early lesion (first 2 weeks) is poorly demarcated and is usually associated with edema around the site. This is called the "stage of cerebritis" [3]. The brain

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_3

cells are destroyed; necrosis and liquefaction occur. A capsule is formed around the lesion, and the abscess is localized to a specific site. It takes about 2 weeks for the encapsulation to occur.

Question 3:
What are the common organisms isolated from the brain abscess? Why is this important?

Answer:
The most common organisms isolated from the brain abscess are *Streptococcus viridans* and *Staphylococcus aureus* [4]. The type of organism found in the abscess depends on the predisposing condition or on the primary source of infection. It is important to identify the organism as the treatment can be specifically directed toward the organism causing the infection [5].

Primary infection source	Pathogen
Otogenic	Streptococcus, Enterobacteriaceae, Bacteroides
Paranasal sinuses	Streptococcus, Bacteroides, Haemophilus
Dental	Streptococcus, Bacteroides, Fusobacterium
Trauma/post-neurosurgical procedures	*Staphylococcus aureus*, Enterobacter, Streptococcus
Endocarditis	*Streptococcus viridans*, *Staphylococcus aureus*, enterococci
Immunocompromised	*Toxoplasma gondii*, *Listeria monocytogenes*, nocardia asteroides, fungal (Aspergillus, Cryptococcus, Coccidioides, Histoplasma)
Congenital cyanotic heart disease	Streptococcus, Haemophilus

Question 4:
Discuss the clinical presentation of a patient with brain abscess?

Answer:
Headache is the most common initial symptom of brain abscess. Fever may be present depending on the source of infection. As the abscess enlarges and becomes more organized, it can compress the adjacent structures causing focal neurological deficits [6]. These three symptoms (headache, fever, and neurological deficits) are believed to be the classic triad of brain abscess but have been identified in only 20% of the patients.

A large abscess can also cause an increase in intracranial pressure (ICP) that presents as headache, vomiting, papilledema, and coma. Seizures can occur in about 40% of the patients. Inflammation process around the abscess can result in severe cerebral edema that can cause changes in mental status and can progress to brain herniation [7]. Occasionally, the abscess can rupture into the ventricular space causing abrupt onset of ventriculitis that presents with meningeal signs like headache, fever, neck stiffness, and altered sensorium.

Question 5:
How would you diagnose a brain abscess?

Answer:
In the setting of the above-mentioned symptoms, CT scan with contrast or magnetic resonance imaging (MRI) should be performed. Imaging of the brain helps identify the location, size, number, and mass effect caused by the abscess. In some cases where the spread is from the paranasal sinuses or mastoids, these structures could be imaged in the same setting as well.

MRI is the imaging modality of choice for diagnosing brain abscess. On T1-weighted images, brain abscess is seen as hypointense area with ring enhancement after the administration of intravenous (IV) gadolinium (Fig. 3.1) [8]. On T2-weighted images, the abscess is visualized as hyperintense area of pus with a well-defined capsule (Fig. 3.2). MRI is sensitive for diagnosing early cerebritis and for accurately estimating the extent of the abscess. MRI with diffusion weighting is useful in differentiating an abscess from a neoplastic cystic lesion.

Although CT scan is not as sensitive as MRI, it is easy to obtain. When CT scan with contrast is used, the abscess is seen as a ring-enhancing lesion with cerebral edema surrounding it (Fig. 3.3) [9].

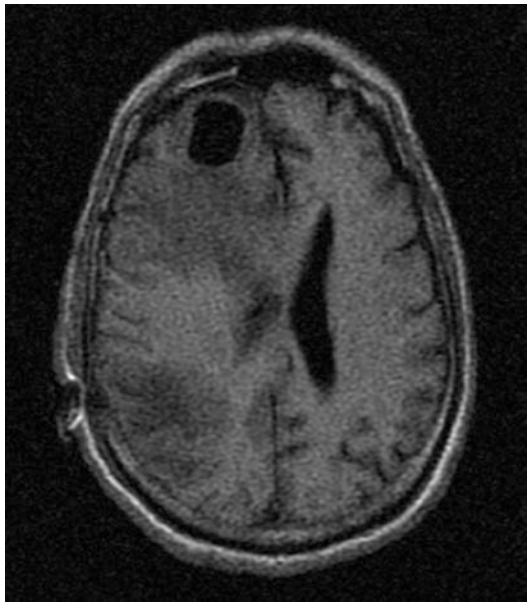


Fig. 3.1 T1-weighted MRI image showing a hypointense brain abscess in the frontal region

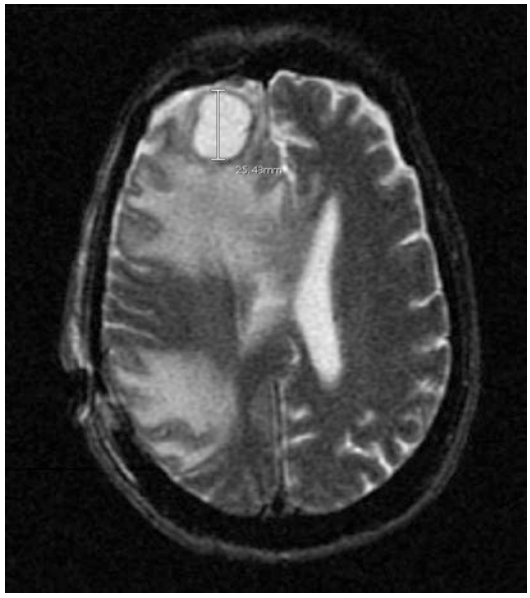


Fig. 3.2 T2-weighted MRI image showing a hyperintense brain abscess in the frontal region

Question 6:
Can lumbar puncture help with the diagnosis?

Answer:
Lumbar puncture is contraindicated in patients with increased ICP or in those presenting with

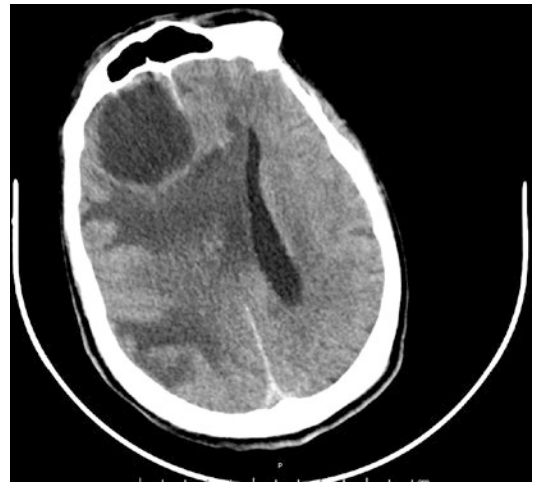


Fig. 3.3 CT scan with contrast showing the frontal abscess

focal signs or symptoms, as it can potentially cause transtentorial or transforaminal herniation and death. As the early symptoms of abscess are similar to meningitis, inadvertent lumbar punctures have been performed in patients with brain abscess with some grave complications [10]. In patients with unruptured abscess, the cerebrospinal fluid analysis does not detect any organism hence, is of no benefit for the diagnosis or management of the abscess [11].

Question 7:
What is the management of brain abscess?

Answer:
Similar to the management of abscess anywhere in the body, the management of the brain abscess is drainage of the pus followed by antibiotic therapy for 4–8 weeks. The surgical drainage of the abscess is preferably done by needle aspiration as this has fewer neurological complications when compared to a craniotomy. The aspiration can be done under CT guidance or ultrasound guidance through a burr hole. Empiric antibiotic therapy is started and the aspirate is sent for culture sensitivity.

When the source of the abscess is unknown, a combination of IV vancomycin, third-generation cephalosporin, and metronidazole is recommended, and the antibiotics are changed later, depending on culture sensitivity [12]. The

empiric therapy can be based on the source if the source is known. Penicillin G provides excellent coverage for oral flora while ceftriaxone and cefotaxime provide good coverage for sinus or otogenic infection source. Vancomycin should be used in patients with abscess from hematogenous spread or in patients with penetrating head injury where methicillin-resistant *Staphylococcus aureus* (MRSA) infection is suspected [13]. First-generation cephalosporins, clindamycin, aminoglycosides, and other antibiotics that do not cross the blood–brain barrier should not be used to treat brain abscess. Once the culture results are available, the management should be tailored to target the specific organism causing the infection.

The duration of therapy for brain abscess ranges from 4 to 8 weeks. Patients with early cerebritis require shorter duration of therapy than patients with organized capsule. Multiloculated abscess and immunocompromised patients require longer duration of treatment. The response to treatment is typically assessed based on the clinical response and improvement in imaging. CT scan is done every week initially and then biweekly to assess the response to treatment. MRI is not recommended for follow-up imaging as the abnormalities persists for months and hence not useful.

Question 8:
When would craniotomy be preferred over needle aspiration? What are the advantages of craniotomy?

Answer:
Surgical excision by craniotomy is considered under certain circumstances [14]:

- Abscess that are enlarging or showing no clinical signs of improvement despite aspiration and antibiotic therapy.
- Multiloculated abscesses and large lesions that are superficially located.
- Traumatic abscesses where a foreign body is present in the brain.

Although surgical excision has increased risk of neurological deficits, there are some benefits [15]:

- The abscess is removed along with the capsule, and hence, the risk of repeated collection of pus is eliminated.
- Abscess arising from contiguous spread like the middle ear infection can be operated upon during the same encounter.
- There is decreased need for repeated weekly imaging.
- Shorter hospital stay.

3.1 Preoperative Period

Question 9:
What are the preoperative concerns in the patient with brain abscess for aspiration or for craniotomy? What premedications would you choose?

Answer:
A thorough preoperative evaluation should be performed and other comorbid conditions that can affect the anesthetic management should be taken into consideration while making anesthetic plans. Patients with symptoms of increased ICP like nausea, vomiting, papilledema, or altered level of consciousness should be managed meticulously to avoid further increase in ICP. CT scan and MRI should be reviewed for the location and number of abscesses and for the presence of cerebral edema or midline shift. Antibiotics at scheduled doses should be given during the perioperative period. Informed consent for the procedure can be obtained from the patient if they are alert and oriented, but if the sensorium is altered, then the next of kin should be consented.

Preoperative medications: Sedatives and opioids are generally avoided in patients with intracranial abscess. Opioids can cause hypoventilation, which leads to the accumulation of arterial carbon dioxide leading to further increase in ICP. Using longer acting benzodiazepines alters the ability to accurately assess the changes in neurological conditions postoperatively and hence is usually avoided. In patients who are anxious but alert, a small dose of midazolam can be used for anxiolysis but should be decided on case-by-case basis.

Question 10:
How would you monitor the patient in the operating room?

Answer:
The patient should be monitored using the standard ASA monitors [16]

- Electrocardiogram (ECG)—five-lead ECG is used to monitor V_5 and II.
- Blood pressure—noninvasive blood pressure monitoring is used initially, and peripheral arterial catheter can be placed after induction for craniotomy to obtain continuous blood pressure monitoring.
- Pulse oximetry—used to assess arterial oxygenation.
- Oxygen analyzer—to determine the fraction of inspired oxygen.
- Capnography—to estimate the end-tidal CO_2 ($ETCO_2$) level.
- Temperature probe in the esophagus or bladder—to maintain the core temperature.

3.2 Intraoperative Period

Question 11:
How would you preform the anesthetic management of this patient for craniotomy and excision of brain abscess?

Answer:
The goals of anesthetic management for a craniotomy is similar to any patient with intracranial mass.

- Management of cerebral blood flow (CBF) and cerebral perfusion pressure (CPP).
- Control of ICP.
- Optimization of surgical exposure.
- Facilitation of early neurological assessment.

Depending on the coexisting disease, induction can be achieved rapidly and reliably with thiopental, etomidate, or propofol. A nondepolarizing muscle relaxant is used to facilitate tracheal intubation. In patients with difficult airway or full stomach, succinylcholine can be used although this may be associated with transient increase in ICP [17]. Maintaining an adequate depth of anesthesia and muscle paralysis prior to intubation is necessary as coughing or bucking over the endotracheal tube can increase CBF and ICP. Lidocaine 1–1.5 mg/kg or short-acting opioid-like fentanyl 1–2 μg/kg can be used with induction drugs to blunt the intubation response. Following intubation, the patient's lungs are ventilated to maintain a $PaCO_2$ of 35 mmHg. Small amount of positive end-expiratory pressure (PEEP) can be used to avoid postoperative atelectasis. Higher levels of PEEP can result in increase in ICP and, hence, should be avoided or used cautiously. Anesthesia is maintained using a combination of opioids, volatile anesthetics, propofol, and non-depolarizing muscle relaxant. Sudden increase in systemic blood pressure should be avoided as this can cause undesirable increase in CBF, CBV, and ICP, resulting in worsening of cerebral edema. Prolonged hypotension can worsen brain ischemia and is better avoided in patients with increased ICP. At the end of the surgery, the effects of muscle relaxants are pharmacologically reversed, and the patient is extubated when the criteria for extubation are met.

Question 12:
What anesthetic technique would you use if the patient has to undergo aspiration of brain abscess?

Answer:
Aspiration of brain abscess can be performed through a burr hole using CT guidance or ultrasound guidance under local anesthesia or general anesthesia. Minimally invasive stereotactic interventions are generally less invasive with fewer complications and, hence, preferred method for drainage of superficial or large abscesses [18]. The goals of general anesthetic management are the same as above which includes smooth induction and intubation, management of CPP, CBF, and avoiding any increase in ICP. In patients who have other coexisting disease and in whom there is an increased risk of morbidity with general anesthesia, local anesthesia with conscious sedation has been successfully utilized. Scalp block can be

performed instead of local infiltration at the surgical site to provide better postoperative pain relief [19]. Dexmedetomidine infusion can be considered for sedation instead of benzodiazepines and opioids as it causes less respiratory depression and maintains the normal $PaCO_2$ levels [20].

Question 13:
Would the anesthetic considerations be different if this patient had congenital CHD?

Answer:
CHD accounts for 12–69% of all the brain abscesses with identifiable risk factors. Tetrology of Fallot is the most common cardiac anomaly associated with brain abscess while others like transposition of great vessels, tricuspid atresia, and pulmonary stenosis have also been reported to predispose to brain abscess.

Normally, when the blood flows through the pulmonary circulation, many of the bacteria present in the blood are removed by phagocytosis in the lung. However, in patients with right-to-left shunts, the blood bypasses the pulmonary circulation and hence carries the bacteria to the brain. In addition, patients with CHD have areas of low perfusion in the brain due to chronic hypoxemia and increased viscosity due to polycythemia that provide a good nidus for bacterial growth. Most of the abscess are supratentorial in location and occur in the distribution of the middle cerebral artery.

The management of brain abscess includes aspiration of the pus and antibiotic therapy. The anesthetic goals specific to a patient with CHD includes:

- Avoidance of hypoxemia, acidosis, and hypercarbia that can increase pulmonary vascular resistance and, hence, the shunt volume [21].
- Ensuring adequate hydration and maintenance of systemic vascular resistance (SVR) to prevent further increase in right-to-left shunting.

Smooth induction and deeper planes of anesthesia required for maintaining the ICP in patients with brain abscess can be challenging in patients with CHD as vasodilatation with anesthesia can worsen right-to-left shunting by decreasing SVR. Oxygen saturation is usually maintained around 80–85% as these patients are chronically hypoxic from the shunt. $ETCO_2$ monitor routinely used to indirectly assess the $PaCO_2$ cannot be used in this setting due to variable dead space and a large difference between $ETCO_2$ and $PaCO_2$. The gradient increases with acute reduction in the pulmonary blood flow from shunting or from decrease in cardiac output. In addition, all IV lines have to be free of air to prevent air embolism. Due to the complexity of the cardiopulmonary system, general anesthesia can be avoided and local anesthesia with sedation can be used instead, in cooperative patients undergoing drainage of the brain abscess [22].

3.3 Postoperative Period

Question 14:
What is the usual postoperative course?

Answer:
Most patients are extubated at the end of the neurosurgical procedure and transferred to the intensive care unit, so that early and repeated neurological assessment can be performed. Any delay in emergence or occurrence of new neurological events in the immediate postoperative period may be due to complications from surgery like intracranial bleed, vascular occlusion, or seizure and warrants an investigation with CT scan of the brain. Postoperative edema begins to subside on the first or the second postoperative day, and an improvement in the neurological status may be noted. The antibiotic coverage is changed based on the culture and sensitivity obtained from the pus and should be continued for at least 4–8 weeks. The British Society for Antimicrobial Chemotherapy recommends 1–2 weeks of IV antibiotics followed by oral medications for 4–6 weeks [23]. These patients can be discharged home with a follow-up CT in every1–2 week to assess the effect of therapy.

Question 15:
What is the outcome?

Answer:
Early diagnosis and treatment have resulted in complete recovery with minimal neurological sequelae in about 80% of the patients [24]. Improvements in imaging technique, minimally invasive neurosurgical procedures, and advancement in antibiotic treatment have all contributed to a decline in mortality from 40% in 1960 to 15% in 2010 [25]. Intraventricular rupture of the abscess and poor Glasgow Coma Scale at presentation has been associated with worse outcomes. Some of the long-term sequelae from the brain abscess include persistent focal neurological deficits, seizures, tremors, and cognitive dysfunction.

Multiple Choice Questions

1. The gold standard for the diagnosis of brain abscess is
   (a) CT scan
   (b) MRI
   (c) Lumbar puncture
   (d) Ultrasound
   Answer: b
   MRI of the brain is imaging modality of choice for diagnosing brain abscess. MRI is sensitive for diagnosing early cerebritis and for accurately estimating the extent of the abscess. MRI with diffusion weighting is useful in differentiating an abscess from a neoplastic cystic lesion that the CT scan cannot differentiate. Lumbar puncture is contraindicated in brain abscess due to the risk of herniation.
2. Risk factors for brain abscess include
   (a) Immunocompromised patients
   (b) Cyanotic congenital heart disease
   (c) Mastoiditis
   (d) All of the above
   Answer: d
   All the patients mentioned above have an increased risk of developing brain abscess. In patients with middle ear infection or mastoiditis, the spread is directly to the adjacent brain area, which is the temporal lobe. In immunocompromised patients and in those with cyanotic congenital heart disease, the spread is hematogenous.
3. In patients with brain abscess where the source of the abscess is unknown, the antibiotic medications to be prescribed should include
   (a) Cefazolin, metronidazole
   (b) Penicillin G, vancomycin, clindamycin
   (c) Cefotaxime, metronidazole, vancomycin
   (d) Aminoglycocide, clindamycin
   Answer: c
   A combination of third-generation cephalosporin, metronidazole, and vancomycin is used to treat brain abscess until the culture and sensitivity results are available. First-generation cephalosporin, aminoglycosides, and clindamycin do not cross the blood–brain barrier and is useless in the treatment of brain abscess.
4. The symptom triad for the diagnosis of brain abscess includes all except
   (a) Headache
   (b) Fever
   (c) Vomiting
   (d) Focal neurological deficits
   Answer: c
   The triad of symptoms that help with the diagnosis of brain abscess include headache, fever, and focal neurological deficits. However, all the three symptoms are present in only 20% of the patients with brain abscess.
5. The recommended duration of treatment with antibiotics for the brain abscess is
   (a) 10–14 days
   (b) 4–8 weeks
   (c) 3 months
   (d) 6 months
   Answer: b
   The duration for treatment is 4–8 weeks. The initial treatment is with IV antibiotics for 1–2 weeks and can be changed to oral medications for the remaining 4–6 weeks.
   Weekly or biweekly CT scan is done to assess the response to antibiotics. The decrease in the size of the abscess is usually seen around 2.5–3 weeks.

References

Question 1

1. Brouwer MC, Tunkel AR, McKhann GM 2nd, van de Beek D. Brain abscess. N Engl J Med. 2014;371:447–56.
2. Moorthy RK, Rajshekhar V. Management of brain abscess: an overview. Neurosurg Focus. 2008;24:E3.

Question 2

3. Britt RH, Enzmann DR. Clinical stages of human brain abscesses on serial CT scans after contrast infusion. Computerized tomographic, neuropathological and clinical correlations. J Neurosurg. 1983;59:972.

Question 3

4. Brouwer MC, Van de Beek D. Epidemiology, diagnosis, and treatment of brain abscesses. Curr Opin Infect Dis. 2017;30:129–34.
5. Brook I. Microbiology and treatment of brain abscess. J Clin Neurosci. 2017;38:8–12.

Question 4

6. Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess: systematic review and meta-analysis. Neurology. 2014;82:806.
7. Loftus CM, Osenbach RK, Biller J. Diagnosis and management of brain abscess. In: Wilkins RH, Rengachary SS, editors. Neurosurgery. 2nd ed. New York: McGraw-Hill; 1996. p. 3285–98.

Question 5

8. Xu XX, Li B, Yang HF, et al. Can diffusion-weighted imaging be used to differentiate brain abscess from other ring-enhancing brain lesions? A meta-analysis. Clin Radiol. 2014;69:909–15.
9. Muzumdar D, Jhawar S, Goel A. Brain abscess: an overview. Int J Surg. 2011;9:136–44.

Question 6

10. Tattevin P, Bruneel F, Clair B, et al. Bacterial brain abscesses: a retrospective study of 94 patients admitted to an intensive care unit (1980 to 1999). Am J Med. 2003;115:143.
11. Mathisen GE, Johnson JP. Brain abscess. Clin Infect Dis. 1997;25:763–81.

Question 7

12. Brouwer MC, Tunkel AR, McKhann GM 2nd, van de Beek D. Brain abscess. N Engl J Med. 2014;371:447–56.
13. Bodilsen J, Brouwer MC, Nielsen H, Van de Beek D. Anti-infective treatment of brain abscess. Expert Rev Anti Infect Ther. 2018;16:565–78.

Question 8

14. Ratnaike TE, Das S, Gregson BA, Mendelow AD. A review of brain abscess surgical treatment—78 years: aspiration versus excision. World Neurosurg. 2011;76:431.
15. Zhai Y, Wei X, Chen R, et al. Surgical outcome of encapsulated brain abscess in superficial noneloquent area: a systematic review. Br J Neurosurg. 2016;30:29–34.

Question 10

16. American Society of Anesthesiologists. ASA standards for basic anesthetic monitoring. In: ASA house of delegates; 2005.

Question 11

17. Bekker AY, Mistry A, Ritter AA, et al. Computer simulation of intracranial pressure changes during induction of anesthesia: comparison of thiopental, propofol and etomidate. J Neurosurg Anesthesiol. 1999;11:69–80.

Question 12

18. Sonneville R, Ruimy R, Benzonana N, et al. An update on bacterial brain abscess in immunocompetent patients. Clin Microbiol Infect. 2017;23:614–7.
19. Osborn I, Sebeo J. “Scalp block” during craniotomy: a classic technique revisited. J Neurosurg Anesthesiol. 2010;22:187–94.
20. Srivastava VK, agrawal S, Kumar S, et al. Comparative evaluation of dexmedetomidine and propofol along with scalp block on hemodynamic and postoperative recovery for chronic subdural hematoma evacuation under monitored anesthesia care. Turk J Anaesthesiol Reanim. 2018;46:51–6.

Question 13

21. Sethi S, Kapil S. Scalp block for brain abscess drainage in a patient with uncorrected tetralogy of Fallot. World J Clin Cases. 2014;16:934–7.

22. Pardeshi SK, Shetty A, Kulkarni A, Shah V. Brain abscess drainage in a case of uncorrected tetralogy of Fallot under scalp block and dexmedetomidine. J Neurosurg Anesthesiol. 2017;29(2):362–3.

Question 14

23. de Louvois J, Brown EM, Bayston R, et al. The rational use of antibiotics in the treatment of brain abscess. Br J Neurosurg. 2000;14:525–30.

Question 15

24. Chowdhury FH, Haque MR, Sarkar MH, et al. Brain abscess: surgical experiences of 162 cases. Neuroimmunol Neuroinflammation. 2015;2:153–61.

25. Brouwer MC, van De Beek D. Epidemiology, diagnosis and treatment of brain abscesses. Curr Opin Infect Dis. 2017;30:129–34.

Suggested Reading

Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess: systematic review and meta-analysis. Neurology. 2014;82:806–13.

Brouwer MC, Tunkel AR, McKhann GM 2nd, van de Beek D. Brain abscess. N Engl J Med. 2014;371:447–56.

Xu XX, Li B, Yang HF, et al. Can diffusion-weighted imaging be used to differentiate brain abscess from other ring-enhancing brain lesions? A meta-analysis. Clin Radiol. 2014;69:909–15.

4 Management of Patient with Cerebellopontine Angle Tumor

Mia Kang

Stem Case Terminology

A 52-year-old woman with a diagnosis of left-sided vestibular schwannoma (VS) presents to the anesthesia preoperative evaluation clinic for workup 2 weeks before her scheduled resection. She has been experiencing progressive hearing loss on the left and reports that recently she has noticed increasing unsteadiness of gait as well as dizziness. She works as a hairdresser and has been unable to work because the dizziness keeps her from being able to stand for extended periods of time. Her past medical history is significant for hypertension, diabetes and obesity (body mass index [BMI] 39). She had a hysterectomy 5 years ago and has never experienced any complications after undergoing anesthesia. Her social history is significant for tobacco abuse (25-pack years).

4.1 Preoperative Evaluation

Question 1:
How do patients with cerebellopontine angle (CPA) tumors typically present?

Answer:
Approximately 80% of CPA tumors are VSs (also referred to as acoustic neuromas). Other CPA tumors include meningiomas (~10%) and epidermoid tumors (~6%). VSs arise from overgrowth of the sheath of cranial nerve VIII and are typically benign but may result in significant clinical symptomatology because of their location. The lifetime risk of developing a unilateral VS is approximately 0.1% [1]. The mortality rate from VS is only 0.2–1% so patients are typically managed with the goals of preserving hearing and balance and maintaining facial nerve function [1].

VSs are diagnosed based on clinical presentation and imaging studies. Patients with VSs typically present with progressive unilateral hearing loss. Dizziness, tinnitus, and/or vestibular symptoms such as gait instability are less common but also possible, usually associated with larger tumors. If the schwannoma is not treated it may advance in size to the point that it may encroach upon the brainstem which can be life-threatening. The gold standard for diagnosis of CPA tumors is magnetic resonance imaging with gadolinium [1].

Treatment options for VS include observation, medical management, stereotactic radiosurgery, microsurgical resection, or some combination of these options. There is currently no consensus on the optimal treatment for VS [1].

M. Kang (✉)
Division of Neuroanesthesia, Department of Anesthesiology, University of North, Chapel Hill, NC, USA
e-mail: Mia_Kang@med.unc.edu

© Springer Nature Singapore Pte Ltd. 2020
H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_4

Question 2:
What are the surgical approaches for resection of a VS?

Answer:
Surgical approaches for resection include translabyrinthine, transotic, middle cranial fossa (MCF), or retrosigmoid (RS). The last two, MCF and RS, allow for hearing preservation whereas the other three result in profound hearing loss because they breach the vestibular or cochlear apparatus of the inner ear [1]. The RS approach requires a posterior fossa craniotomy which may necessitate that the operation be performed with the patient in sitting position. The advantage of this approach is that it allows access to the CPA, petrous apex, clivus, and internal auditory canal; however, this must be weighed against the significant risks posed to the patient when undergoing a sitting position craniotomy [1]. In addition, this approach also carries a significant risk of postoperative cerebrospinal fluid (CSF) leak, approximately 5–10% [1]. The risks and benefits of each of these approaches, taking into account patient factors, the location and size of the tumor, and surgeon preference, must be carefully considered by the neurosurgeon and anesthesiologist when determining which of these approaches will be used (Fig. 4.1).

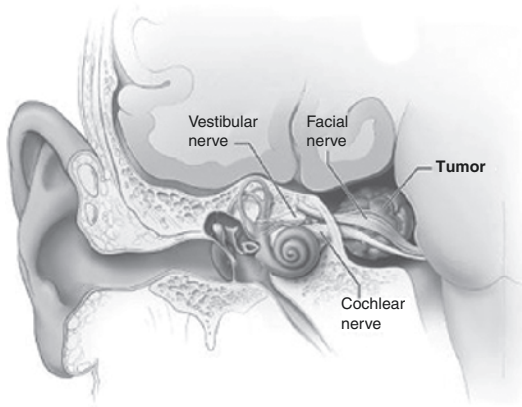


Fig. 4.1 Inner ear with vestibular schwannoma. (Source: NIH/NIDCD (https://www.nidcd.nih.gov/health/vestibular-schwannoma-acoustic-neuroma-and-neurofibromatosis#ref1))

While patients are typically placed in three-quarters lateral position with the head in Mayfield pins facing downward for these procedures at your institution, the surgeon informs you that because of the size of this patient's tumor she would like to have the patient placed in sitting position for the case.

Question 3:
Discuss the various patient positions that are used for VS resection.

Answer:
There are a variety of positions that the patient may be placed in for CPA tumor resection which include sitting, prone, and lateral versus three-quarters lateral versus park bench. Sitting position may provide improved surgical conditions because it reduces dural sinus pressure which may help to decrease venous bleeding (see Table 4.1). (Cottrell) This position optimizes surgical exposure by allowing gravity to pull the cerebellum down away from the field. There are benefits from an anesthetic standpoint as well. The sitting position helps to improve respiratory mechanics because of decreased airway pressures and improved diaphragmatic excursion, particularly in obese patients. Another advantage of this position is that it allows the anesthesia team to readily access the patient's airway.

Table 4.1 Advantages of sitting position craniotomies vs. other positions

Surgical
Improved exposure
Improved anatomical orientation
Improved venous drainage from the surgical field
Improved hemostasis
Gravitational drainage of CSF and blood from the surgical field
Better teaching due to the nonrotated anatomical field
Shorter surgical time
Decreased intracranial pressure (ICP)
Anesthetic
Improved access to the endotracheal tube, chest wall, and arms by the anesthesiologist
Diaphragm is able to move more freely
Ability to observe the face for neuromonitoring
Ability to use transesophageal echocardiography (TEE) for venous air embolism (VAE) detection

Adapted from [7]

Despite these advantages sitting position craniotomies also pose significant challenges for the anesthesiologist. The major concern about sitting position craniotomy, of course, is the increased risk of venous air embolism (VAE). There has been a great deal of variation in the rates of intraoperative VAE for patients undergoing neurosurgical procedures in sitting position reported in the literature. In one systematic review of 4806 patients undergoing surgery in sitting position, 39% of craniotomy patients and 12% of cervical surgery patients were diagnosed with intraoperative VAE [2]. However, it is important to remember that while a relatively high proportion of patients may be diagnosed with intraoperative VAE, very few of these episodes are clinically significant. These rare cases of rapid air entrainment resulting in significant impairment of gas exchange, hemodynamic compromise, or persistent neurologic impairment in patients undergoing surgery in sitting position are referred to as extreme VAE [3]. In one case series of 728 patients undergoing craniotomies in sitting position, there were only 8 cases of extreme VAE (1.1%) [3]. In another case series of neurosurgical procedures performed in sitting position at a single institution, the incidence of VAE was found to be 4.7% but the incidence of clinically significant VAE was only 1% [4]. Relative contraindications to this position include intracardiac septal defects because of the risk of paradoxical air embolism (PAE), pulmonary AV malformations, hydrocephalus, and severe hypovolemia [5].

A modified version of sitting position known as semi-sitting position may be used for resection of lateral tumors. This position was developed in order to reduce the risk of VAE during these procedures [6]. It is similar to standard sitting position in that the bed is flexed at the patient's hips to 90° and the knees are flexed to 30°. However, the entire bed is then reclined so that the vertex and the legs are nearly level. In their case series of 187 craniotomies using this position they report 3 cases of significant VAE (1.6%), with only 1 (0.5%) causing hemodynamic instability. In contrast, the incidence of significant intraoperative VAE during standard sitting position craniotomies cited in the literature is as high as 50% [2].

Placing the patient in prone position decreases the risk of VAE but does not eliminate it since the head is still elevated relative to the heart in order to try to decrease venous bleeding. The risk of vision loss, usually related to ischemic optic neuropathy, may be slightly elevated in prone position as compared to other positions but remains quite low [5]. Patients may also experience significant facial edema, including of the orbit and airway, after surgery in prone position but this should resolve quickly postoperatively once the patient is returned to supine position.

The lateral position may be used for unilateral procedures in the upper posterior fossa while the three-quarter prone position and lateral park bench allow for greater head rotation thereby allowing more access to axial structures [5].

Question 4:
What preoperative workup would you obtain for this patient?

Answer:
A through history and physical should be obtained, with particular emphasis on cardiopulmonary status, prior surgeries, evidence of cerebrovascular compromise, and suitability for central venous access [5]. Laboratory workup should include chemistry and CBC and type and screen. The patient's exercise tolerance should be assessed to determine if further testing is required. If there are any concerns for cardiac issues, baseline electrocardiogram (EKG) and possibly more invasive cardiac testing may be necessary.

The patient should be asked about any cervical spine issues since sitting position may exacerbate any preexisting pathology; however, there is no consensus on what diagnostic tests should be ordered preoperatively. A recent review of current practice found that only one center performs routine extension-flexion radiographs of the cervical spine routinely on all patients presenting for sitting position craniotomies [7]. It appears that most practitioners would obtain imaging studies only in patients with known or suspected cervical spine pathology. Thus, the authors conclude that there is currently no uniform approach that has been established for

preoperative evaluation of possible cervical spine pathology in patients being considered for sitting position craniotomy [7].

Prior to the worsening of her symptoms the patient was active and had good exercise tolerance. However, upon further discussion with the patient she mentions that she has been told that she has a murmur but has never had any symptoms from it and has never been referred to a cardiologist.

Question 5:
What further information would you like for this patient?

Answer:
The presence of a benign murmur raises concerns for the presence of a septal defect. One of the most dreaded complications for patients undergoing sitting position craniotomy is PAE. This risk is increased for patients with intracardiac septal defects so most authors feel that the presence of a patent foramen ovale (PFO) is a relative contraindication to undergoing craniotomy in sitting position. However, there is great variability in the approach to preoperative evaluation for PFO in patients being considered for a sitting position surgery. One review found that three centers refer all patients presenting for sitting position craniotomy for formal diagnostic workup for PFO while others evaluate for the presence of PFO using transcranial Doppler (TCD) only after the induction of anesthesia [7]. Another review of 28 studies found that 10 centers consider PFO an absolute contraindication to sitting position craniotomies whereas 2 of the studies did not [2]. In another review of 977 patients undergoing craniotomies or cervical spine surgeries performed in semi-sitting position, 82 patients were found to have PFOs [8]. Intraoperative VAE was detected in 33 of those 82 patients (40.2%) with no subsequent PAE so the authors conclude that the risk of performing surgery in the semi-sitting position is acceptable even in patients with PFO [8]. Clearly, there is currently no consensus regarding the preoperative evaluation of patients being considered for sitting position craniotomy, but most authors do recommend that formal evaluation for PFO be performed preoperatively for patients being considered for surgery in sitting position, especially for patients like this one who report a benign murmur.

Question 6:
How prevalent is PFO and how is it diagnosed?

Answer:
Approximately, 25% of adults have a PFO [9]. The rate of PFO in patients with a prior history of cryptogenic cerebrovascular accident (CVA) is more than 40% [2, 9]. PFOs are a concern for cases in which the risk of VAE is increased because of the possibility of a PAE. PAE is the passage of air from the venous circulation into the arterial circulation and can result in significant neurologic complications or even death. The rate of VAE for sitting position cases has been cited as ranging from 1 to 76% versus 0 to 12% in horizontal position in various case series [2]. The overall rate of VAE for posterior fossa procedures performed in sitting position is estimated to be about 39% [2]. In three studies which included patients with PFO of patients undergoing sitting position craniotomies, the incidence of PAE was reported as 14%, 0%, and 6.6% (the study reporting a PAE rate of 0% partially excluded patients with PFO) [2]. Thus, it is important to evaluate for the presence of PFO in patients who are presenting for sitting position craniotomy.

While some authors suggest PFO is an absolute contraindication to sitting position craniotomy, others feel that the availability of reliable monitors such as transesophageal echocardiography (TEE) or precordial Doppler allow for timely intervention so that the risk of undergoing a sitting position craniotomy without preoperative evaluation for PFO is acceptable. In one case series of 136 patients operated on in sitting position, 22 patients (16%) were diagnosed with intraoperative VAE [10]. These patients were not screened for PFO prior to surgery so post-induction TCD was performed to evaluate for PFO which was found in only 2 patients (1.4%). Neither of these patients was diagnosed with intraoperative VAE. See Fig. 4.2 for a suggested

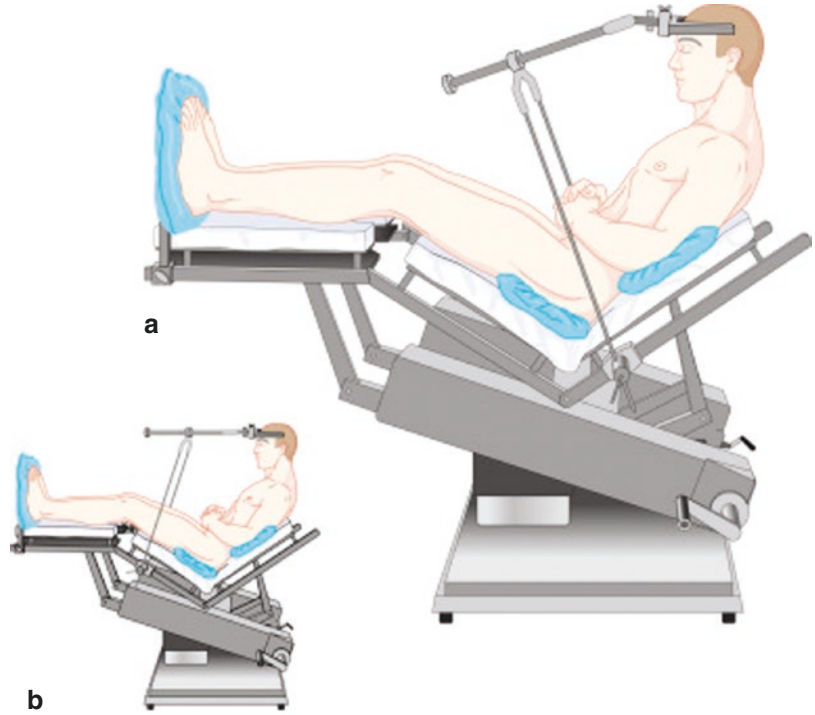


Fig. 4.2 Diagram A shows the correct configuration of the head holder, allowing for the OR table to be flattened and placed into Trendelenburg position without disrupting the position of the head. In Diagram B by contrast the bed cannot be flattened without removing the patient's head from the head holder. Used with permission from *Miller's Anesthesia*, 8th ed., Chap. 70

approach to evaluating a potential candidate for sitting position craniotomy.

There are numerous diagnostic tools that can be used to evaluate for PFO. Transthoracic echocardiography (TTE) has a specificity of 99% and has the benefit of being noninvasive [11]. A PFO study involves the injection of agitated saline into a peripheral vessel while the TTE is being performed. Patients may be asked to perform a Valsalva maneuver during the exam which increases right atrial pressure (RAP) and may encourage the passage of bubbles through any communication. A positive diagnosis is made if bubbles appear in the left atrium within three cardiac cycles. However, TTE's low sensitivity of 46% means that most patients with a negative result will be referred for TEE if there is a high index of suspicion for PFO [11].

Another noninvasive diagnostic test for PFO is TCD. It has the advantages of being less expensive than echocardiography and easy to perform at the bedside. Similar to TTE the patient may be asked to perform a Valsalva maneuver during the exam to elicit evidence of an intracardiac communication. A meta-analysis comparing TCD and TTE of 35 studies which included 3067 patients found that TCD has an overall sensitivity of 96.1% and specificity of 92.4% as compared to TTE with an overall sensitivity of sensitivity of 45.1% and specificity of 99.6%; the authors concluded the TCD's overall diagnostic yield appears to outweigh that of TTE [12].

Currently TEE with contrast remains the gold standard for diagnosis of PFO (89% specificity, 92% sensitivity); however, as compared with TTE and TCD, TEE has several disadvantages. It is more expensive and more invasive with many patients requiring sedation while it is performed so that the patient is likely not able to perform a Valsalva maneuver during the test. Because TCD has been shown to have comparable sensitivity and specificity to TEE, Komar et al., suggest that both TEE and TCD are necessary for a complete evaluation for PFO [13].

The patient is referred to a cardiologist for evaluation of her murmur. A TEE is performed and the patient is found to have a PFO.

Question 7:
What is your next step?

Answer:
The patient should be counseled on the risks of undergoing a craniotomy in sitting position with the increased risk for PAE and the significant neurologic and cardiovascular risks it entails. Percutaneous PFO closure has a >95% success rate and major complication rate (defined as pericardial effusion with tamponade, device embolization requiring surgery, thrombus on device, or CVA/TIA) is reported as 2.4–5.9% [11]. Thus, undergoing a preoperative PFO closure appears to be a safe option for patients being considered for a craniotomy in sitting position.

The patient elects to undergo PFO closure prior to undergoing her surgery because of the risk of PAE. The cardiologist is able to perform a successful percutaneous closure of her PFO.

Question 8:
How soon after the procedure can the patient undergo her planned craniotomy?

Answer:
Patients who undergo PFO closure are typically placed on antiplatelet therapy for several months. A review of 593 patients who had undergone percutaneous PFO closure and were evaluated for thrombus formation at 4 weeks and 6 months reports the incidence of thrombus formation to be 2.5% [14]. Risk factors for thrombus formation include development of atrial fibrillation after closure and persistent atrial septal aneurysm. Therefore, current practice is to place patients on antiplatelet therapy (aspirin and clopidogrel) after the PFO closure for at least 6 months for thrombus prophylaxis [14].

You are informed by the neurosurgeon that she feels that the patient needs to proceed with the surgery soon because of the large size of the patient's tumor as evidenced by her vestibular symptoms. She is concerned about the tumor causing further neurologic compromise. After a lengthy discussion with the neurosurgeon and the cardiologist regarding the risks and benefits of proceeding with surgery versus interrupting the antiplatelet therapy, the patient decides to proceed with the VS resection 2 weeks after the PFO closure.

Question 9:
What is your plan for management of this patient's antiplatelet therapy?

Answer:
In general, there are several options for perioperative management of antiplatelet therapy. For non-neurosurgical cases the patient is often advised to continue with aspirin while holding the clopidogrel for 5–7 days preoperatively. Another option would be to hold both aspirin and clopidogrel for 5–7 days and bridge during this period with an agent such as cangrelor. Cangrelor is an intravenous (IV) agent with a half-life of less than 10 min so the patient would need to be admitted for this. A third option is to continue both aspirin and clopidogrel and transfuse platelets immediately prior to the procedure [15].

You and the neurosurgeon counsel the patient that it is critically important to minimize the risk of perioperative bleeding for her procedure because of the location of her tumor. Collectively you agree that the incidence of thrombus formation is sufficiently low that you feel it is safe for her to discontinue the aspirin and clopidogrel for 7 days prior to her surgery. The patient is advised to take the aspirin and clopidogrel for 1 week and then hold them in preparation for her surgery.

4.2 Intraoperative Management

The patient presents 2 weeks after her PFO closure for surgery. She has appropriately held her aspirin and Plavix for 7 days as instructed.

Question 10:
What is your anesthetic plan for this patient?

Answer:
Typically patients presenting for VS resection have undergone a thorough preoperative evaluation and increased intracranial pressure (ICP) is rarely a concern. The patient may be premedi-

cated with midazolam depending on the patient's comorbidities, neurologic exam, and the anesthesiologist's discretion. Induction is typically performed with fentanyl, lidocaine, propofol, and the depolarizing neuromuscular blocker succinylcholine. If there is a contraindication to succinylcholine, a nondepolarizing neuromuscular blocker such as rocuronium may be used. With the introduction of sugammadex rocuronium can be reliably reversed within seconds. Typically facial nerve electromyography (EMG) is performed intraoperatively so intraoperative neuromuscular blockade is contraindicated. EMG is not affected by volatile agents so volatile agents may be used for maintenance of anesthesia. A propofol infusion may be used depending again on provider preference and patient factors. Remifentanil is a useful adjunct to volatile agent and/or propofol to insure that the patient does not move while not prolonging emergence because of its steady context-sensitive half-time.

Most practitioners opt to avoid the use of nitrous oxide in cases with an increased risk of VAE because of its theoretical potential to dramatically increase the volume of any entrained air. In animal studies NO_2 has been shown to decrease the LD50 for VAE and cause the expansion of bubbles in NO_2-saturated fluid. However, the use of 50% NO_2 has not been shown to worsen hemodynamic changes or neurologic outcomes in patients with intraoperative VAE [3]. Thus, these authors do not consider it necessary to avoid NO_2 in sitting position craniotomies. However, if the provider has opted to use nitrous oxide during the case, most authors do recommend discontinuing it if a VAE is detected.

Question 11:
What monitors will you use intraoperatively if the procedure is being performed in prone or three-quarters lateral position?

Answer:
Intraoperative monitoring for a patient undergoing a VS resection in prone or three-quarters lateral position typically includes standard ASA monitors and an arterial line. Access consisting of two large bore IVs is sufficient. A central venous catheter (CVC) should be placed if peripheral access is insufficient.

The surgeon has discussed with you her preference for performing the case with the patient in sitting position because of the size of the tumor and the goal of preserving hearing and balance.

Question 12:
What concerns do you have about placing this patient in sitting position for her surgery?

Answer:
One of the most concerning risks for patients undergoing sitting position craniotomies is the increased risk of VAE. VAE is the entrainment of air from the operative field into the venous circulation. The risk of VAE is increased when the site being operated on is more than 5 cm above the level of the right atrium and the surgical field for craniotomies in sitting position is several times greater than 5 cm. In addition, there are numerous large, noncompressible venous channels in the surgical field so that the risk of VAE during sitting position craniotomies is among the highest for any surgical procedure [16]. The two factors that determine the severity of clinical symptoms are the volume of air entrained and the rate of accumulation [16]. The lethal volume of air entrainment in adults has been calculated to be 200–300 mL (3–5 mL/kg) [16]. If the rate of air entrained is sufficiently large an air lock may occur whereby forward circulatory flow is impeded because of outflow obstruction of the right ventricle from inability to decompress the ventricular wall [16]. This rapidly leads to right heart failure and subsequent cardiovascular collapse.

Even VAE that accumulates more gradually may result in significant pathologic changes that may make ventilation and maintaining hemodynamic stability quite challenging for the anesthesiologist. VAE leads to increased microvascular permeability. Pulmonary hypertension may be induced by the release of endothelin 1 from the pulmonary vasculature. In addition, microbubbles from the VAE may lead to platelet aggregation and the release of platelet activator inhibitor. This may in turn lead to a systemic inflammatory response [16].

As noted previously the rates of intraoperative VAE during sitting position craniotomy that have been reported in the literature vary greatly. However, the rate of clinically significant VAE, usually defined as resulting in hemodynamic or respiratory compromise is generally much lower. A recent review of 450 suboccipital procedures performed in sitting position at a single institution evaluated for the incidence of clinically significant VAE [4]. Episodes of intraoperative VAE were defined as mild if no intervention was required, moderate if there was a significant drop in end-tidal CO_2 ($ETCO_2$) or hemodynamic instability, or severe if the criteria for moderate VAE were met and in addition repositioning was necessary and/or advanced cardiopulmonary life support (ACLS) needed to be performed [4]. There were 12 cases of clinically significant VAE (2.7%) [4]. Similarly another review of 600 patients calculated the intraoperative incidence of VAE to be 19% but the incidence of VAE resulting in hemodynamic or respiratory compromise was 3.3% [17].

A significant concern for patients with a communication between the right and left heart is that a VAE may develop into a PAE whereby the air embolism travels from the venous circulation into the arterial circulation. PAEs can result in catastrophic neurologic injury and even death. Although the exact pressure gradient necessary to push air across an intraseptal cardiac defect is unknown, it is thought to be at least 5 mmHg [18]. Mammoto et al. found that PAE occurred only with the entrainment of significant volumes of air so it is possible that a significant increase in right heart pressure is necessary for a VAE to result in a PAE [19]. (Mammoto) Factors that affect the RAP to left atrial pressure (LAP) gradient include PEEP which increases it and generous fluid administration which decreases it [18].

Physiologic changes that can be expected if the patient has sustained a VAE include a rapid significant decrease in $ETCO_2$ because of the disruption in circulation. In one case series of sitting position craniotomies, the average time for $ETCO_2$ to fall from baseline to minimum was about 11 min after VAE was detected, falling on average by 38% [3]. If end-tidal nitrogen (ETN_2) is being monitored, there may be a spike in N_2 levels with the entrainment of room air in the systemic circulation. The average time for mean arterial pressure (MAP) to drop from baseline to minimum recorded was 9.8 min, with MAPs falling on average by 46% [3]. The oxygen saturation levels may drop but depending on the amount of entrained air this may be a later finding. EKG tracing may demonstrate right-sided heart strain and ST-T segment changes. If a TEE is performed there may be evidence of right-sided heart strain as well with a full right heart and a relatively empty left heart.

Question 13:
What additional monitors will you want for this patient if she is to be placed in sitting position for her surgery?

Answer:
If the patient is undergoing surgery in sitting position monitoring should standard ASA monitors, arterial line, plus a TEE or precordial Doppler for detection of VAE. According to Chang et al., "Among the treatments of venous air embolism, aspirating air through the right atrial catheter has proven to be the most effective" [20]. Thus, placing a CVC to facilitate aspiration of a possible VAE is also considered standard of care.

There is a great deal of debate in the literature about the type of CVC that should be placed and its optimal location and positioning. CVCs are commonly placed in the subclavian vein instead of the internal jugular (IJ) vein for craniotomies so as not to compromise venous drainage; however, the risk of compromising venous outflow posed by placing the CVC in the IJ should be sufficiently low for most patients unless there is significant concern about elevated ICP. Some institutions instead place a long arm CVC in the basilica or cephalic vein (Arrow Multiorificed Antecubital Central Venous Catheterization Kit—AK-04250; Teleflex Inc., Morrisville, NC) [3, 4].

Similarly there has been a great deal of discussion about where the tip of the CVC should be

placed. Bunegin, et al. recommend that a multi-orifice catheter should be placed 2 cm below the SVC-atrial junction, but a single-orifice catheter should be placed 3 cm above the SVC-atrial junction (see Fig. 4.3) [21]. However, this distinction is most likely important only when aspirating smaller volumes of air. While there has not been a great of investigation regarding the optimal placement of the tip of the CVC, most practitioners feel that positioning it anywhere in the right atrium will allow for the aspiration of large volumes of air [18]. Two methods are available for confirming the position of the CVC tip, radiography, and intravascular electrocardiography (ECG) but there has been little data to support the superiority of either method. Indeed, most authors feel that positioning the CVC tip at the level of the second or third intercostal space is sufficient [18].

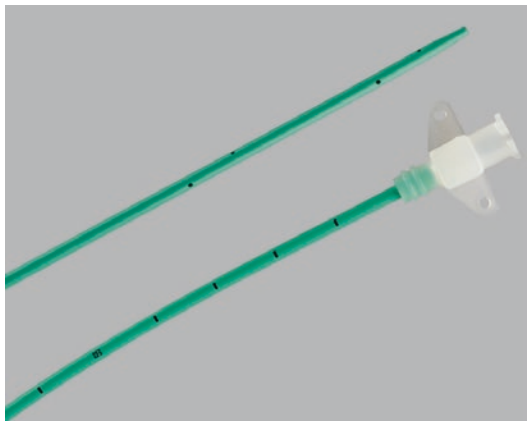


Fig. 4.3 Bunegin-Albin multiorifice catheter. Permission for use granted by Cook Medical, Bloomington, Indiana (https://www.cookmedical.com/products/cc_vas_webds/)

The type of CVC placed for a sitting position craniotomy may also be important to the success rate of attempts to aspirate air when a VAE is detected. For multilumen CVC and Swan-Ganz catheters, the success rate of attempted aspiration has not been very promising with reports in the literature of 6–16% [16]. Better success rates of 30–60% have been reported with the Bunegin-Albin multiorifice catheter (Cook Critical Care) [21] (Fig. 4.4).

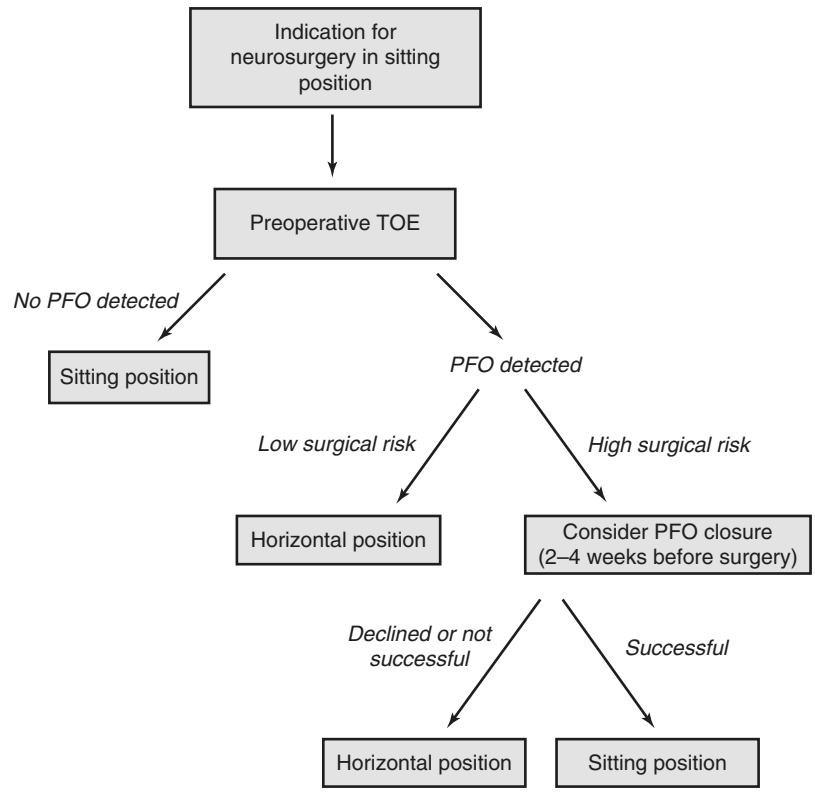


Fig. 4.4 Suggested algorithm for evaluating a patient for sitting position craniotomy [7]

One caveat about aspirating air via CVC in the event of VAE that must be kept in mind is that most of the data comparing the efficacy of the various types of CVCs are from animal studies and not humans. Interestingly in a recent case series of 136 sitting position surgeries (93 craniotomies and 43 cervical spine procedures), 22 episodes of VAE (21.5% of craniotomies and 4.7% of the spine cases) were detected, and the authors report that air was successfully aspirated via CVC in 59% of those cases [10]. However, in a case series of 798 neurosurgical procedures performed with the patient in sitting position examining the incidence of extreme VAE, the authors felt that appreciable air was aspirated via CVC in only one case [3]. Thus, it is considered standard of care to place a CVC during sitting position craniotomies in order to facilitate the aspiration of air in the event of an intraoperative VAE; however, there is very little data reported in the literature regarding the success rates of these maneuvers in humans.

Monitors for the detection of VAE are critical during a sitting position case. The monitor should have high sensitivity and specificity, allow for a rapid response and provide feedback about recovery from the event. The most sensitive monitor for detection of VAE is TEE, which can detect volumes as small as 0.02 mL/kg of intravascular air. However, the feasibility of monitoring TEE for a prolonged case. As well as the safety concerns of leaving an ECHO probe inserted for such a long duration. Make this modality impractical for many institutions.

Precordial Doppler is nearly as sensitive as TEE for detecting VAE allowing for the detection of volumes as small as 0.05 mL/kg of intravascular air. It also has the advantage of being noninvasive. The Doppler probe should be placed either left or right parasternally between the second and third or third and fourth ribs. As a check that the probe is positioned properly a bubble test may be performed by injecting 9 mL of saline mixed with 1 mL of air into the CVC. The rhythmic sound of normal heart tones will be replaced with turbulent flow, often referred to as a "mill wheel" sound. Other modalities for intraoperative monitoring for VAE include TCD ultrasound, pulmonary artery catheter, ETN_2 detector, and $ETCO_2$ detector. Currently the combined use of precordial Doppler and continuous $ETCO_2$ monitoring is the standard of care for detection of intraoperative VAE [18].

After a smooth induction the patient is positioned in sitting position. Approximately, 4 h into the case, the patient begins to have significant arrhythmias and her heart rate is noted to be in the 30s.

Question 14:
What is the likely cause and what is your next step?

Answer:
Manipulation of the pons and/or lower medulla, as well as the extra-axial portion of the vagus nerve can all result in significant dysrhythmias and hemodynamic changes. These may include bradycardia, tachycardia, hypertension, hypotension, premature ventricular contractions, or even asystole. Immediately inform the surgeon of these changes and request that any retraction be released immediately. While the temptation is to treat such hemodynamic changes pharmacologically, such interventions may mask warning signs regarding potential injury to these vital structures [18]. Thus, timely communication with the neurosurgeons about any arrhythmias or sudden hemodynamic changes is critically important.

You notify the neurosurgeons about the patient's bradycardia and they relax their retraction. The bradycardia quickly resolves and the case proceeds without a return of the significant bradycardia. Approximately, 6 h into the case, turbulent flow is detected on the precordial Doppler and the patient's blood pressure is noted to drop precipitously with systolic pressures falling to the 50s.

Question 15:
What is the most likely etiology of these derangements and what are your next steps?

Answer:
The patient has likely sustained a VAE. The surgeon needs to be informed immediately. He/she should flood the field with irrigation. The surgical field should be lowered as close to the level of the heart as possible to prevent further entrainment of air, and if necessary the patient should be placed in Trendelenburg position. It is not necessary to take the patient out of the head holder; rather, the entire bed should be placed so that the head is level with the heart. This allows the entire table to be put into Trendelenburg to level the head with the heart as opposed to flattening out the entire bed. It is important to place the head supports on the portion of the operating room table that is raised to achieve sitting position so that the bed can be flattened to facilitate chest compressions if necessary (Fig. 4.2).

Jugular venous compression has been shown to be effective at limiting the entry of air into the chest from face and head sources; however, the subsequent increase in ICP should be taken into account during a craniotomy [16]. If there is hemodynamic collapse, ACLS including chest compressions should be initiated as rapidly as possible. Another benefit of chest compressions may be to help force air out of the pulmonary outflow tract back into smaller pulmonary vessels which may help with forward blood flow [16]. IV fluids should be running wide open, also to encourage forward flow. An attempt to aspirate air from the right atrium via a CVC should be considered.

Once these immediate interventions have been attempted the patient may need hemodynamic support including vasopressors. The goals would be to optimize myocardial perfusion and provide inotropic support of the right ventricle [16]. Blood pressure should be supported with vasopressors. Dobutamine has been shown to increase cardiac index and stroke volume and reduce pulmonary vascular resistance in the setting of VAE [16]. Norepinephrine has been suggested as another alternative and has been shown to increase blood pressure without increasing pulmonary vascular resistance.

Upon being informed about the hemodynamic changes the surgeons immediately flood the field with irrigation and the operating table is put into Trendelenburg position to place the patient's head approximately level with the heart. Fluids are opened and phenylephrine is administered with good response and the patient's systolic blood pressure increases to the 100s. A TEE is performed which demonstrates right ventricular strain and a relatively empty left-sided heart. As the patient's blood pressure stabilizes a repeat TEE shows resolution of the right ventricular overload. Once the patient has been successfully resuscitated and is hemodynamically stable, her oxygenation and ventilation status also stabilize so after a discussion with the neurosurgeons the decision is made to continue with the case. The rest of the surgery proceeds uneventfully and the surgeons finish the procedure which started at 7:30 am around 7:00 pm. At the end of the case all anesthetic agents are discontinued. After 30 min the patient continues to require ventilatory support and is not responding to aggressive stimulation.

4.3 Postoperative Management

Question 16:
What is delayed emergence?

Answer:
Delayed emergence after anesthesia does not have a precise definition in the literature but is generally agreed to be the failure of a patient to regain the expected level of consciousness about 30–60 min after all anesthetic agents have been discontinued [22]. Some authors suggest that emergence is delayed if the appropriate level of consciousness is not regained within 15 min after discontinuation of all anesthetic agents [23]. Frost suggests that causes for delayed emergence can be categorized into four broad categories: patient factors, drug factors, surgical factors, and metabolic factors [22]. This schematic may be helpful in determining possible etiologies that are more likely when faced with a case of delayed emergence. Patient factors include extremes of age, genetic variation,

body habitus, comorbidities, obstructive sleep apnea (OSA), preexisting cognitive dysfunction, seizures, and CVA. Drug factors include overdose, prolonged exposure to inhaled or IV agents, residual neuromuscular blockade, potentiation by other drugs, local anesthetic toxicity, and fluid overload. Surgical factors include long duration and of course, type of surgery [22]. Neurosurgical procedures have the highest risk for delayed emergence [22]. Causes of delayed emergence specific to neurosurgical cases include pneumocephalus, CVA, CSF hypotension, and seizure [23].

In neurosurgical cases one of the priorities in terms of anesthetic management is rapid recovery from anesthesia so that a postoperative neurologic assessment can be obtained as quickly as possible. However, in some procedures gradual emergence may in fact be desired and is planned so as to have a controlled extubation. For instance prone positioning may result in macroglossia and concern for airway edema so the emergence may be delayed to allow the edema to improve. The region of the brain being operated on also plays an important role in determining how quickly the patient emerges from anesthesia. In one series of 800 patients undergoing infratentorial procedures, there were 398 cases (50%) of delayed emergence [24].

Question 17:
What are some likely causes for this patient's delayed emergence?

Answer:
Along with the likely causes that may contribute to delayed emergence from anesthesia in general, this patient is at increased risk for several complications related to the location of her surgery. Patients having posterior fossa procedures are at increased risk for postoperative edema because of the relatively confined space. The respiratory centers in the brainstem may have been affected from aggressive retraction or edema so it is critical that patients demonstrate a good respiratory pattern both in terms of frequency and adequate tidal volumes. Patients undergoing surgery in prone position are at increased risk of developing facial and airway edema. They may also have significant macroglossia. A leak test should be considered prior to extubating the patient to ensure adequate patency of the airway. In addition, these patients are also more likely to have PONV so it is crucial that their level of consciousness be sufficient for them to protect their airway. Because of these concerns, some neuroanesthesiologists advocate waiting to extubate patients who have undergone posterior fossa procedures for 1–2 h after they have completely recovered from anesthesia [23].

Patients undergoing a sitting position craniotomy also have an increased likelihood of clinically significant pneumocephalus and in particular ventricular tension pneumocephalus (VTP). Risk factors for the development of pneumocephalus include long duration of surgery, intraoperative use of nitrous oxide, preoperative hydrocephalus, intraoperative osmolar therapy, hyperventilation, spinal anesthesia, barotrauma, and continuous CSF drainage via a lumbar drain [25]. The risk of VTP is increased in sitting position craniotomy because of the "inverted bottle phenomenon" whereby hydrostatic pressure causes CSF to drain and be replaced by air which rises and cannot exit [25]. Higher volumes of intraventricular air are associated with the development of VTP with average volumes of 48.5 mL in symptomatic vs. 7.4 mL in asymptomatic patients [25]. The strongest risk factor for the development of VTP was intraoperative opening of the fourth ventricle with an OR of 34.7 (CI 95% [4.4–273.5], $p = 0.001$) [25]. While some neurosurgeons may opt to place an external ventricular drain (EVD) prophylactically in order to be able to treat potential VTP, there is no data in the literature to support this practice [25].

The rates of VTP reported in the literature vary but in general are low. In a review of 307 patients undergoing craniotomy in sitting position at a single institution, 12 patients (3.9%) were diagnosed with VTP [25]. In comparison, another recent case review of 450 suboccipital craniotomies performed in sitting position reports the rate of VTP to be only 0.2% [4]. VTP is managed by placement of an EVD. Of the 12 patients with VTP, 5 improved immediately after placement

of the EVD and woke up while 4 experienced a more gradual improvement in neurologic status over the next several days [25].

The decision is made to leave the patient intubated and she is transferred to the neurosurgical intensive care unit for further management. She is still not responding to painful stimulus on postoperative day (POD) 1 so she is transported to the computed tomography (CT) scanner for STAT imaging. The head CT shows significant pneumocephalus with other expected postoperative changes. An EVD is placed and the patient begins to demonstrate an improved respiratory pattern over the next several days. She is following commands and is extubated on POD 4. Her neurologic exam is consistent with her preoperative baseline. She is transferred to the floor on POD 6 and is discharged home on POD 8.

4.4 Conclusion

CPA tumors are not uncommon and their resection poses many challenges for the anesthesiologist and neurosurgeon. These procedures can be performed with the patient in a variety of positions. Currently these surgeries are performed with the patient in sitting position less and less commonly because of the concern for increased risk of VAE. Sitting position does offer numerous advantages in terms of surgical exposure and anesthetic management. There is currently no consensus about the need for formal preoperative evaluation for PFO in patients who are being considered for surgery in sitting position. Several recent formal case reviews do suggest that the risk of VAE resulting in PAE is extremely low; however, most authors do continue to recommend that patients with known PFO not undergo sitting position craniotomies.

Continuous monitoring for VAE during a craniotomy in sitting position is mandatory. While TEE is most sensitive for detection of VAE, most authors agree that the current standard of care, which is the use of precordial Doppler in conjunction with $ETCO_2$ monitoring, is sufficient. A CVC is required for craniotomies in sitting position in the event that it is necessary to aspirate air from the right atrium. The Bunegin-Albin catheter has been shown to result in higher success rates in aspirating air in animal models; however, there has been very little data published in the literature on the efficacy of aspirating air via CVC in humans.

Finally patients undergoing surgical resection of CPA tumors have an increased incidence of numerous postoperative complications, including impaired respiratory drive, airway edema depending on the intraoperative positioning, and clinically significant VTP. Therefore, it is critical to make sure that patients have completely emerged from anesthesia and are demonstrating a regular respiratory pattern and ability to protect their airway before extubation.

Multiple Choice Questions

1. What is the gold standard for diagnosis of PFO?
   (a) TTE
   (b) TEE
   (c) TCD
   (d) TCD and TEE
   Answer: b
   The gold standard for diagnosis of PFO is TEE because it is most sensitive. Some authors advocate for performing TCD in conjunction with TEE for diagnosis of VAE.
2. What is the current standard of care for detection of intraoperative VAE?
   (a) TTE
   (b) TEE
   (c) Precordial Doppler
   (d) Precordial Doppler and $ETCO_2$ detector
   Answer: d
   The current standard of care for detection of intraoperative VAE is the use of precordial Doppler along with continuous $ETCO_2$ monitoring. TEE is the most sensitive diagnostic modality for detection of VAE but is invasive and may require additional personnel certified in ECHO to interpret the findings. Precordial Doppler is nearly as sensitive as TEE and has the advantages of being noninvasive and not requiring special training to interpret

3. A VAE is detected in a 45-year-old woman undergoing CPA tumor resection in sitting position. Her MAPs are in the 50s. Which of the following vasopressors is the best choice?
   (a) Phenylephrine
   (b) Vasopressin
   (c) Dobutamine
   (d) Epinephrine
   Answer: c

   Dobutamine has been shown to increase cardiac index and stroke volume and reduce pulmonary vascular resistance in the setting of VAE. Vasopressin is a viable alternative because it does not increase PVR.
4. During a VS resection in you notice significant bradycardia to the 30s on the patient's EKG reading. What is your next step?
   (a) Administer atropine
   (b) Inform the surgeons
   (c) Administer epinephrine
   (d) Administer ephedrine
   Answer: b

   During posterior fossa procedures, manipulation of the pons, medulla, and/or vagus nerve can result in significant arrhythmias and hemodynamic changes. While the immediate impulse is to treat such disturbances pharmacologically, doing so may risk warning signs of impending damage to these structures. Thus, the initial response should be to inform the surgeons to see if releasing retraction and modifying their approach will result in improvement of these hemodynamic disturbances.

References

1. Kaul V, Cosetti MK. Management of vestibular schwannoma (including NF2). Otolaryngol Clin N Am. 2018;51(6):1193–212.
2. Fathi AR, et al. Patent foramen ovale and neurosurgery in sitting position: a systematic review. Br J Anaesth. 2009;102(5):588–96.
3. Abcejo AS, et al. Urgent repositioning after venous air embolism during intracranial surgery in the seated position. J Neurosurg Anesthesiol. 2019;31(4):413–21. https://doi.org/10.1097/ANA.0000000000000534.
4. Himes BT, et al. Contemporary analysis of the intraoperative and perioperative complications of neurosurgical procedures performed in the sitting position. J Neurosurg. 2017;127:182–8.
5. Schlichter RA, Smith DS. Chap. 12: Anesthetic management for posterior fossa surgery. In: Cottrell J, Patel P, editors. Cottrell and Patel's neuroanesthesia. 6th ed; 2017.
6. Jadik S, et al. A standardized protocol for the prevention of clinically relevant venous air embolism during neurosurgical interventions in the semisitting position. Neurosurgery. 2009;64:533–9.
7. Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. Curr Opin Anaesthesiol. 2014;27(5):474–83. https://doi.org/10.1097/ACO.0000000000000104.
8. Klein J, et al. A systematic review of the semi-sitting position in neurosurgical patients with patent foramen ovale: how frequent is paradoxical embolism? World Neurosurg. 2018;115:196–200.
9. Hagen PT, et al. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc. 1984;59:17–20.
10. Hervias A, et al. Detection of venous air embolism and patent foramen ovale in neurosurgery patients in sitting position. Neurocirugia (Astur). 2014;25(3):108–15.
11. Yuan K, Kasner SE. Patent foramen ovale and cryptogenic stroke: diagnosis and updates in secondary stroke prevention. Stroke Vasc Neurol. 2018;3(2):84–91. https://doi.org/10.1136/svn-2018-000173.
12. Katsanos AH, et al. Transcranial Doppler versus transthoracic echocardiography for the detection of patent foramen ovale in patients with cryptogenic cerebral ischemia: a systematic review and diagnostic test accuracy meta-analysis. Ann Neurol. 2016;79(4):625–35.
13. Komar M, et al. Transcranial Doppler sonography should it be the first choice for persistent foramen ovale screening? Cardiovasc Ultrasound. 2014;12:16. https://doi.org/10.1186/1476-7120-12-16.
14. Krumsdorf U, et al. Incidence and clinical course of thrombus formation on atrial septal defect and patent foramen ovale closure devices in 1,000 consecutive patients. JACC. 2004;43(2):302–9.
15. Tafur A, Douketis J. Perioperative management of anticoagulant and antiplatelet therapy. Heart. 2018;104:1461–7.
16. Mirski MA, et al. Diagnosis and treatment of venous air embolism. Anesthesiology. 2007;106(1):164–77.
17. Gaslandt O, et al. The sitting position in neurosurgery: indications, complications and results: a single institution experience of 600 cases. Acta Neurochir (Wien). 2013;155(10):1887–93. https://doi.org/10.1007/s00701-013-1822-x. Epub 2013 Aug 8.
18. Drummond J, et al. Chap. 70: Anesthesia for neurologic surgery. In: Miller RD, editor. Miller's anesthesia. 8th ed; 2015.
19. Mammoto T, et al. Incidence of venous and paradoxical air embolism in neurosurgical patients in the sitting

position: Detection by transesophageal echocardiography. Acta Anaesthesiol Scanda. 1998;42(6):643–7.
20. Chang JL, et al. Analysis and comparison of venous air embolism detection methods. Neurosurgery. 1980;7(2):135–41.
21. Colley PS, Artru AA. Bunegin-Albin catheter improves air retrieval and resuscitation from lethal venous air embolism in upright dogs. Anesth Analg. 1989;68:298–301.
22. Frost EAM. Differential diagnosis of delayed awakening from general anesthesia: a review. Middle East J Anaesthesiol. 2014;22(6):537–48.
23. Ecchevarria M, et al. Chap. 13: Emergence from anesthesia. In: Prabhakar H, editor. Essentials of neuroanesthesia; 2017.
24. Cai YH, et al. Factors influencing delayed extubation after infratentorial craniotomy for tumour resection: a prospective cohort study of 800 patients in a Chinese neurosurgical centre. J Int Med Res. 2013;41(1):208–17.
25. Sachkova A, et al. Predictors of tension pneumocephalus after posterior fossa surgery in the sitting position. Acta Neurochir. 2018;160(3):525–38. https://doi.org/10.1007/s00701-017-3444-1. Epub 2018 Jan 6.

Suggested Reading

Fathi AR, et al. Patent foramen ovale and neurosurgery in sitting position: a systematic review. Br J Anaesth. 2009;102(5):588–96.
Mirski MA, et al. Diagnosis and treatment of venous air embolism. Anesthesiology. 2007;106(1):164–77.
Schlichter RA, Smith DS. Chapter 12: Anesthetic management for posterior fossa surgery. In: Cottrell J, Patel P, editors. Cottrell and Patel's Neuroanesthesia. 6th ed. 2017.

5 Management of Patient with Aneurysmal Subarachnoid Hemorrhage

Charu Mahajan, Indu Kapoor, and Hemanshu Prabhakar

Stem Case Terminology

A 54-year-old male was brought in the emergency department by his son. He was apparently alright until 6 h back when he complained of sudden onset of severe headache followed by vomiting and transient loss of consciousness. He was a known case of hypertension on Tab. amlodipine 10 mg OD. On examination, the patient had a GCS score of E4V5M6 (drowsy), with pupils bilaterally equal in size and reacting to light. There was presence of neck rigidity and no other motor/sensory deficit. Heart rate—92/min, blood pressure—178/92 mmHg, respiration: 20/min, temperature: 37.2 °C, SpO_2—97% on face mask with oxygen flow @ 6 L/min. Chest and CVS examination findings were normal. Mallampati score could not be assessed but from other external parameters, airway appeared normal. Samples for routine investigations were sent.

5.1 Preoperative

Question 1:
What is your differential diagnosis? How will you proceed?

Answer:
Development of sudden and severe headache with vomiting, loss of consciousness, and focal neurological deficit points toward an intracranial event like:

1. Hemorrhagic stroke
2. Aneurysmal subarachnoid hemorrhage (SAH)—strong possibility because of abrupt onset
3. Pituitary apoplexy: odd: hypertension
4. Tumor bleed: No prior positive history
5. Meningitis: No previous positive history, no fever
6. Migraine: Odd-loss of consciousness, presence of focal deficits

After stabilization of the patient, we will get an urgent non-contrast computed tomography (NCCT) scan done.

Question 2:
NCCT shows blood in right sylvian fissure with no other positive findings. For confirmation of diagnosis, how shall one proceed?

Answer:
Presence of blood in subarachnoid space usually points toward an aneurysmal bleed. Once the diagnosis of SAH is confirmed on computed tomography (CT) scan, the site of

C. Mahajan (✉) · I. Kapoor · H. Prabhakar
Department of Neuroanesthesiology and Critical Care, All India Institute of Medical Sciences (AIIMS), New Delhi, India

© Springer Nature Singapore Pte Ltd. 2020
H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_5

bleed has to be determined by invasive tests digital subtraction angiogram (DSA) or non-invasive ones like CT angiography (CTA) or MR angiography (MRA), depending on the availability, expertise, and patient factors. Though DSA is still considered the gold standard, CTA or MRA can be carried out in cases where DSA cannot be performed in a timely manner [1]. Newer imaging techniques like multidetector CTA, 3 T field strength MRA, time-of-flight sequence, and three-dimensional reconstruction have improved the accuracy of these tests.

The patient underwent DSA under local anesthesia. It revealed right-sided middle cerebral artery (MCA) bifurcation aneurysm of size 4.24 × 3.18 × 2.42 mm pointing anteriorly and slightly superiorly having a neck diameter of 2.4 mm.

Question 3:
What are the other common sites for intracranial aneurysm formation?

Answer:
The intracranial aneurysms usually form at branching sites where the hemodynamic stress is maximum. These are most commonly located in anterior circulation (85–95%), at anterior communicating artery (30%), posterior communicating artery (25%), and MCA (20%). The posterior circulation involving basilar and vertebral artery form the rest of the 5–15% aneurysms and carry a grave prognosis if they rupture.

Question 4:
Enumerate the risk factors for the development of intracranial aneurysms.

Answer:
Various risk factors are age, hypertension, family history, smoking, drug abuse (cocaine), etc. Few conditions like autosomal polycystic kidney disease, type IV Ehlers-Danlos syndrome, coarctation of aorta, connective tissue disorders, and arteriovenous malformations have a propensity for the development of an intracranial aneurysm.

Question 5:
What are the different SAH scores and how are they helpful?

Answer:
There are a variety of SAH scores, but only few are validated and are in common use. These scales help in prognostication of patients and assessment of risk of surgery, guide treatment decisions based on severity and for effective communication of patient's condition among healthcare staff.

The commonly used scales are as follows:

Hunt and Hess scale (1968) [2]: It is the most widely used scale because of its ease of assessment. It consists of five following grades:

- Grade 1: Asymptomatic or mild headache and slight nuchal rigidity
- Grade 2: Moderate to severe headache, stiff neck, no neurologic deficit except cranial nerve palsy
- Grade 3: Drowsy or confused, mild focal neurologic deficit
- Grade 4: Stupor, moderate, or severe hemiparesis
- Grade 5: Deep coma, decerebrate posturing

The patient is allotted to one grade higher in the presence of serious systemic disease (hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease) or vasospasm on angiography.

Hunt and Kosnik [3] modified it to add	– Grade 0: Unruptured aneurysms
	– Grade 1a: fixed neurologic deficit

World Federation of Neurological Surgeons grading scale (1988) [4]

- Grade 1: GCS score 15, no motor deficit
- Grade 2: GCS score 13–14, no motor deficit
- Grade 3: GCS score 13–14, with motor deficit
- Grade 4: GCS score 7–12, with or without motor deficit
- Grade 5: GCS score 3–6, with or without motor deficit

Fisher Scale (1980) [5]

- Group 1: No blood detected
- Group 2: Diffuse deposition or thin layer with all vertical layers of blood (in interhemispheric fissure, insular cistern, or ambient cistern) less than 1 mm thick
- Group 3: Localized clots and/or vertical layers of blood 1 mm or more in thickness
- Group 4: Intracerebral or intraventricular clots with diffuse or no subarachnoid blood

Few others to name are modified Fisher scale, Claassen CT rating scale, the VASOGRADE, Ogilvy and Carter grading system, etc.

Question 6:
To which grade does this patient belong to?

Answer:
This patient belongs to Hunt Hess grade 3 (II + I), WFNS score of grade 2, and Fisher grade 2.

Question 7:
What are the different radiological scales and how are they helpful?

Answer:
The different radiological scales are Fisher scale [5], modified Fisher scale [6], Hijdra sum score [7], and Claassen CT rating scale [8].

Modified Fisher scale comprises of four grades (0–4). Grade 0—no SAH, no intraventricular hemorrhage (IVH). Grade 1—thin (≤1 mm) diffuse or focal SAH; no IVH. Grade 2—thin (≤1 mm) diffuse or focal SAH; no IVH. Grade 3—thick (>1 mm) diffuse or focal SAH, no IVH. Grade 4—thick (>1 mm) diffuse or focal SAH, with IVH.

The risk of delayed cerebral ischemia (DCI) increases with increasing score and is maximum with grade 4 modified fisher scale. The modified Fisher scale is more significantly associated with clinical DCI than the Fisher scale and may have an advantage over it [9].

Hijdra sum score grades the amount of blood on computed tomography from 0 to 42, based on the presence of blood in fissure/cisterns and ventricles. However, it is tedious when applied clinically.

Claassen CT rating scale also gives an index of risk of DCI due to vasospasm depending upon the amount of SAH and IVH. However, it is also not clinically established.

Question 8:
What is early brain injury caused by an aneurysm rupture?

Answer:
When an aneurysm ruptures, blood extravasates into subarachnoid space under high pressure, resulting in increase in intracranial pressure (ICP). The sudden increase in ICP leads to decrease in cerebral blood flow (CBF), global cerebral ischemia, and loss of consciousness. Blood and its breakdown products hinder in the free flow of CSF, causing hydrocephalous. All these early changes result in neuroinflammation, endothelial injury, microthrombosis, and excitotoxicity. These early changes which typically occur in the first 72 h are considered as factors further contributing to DCI, which we will be discussing later.

Question 9:
The patient was shifted to neuro-intensive care unit (ICU) for further management until preparation for surgery was made. What are the initial concerns in such a patient and how will you manage each?

Answer:
The initial concerns in such a patient relate to:

- Management of blood pressure
- Rebleeding
- Development of early hydrocephalus
- Seizures
- Fever
- Anemia
- Electrolyte abnormalities
- Cardiopulmonary dysfunction

Blood pressure: Acute increase in blood pressure of SBP >160 mmHg in patients with unsecured aneurysms may lead to rebleeding and cerebral edema [10]. This should be avoided and

managed promptly. Similarly cerebral perfusion pressure (CPP) should be maintained >70 mmHg to prevent metabolic crisis [11].

Rebleeding: A major concern in the early phase of aneurysmal SAH is rebleeding as it is associated with high mortality and morbidity. About 15–20% of the patients suffer rebleeding within first 14 days if not treated. The maximum risk is on the first day of ictus (9–17%) and then about 1–2% daily for next 2 weeks. The risk factors for rebleeding are higher Hunt and Hess grade, large size of aneurysm, intracerebral hematoma, delay in definitive treatment, cerebrospinal drainage, hypertension, and seizures [10].

The use of antifibrinolytics decreases the risk of rebleeding but increases the ischemic changes resulting in no overall benefit in improving the outcome. But, based on its important effect on stabilization of clot, a short course (<72 h) of tranexamic acid or aminocaproic acid may be given in patients in whom there is delay in definitive treatment of aneurysm but have no major contraindications to its use [1].

Any surge in blood pressure can result in rebleeding from the aneurysm. It is safe to keep the systolic blood pressure (SBP) below 160 mmHg.

Hydrocephalus: The incidence of acute hydrocephalus is about 20–30%. If it is symptomatic, external ventricular drainage (EVD) may be required in early stage. The CSF drainage should be done very slowly and in small aliquots. As transmural pressure (TMP) = mean arterial pressure (MAP) −ICP, so any rapid lowering of ICP may result in increase in TMP and re-rupture of aneurysm.

About 50% of these patients may develop chronic hydrocephalous because of silting of arachnoid granulations and pia-arachnoid adhesions, which interfere with the outflow and absorption of CSF. These patients subsequently require permanent shunting procedures.

Seizures: It occurs in about 26% of SAH patients, associated with poor grade SAH, thick blood clot, hematoma, infarction, and MCA aneurysms. A greater subarachnoid blood clot burden and subdural hematomas are important covariates for the occurrence of seizures [12].

Seizures occurring prior to definitive management of aneurysm may lead to rebleeding. The routine use of antiepileptics has no role in the management, and long-term therapy is not recommended. However, a short course of AED (<7 days) may be given in early days after ictus [13].

Fever: Fever during early stage after bleeding can increase the secondary brain injury and is associated with DCI and poor outcome [14]. Factors like poor Hunt and Hess grade, presence of IVH, and older age are independent predictors of fever in SAH [15]. Pharmacological treatment along with cold sponging methods may help. Endovascular cooling devices have also been used, but no beneficial effect on outcome has been found.

Anemia: Anemia has been associated with poor outcome as the ongoing ischemia further compromises the brain metabolic supply in these patients. On the other hand, blood transfusion has failed to show any improvement in outcome. In a recent study, the effect of transfusion on cerebral oxygenation was investigated by using multimodality monitoring in 15 consecutive patients with SAH. Packed red blood cell transfusion was associated with improvement in brain tissue oxygen [16].

Electrolyte abnormalities: Sodium abnormalities especially hyponatremia are very common after SAH. This can be because of syndrome of inappropriate secretion of anti-diuretic hormone (SIADH), cerebral salt wasting syndrome (CSW), dilutional hyponatremia, use of diuretics, and corticotropic hormonal deficiency. SIADH and CSW can be differentiated by serum osmolality (<275 mOSm/Kg in SIADH), urine sodium (>40 meq/L in SIADH), urine osmolality (>100 mOSM/Kg *in SIADH*), hematocrit levels (decreased in SIADH), and urinary output (increased in CSW). The patient will be normovolemic/hypervolemic in SIADH but will be hypovolemic in CSW because of loss of water and sodium. Management depend-

ing upon the cause should be carried out. Normovolemia should be maintained at all times. Hypernatremia can occur due to dehydration or central diabetes insipidus (DI). Accurate diagnosis of DI and management is essential. It should be slowly corrected to avoid complications.

Cardiac abnormalities: Spectra of cardiac abnormalities can be seen in these patients varying from benign electrocardiographic (ECG) abnormalities, arrhythmias, ST segment changes mimicking myocardial infarction (MI) to serious echocardiographic changes like wall motion abnormalities. Neurogenic stunned myocardium develops as a result of intense sympathetic surge resulting in cardiac dysfunction. It comprises left ventricular dysfunction, ECG changes, and elevation in cardiac enzymes. Its diagnosis is a challenge and has to be differentiated from acute MI. Early goal-directed therapy guided by preload volume and cardiac output monitoring by transpulmonary thermodilution was found to be beneficial for reducing DCI and improving functional outcome in patients with poor clinical grade [17].

Pulmonary edema: The patient can develop dyspnea, hemoptysis, tachypnea, tachycardia, and basal rales. Intense sympathetic stimulation may lead to increase in pulmonary pressures resulting in neurogenic pulmonary edema. The criteria for diagnosis of NPE has been proposed which includes bilateral opacities, PaO_2/FiO_2 ratio <220, no evidence of LAH, presence of severe CNS injury, and absence of other causes of respiratory failure [18]. However, in patients with pre-existing cardiac disease, cardiogenic pulmonary edema may also arise. Even severe neurogenic pulmonary edema may also lead to features of cardiac failure and exacerbation of pulmonary edema. There is high probability of overlap of these two different types of pulmonary edema, and their differentiation is difficult.

The treatment should be supportive with oxygen inhalation and mechanical ventilation when required. Lowering of raised ICP is beneficial for neurogenic pulmonary edema.

Question 10:
When should definitive treatment be instituted, early or late?

Answer:
The results of international cooperative study indicated no difference in outcome in patients operated early (0–3 days) or late (11–14 days) [19]. The definitive treatment of ruptured cerebral aneurysms should be done as early as possible.

It was decided to take up the patient for open craniotomy and clipping of aneurysm.

Question 11:
How does one decide between surgical clipping and endovascular coiling?

Answer:
The factors taken into consideration for deciding the mode of treatment are age, general condition, location, size of aneurysm, whether wide-necked aneurysm, perforators originating from wall, coexisting hematoma, large blood load, etc.

For an aneurysm that is technically equally amenable to surgical clipping and endovascular coiling, latter is preferred. Patients having large intraparenchymal hematomas and MCA aneurysms are preferred candidates for surgical clipping. Ruptured aneurysms in elderly patients (>70 years), poor-grade patients (WFNS IV/V), and aneurysms of basilar apex are chosen for endovascular coiling [1].

Balloon remodeling and intracranial stenting are the endovascular techniques used to assist coiling in wide-necked aneurysms. The role of flow divertors in unruptured aneurysms is quite established but now it is also being used in carefully selected set of patients having aneurysmal SAH.

Question 12:
How will you evaluate the patient before surgery?

Answer:
Before surgery, the patient has to be evaluated for clinical features, days to ictus, neurological deficits, comorbidities, and SAH grade. Systemic examination tells about the hemodynamic variables and the presence of other non-neurological

complications. Investigations that are required before taking up the patient for surgery include complete hemogram, renal function tests, serum electrolytes, blood sugar, coagulation profile, X-ray chest, and ECG. CT scan should be reviewed for assessing the presence of hydrocephalous, blood load and any hematoma, Fisher grade, or infarct. The location and size of aneurysm and the presence of angiographic vasospasm can be known from the angiographic films.

Question 13:
Will you premedicate this patient?

Answer:
I will not premedicate this patient with any sedatives as he is already drowsy, and administration of such drugs may interfere with neurological examination. I shall order continuation of Tab. nimodipine 60 mg every 4 h and Tab. amlodipine 10 mg OD. H_2-blocker may be given in the morning of surgery.

5.2 Intraoperative

Question 14:
What are your anesthetic goals?

Answer:
1. Strict control of hemodynamics
2. Prevent any fluctuations in ICP
3. Maintain adequate CPP
4. Make the brain slack enough for adequate surgical exposure and safe clipping.
5. Provision of neuroprotection when prolonged temporary clipping time is anticipated
6. Enable neuromonitoring and evoked potential recording
7. Smooth emergence

Question 15:
How should induction of anesthesia be carried out in this patient?

Answer:
In the operating room, we will attach routine monitors like ECG, NIBP, and SpO_2. Direct blood pressure may be transduced from an arterial line secured under local anesthesia. General anesthesia will be induced with 2 μg/kg fentanyl, 2–2.5 mg/kg propofol, and 0.8 mg/kg rocuronium. To blunt the pressor response just before laryngoscopy, an additional small dose of hypnotic agent may be administered. A gentle and quick laryngoscopy is done, and airway is secured with a tracheal tube. Anesthesia can be maintained with oxygen in nitrous oxide or air along with inhalational agent sevoflurane. There is no evidence that nitrous oxide is associated with poor outcome in these patients [20].

Question 16:
How does anesthetic technique affect the aneurysm?

Answer:
The major *concern* during intraoperative care is to prevent aneurysm rupture. Blood pressure variation and levels of arterial carbon dioxide play an important role in maintaining brain homeostasis. TMP is the pressure present across the aneurysmal wall, which if rises, can lead to aneurysm rupture. It is calculated as TMP = MAP − ICP. So, increase in blood pressure will increase the TMP and hence the risk of rupture also rises. On the other hand, CPP has to be maintained around 70 mmHg to prevent ischemia of the brain.

Similarly, any vigorous hyperventilation in good grade patients can lower ICP and lead to increase in TMP, further subjecting the patients to risk of rupture. But, in poor-grade patients, hyperventilation will be required to lower the ICP and to maintain CPP.

Question 17:
What are the monitoring modalities which you can use intraoperatively?

Answer:
Other than *the* standard ASA monitoring like ECG, NIBP, SpO_2, $EtCo_2$, and urine output, we would like to do invasive beat-to-beat blood pressure monitoring by an arterial line. We will also insert a central line 7 F in the right internal jugular vein. Patients might need a BIS/entropy

monitor to titrate the anesthetic agent according to burst suppression ratio (BSR), in case prolonged temporary clipping is required. The use of somatosensory evoked potentials (SSEP) and motor evoked potentials (MEP) monitoring intraoperatively requires modification of the anesthetic technique to TIVA/opiod infusion and omission of muscle relaxants for the maintenance of anesthesia. The other intraoperative neuromonitoring modalities which can be used are near infrared spectroscopy (NIRS) and jugular venous oximetry for assessing the brain oxygenation. Transcranial Doppler (TCD) has also been used intraoperatively to study CBF changes but is logistically difficult. A rapid sampling microdialysis catheter can be used intraoperatively to study the brain metabolism of at-risk area [21].

The surgeon is dissecting around the aneurysm and suddenly rupture occurs.

Question 18:
How will you manage?

Answer:
The treatment of aneurysm rupture is mainly supportive with fluid and blood resuscitation. Adenosine can also be used for the purpose of transient profound hypotension or cardiac arrest in cases of frank intraoperative aneurysm rupture, where the surgeon requires visualization of clear surgical field for clipping of aneurysm. Adenosine 0.3–0.4 mg/kg administered intravenously through a central line or a large vein induces a state of profound hypotension for a period of about 45 s [21]. This can be useful when application of temporary clip is not feasible, as in complex aneurysms or in cases where rupture of aneurysm blinds the surgical field. Adenosine in latter condition, by virtue of its transient but profound hypotensive effect, can reduce the bleeding and enable the surgeon to apply an aneurysm clip successfully. Escalating doses of adenosine (6, 12, 18, 24, and 36 mg) may be given and titrated to achieve approximately 30 s of asystole [23]. Few contraindications for adenosine administration are patients with coronary artery stenosis, atrioventricular (AV) conduction defects (second degree AV block), severe reactive airway disease, and sick sinus syndrome/heart block.

Question 19:
What are the neuroprotective modalities employed during surgery?

Answer:
Agents like thiopental and propofol reduce the cerebral metabolic rate and allow brain to tolerate longer ischemic times during temporary clipping. The hypotension occurs during administration of such agents, and concurrent infusion of vasopressor is needed. However, there is no definite proven role of improvement in the outcome by any pharmacological agent [24]. Hypothermia which has a beneficial effect in global ischemia does not confer much protection during this surgery [25]. The best method is to maintain systemic and brain homeostasis by maintaining normotension, normoxia, normocapnia, normothermia, and normoglycemia.

The surgeon is able to clip the aneurysm. Now, he wants to perform intraoperative videoangiography.

Question 20:
How is it performed?

Answer:
Any residual aneurysm or any parent/perforator occlusion can be checked and corrected on table by means of indocyanine green videoangiography (ICG-VA). A special microscope with an integrated infrared fluorescence module is required to visualize the real-time flow of dye through the cerebral vessels, within seconds after its intravenous administration. An intravenous dose of 0.2–0.5 mg/kg is generally used with a maximum permissible dose of 5 mg/kg/day. Few side effects like anaphylaxis and transient oxygen desaturation may occur rarely.

Question 21:
Will you extubate this patient on OR or ventilate postoperatively?

Answer:
A patient of HH grade III may be extubated in OR depending upon his condition and other intraoperative variables. In view of the intraoperative rupture of the aneurysm, I would like to ventilate this patient in postoperative period.

5.3 Postoperative

The patient is shifted to neurosurgical ICU for postoperative ventilation and extubated on postoperative day (POD) 2. On the 6th POD, the patient becomes drowsy. What can be the possible reasons for change in consciousness?

Change in consciousness can be primarily due to hypotension, hydrocephalous, sodium disturbances, rebleeding, seizures, DCI, or development of an infarct.

Question 22:
What do you mean by terms vasospasm and DCI?

Answer:
The term vasospasm is reserved for angiographic evidence of narrowed cerebral arteries. On the other hand, DCI is defined as the development of neurological deterioration with the presence of focal neurological signs and/or presence of radiographic evidence (CT/magnetic resonance imaging [MRI]) of ischemia [26]. While 70% of SAH patients have angiographic vasoconstriction, only 20–30% develop DCI [27]. It occurs mainly 3–14 days after ictus.

DCI has a multifactorial pathophysiology like cortical spreading depolarization, cerebral vascular dysregulation, microthrombosis, and neuroinflammation. It is associated with significant morbidity and mortality. The patient presents with delayed neurological deterioration and development of new neurological deficits. The therapies targeted to resolve cerebral vasospasm often fail to improve the outcome in these patients. Over the time, now DCI and vasospasm are known to be two separate entities with vasospasm being just one but an important out of the several factors involved in pathogenesis of DCI.

Question 23:
How will you diagnose cerebral vasospasm?

Answer:
Various modalities for diagnosis of cerebral vasospasm are:

Clinical: In neurologically intact patients, serial clinical examinations help to detect any alteration in consciousness or development of any focal neurological deficit that cannot be owed to any other probable cause. However, in poor-grade patients, subtle changes will not be evident early, and other diagnostic modalities become more important.

Digital subtraction angiography: It is considered as gold standard for the diagnosis of narrowing of cerebral vessels. At the same time, it also allows endovascular interventions and intra-arterial administration of various therapeutic agents for reversing vasospasm. CTA is another noninvasive alternative to DSA, which can detect vasospasm with high sensitivity and specificity [28]. Magnetic resonance angiography-time-of-flight sequence is specific for diagnosis of cerebral vasospasm.

TCD ultrasonography: Cerebral vasospasm causes narrowing of blood vessels which lead to an increase in CBF velocity. This can be measured noninvasively by TCD ultrasonography. Normal MCA CBF velocity values are taken as <120 cm/s and velocity >180 cm/s has high positive predictive value [29]. To differentiate hyperemia from vasospasm, Lindegaard index is used which is a ratio of MCA mean CBF velocity and extracranial internal carotid artery mean CBF. Value of 3–6 indicates mild-moderate vasospasm and >6 indicates severe vasospasm [30]. TCD has a sensitivity of 90%, specificity 71%, positive predictive value 57%, and negative predictive value 92% for the diagnosis of vasospasm. TCD evidence of vasospasm is highly accurate for the prediction of DCI [31]. However, it also has many limitations pertaining to anatomical variation, technical challenges, and inability to assess distal vasculature.

Brain perfusion imaging: Various modalities for measuring perfusion are Xenon CT, computed tomographic perfusion, single-photon emission computed tomography, positron emission tomography, MR perfusion-weighted imaging, and Xenon CT. A decrease in regional blood flow or increase in mean transit time (MTT) >5–6.4 s correlates well with DCI [32]. Brain perfusion studies can detect even microcirculatory cerebral vasospasm even when cerebral angiogram depicts no apparent visible narrowing.

Electroencephalography: Reduction in alpha/delta ratio or alpha variability is sensitive and

specific for predicting DCI before the onset of symptoms [33]. Subcortical electrocorticography and intracranial EEG may detect changes even earlier than scalp EEG [34].

Other neuromonitoring: NIRS is a noninvasive means to detect cortical oxygen desaturation as may occur during cerebral vasospasm. It can alert the physician to carry out other more sensitive and specific tests for the detection of vasospasm.

Jugular venous oximetry: It is one of the invasive methods to detect cerebral ischemia (value <55%), but is less sensitive to detect vasospasm as it provides us with more of a global value rather than regional values.

Cerebral microdialysis: The microdialysis catheter placed in the parent vessel territory of ruptured aneurysm or within the watershed area is able to sample the interstitial metabolic milieu. Increase in values of lactate: pyruvate ratio >40 and decrease in glucose levels have occurred, hours before DCI onset [35]. The trend monitoring may provide information about a window period during which therapeutic interventions may be applied to improve the outcome.

Question 24:
Discuss the management of DCI.

Answer:
Prevention, early detection, and management are important for improving the outcome of these patients. Nimodipine is the only drug which has been found to be associated with better outcome in aneurysmal SAH patients despite having no role in improving the angiographic vasospasm [36]. It is prescribed as 60 mg orally, 4 h for 21 days. A phase 3 clinical trial has been planned to assess the safety and efficacy of intraventricular EG-1962 (extended-release microparticle formulation of nimodipine) to standard oral nimodipine in improving the neurological outcome of these patients [37].

Several other interventions like clazosentan [38], erythropoietin [39], magnesium [40], statins [41], prophylactic angioplasty [42], prophylactic hypervolemia, and prophylactic hypertension [43] have been tried for cerebral vasospasm or DCI prevention, but with no beneficial role in improving the outcome. Prophylactic hypervolemia is associated with additional cost and complications while having no beneficial effect on reducing vasospasm or DCI. Maintenance of euvolemia and normal serum sodium levels may help in the prevention of DCI [44]. Even use of cisternal irrigation with saline at the time of open surgery to clear away blood and its breakdown products has no proven evidence in improving outcome. Intraoperative cisternal/ventricular instillation of tissue plasminogen activator and lumbar drainage of CSF to enhance the clearance of blood and its breakdown products have also been found not to improve neurologic outcome [45, 46].

For the treatment-delayed cerebral ischemia, a three-stage algorithm has been suggested [47]. For the new-onset DCI, the first step suggested is induced hypertension with target SBP of 160–220 mmHg, along with the maintenance of euvolemia. This was based on the evidence that hypertension was the most important out of triple "H" therapy and thus hypervolemia and hemodilution fell out of favor. The AHA guidelines recommend induced hypertension for the treatment of DCI, provided cardiac status permits it [1]. However, results from a premature halted HIMALAIA trial due to slow recruitment does not add to any evidence to support induced hypertension [48]. From a recent retrospective study involving 1647 patients, hypertension induction in patients having clinical signs of DCI reduced the development of cerebral infarcts and poor clinical outcome [49].

The next step is the rescue therapy—tier 1 and 2. Tier 1 therapy includes endovascular therapy for medically refractory cases. This can be performed by mechanical angioplasty or intra-arterial infusion of vasodilators. Proximal vasospastic vessels can be dilated by angioplasty, but pharmacological angioplasty is effective for distal vasculature also. Various agents used for this purpose are nimodipine, nicardipine, verapamil, milrinone, papaverine, and fasudil. The consequent hypotension secondary to these agents needs to be taken care of. Milrinone, a phosphodiesterase inhibitor, is used for intra-arterial administration at dose of 8 mg over 30 min with a maximum dose of 24 mg [50]. The intravenous dose is 1 μg/kg/min given usually for 5–7 days and then gradually tapered. The continuous intravenous infusion has been found to be as efficient as combined

intra-arterial + intravenous infusion and has been suggested as first easy-to-use option [51]. Though it improves the vasospasm, its beneficial effect in improving outcome is uncertain due to the variability in dosing and route of administration [52].

The other tier 1 rescue therapy includes cardiac output optimization (Cardiac index >4.0 L/min/m^2) and maintenance of hemoglobin above 8–10 g/dL, with higher levels appropriate for patients having DCI [53]. The tier 2 therapy includes use of therapeutic hypothermia, administration of intrathecal vasodilators, use of hypertonic saline in raised ICP cases and experimental use of aortic flow diversion and intra-aortic balloon pump with no evidence to prove their actual utility.

Vasospasm and DCI are much beyond just the large vessel narrowing with multiple parallel pathogenic arms. Therapies to target it at multiple levels might be of some help.

Multiple Choice Questions

1. Which one of these is a Class I, level A recommendation?
   (a) Hypertension should be treated, and such treatment may reduce the risk of DCI.
   (b) Oral nimodipine should be administered to all patients with aSAH.
   (c) Complete obliteration of the aneurysm is recommended whenever possible.
   (d) Maintenance of euvolemia and normal circulating blood volume is recommended to prevent DCI.
   Answer: b
2. Risk of cerebral vasospasm is highest in patients of which grade?
   (a) Modified Fisher grade 4
   (b) Modified Fisher grade 3
   (c) Fisher grade 4
   (d) Hunt and Hess grade 2
   Answer: a
3. Intraoperative bolus of adenosine may be used for the purpose of all except:
   (a) Flow arrest during clipping
   (b) Aneurysm rupture
   (c) Neuroprotection
   (d) Paroxysmal supraventricular tachycardia
   Answer: c
4. The present modalities for managing delayed cerebral vasospasm are all except:
   (a) Nimodipine
   (b) "Triple H" therapy
   (c) Hypertension
   (d) Intravenous milrinone
   Answer: b
5. Lindegaard ratio less than 3 indicates:
   (a) Mild vasospasm
   (b) Moderate vasospasm
   (c) Severe vasospasm
   (d) Hyperemia
   Answer: d

References

1. Connoly ES Jr, Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida R, et al. Guidelines for the management of aneurysmal subarachnoid haemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012;43:1711–37.
2. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. J Neurosurg. 1968;28:14.
3. Hunt WE, Kosnik EJ. Timing and perioperative care in intracranial aneurysm surgery. Clin Neurosurg. 1974;21:79.
4. Report of World Federation of Neurological Surgeons Committee on a universal Subarachnoid Hemorrhage Grading Scale. J Neurosurg. 1988;68:985.
5. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualised by computed tomographic scanning. Neurosurgery. 1980;6:1.
6. Frontera JA, Claassen J, Schmidt JM, Wartenberg KE, Temes R, Connolly ES Jr, et al. Prediction of symptomatic vasospasm after subarachnoid haemorrhage: the modified fisher scale. Neurosurgery. 2006;59:21–7.
7. Dupont SA, Wijdicks EF, Manno EM, Lanzino G, Rabinstein AA. Prediction of angiographic vasospasm after aneurysmal subarachnoid hemorrhage: value of the Hijdra sum scoring system. Neurocrit Care. 2009;11:172–6.
8. Claassen J, Bernardini GL, Kreiter K, Bates J, Du YE, Copeland D, et al. Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid haemorrhage: the Fisher scale revisited. Stroke. 2001;32:2012.
9. Van der Steen WE, Leemans EL, van den Berg R, et al. Radiological scales predicting delayed cerebral ischemia in subarachnoid hemorrhage: systemic review and meta-analysis. Neuroradiology. 2019;61(3):247–56. https://doi.org/10.1007/s00234-019-02161-9.

10. Ohkuma H, Tsurutani H, Suzuki S. Incidence and significance of early aneurysmal rebleeding before neuro-surgical or neurological management. Stroke. 2001;32:1176–80.
11. Schmidt JM, Ko SB, Helbok R, Kurtz P, Stuart RM, Presciutti M. Cerebral perfusion pressure thresholds for brain tissue hypoxia and metabolic crisis and poor grade subarachnoid haemorrhage. Stroke. 2011;42:1351–6.
12. Ibrahim GM, Fallah A, Macdonald RL. Clinical, laboratory and radiographic predictors of the occurrence of seizures following aneurysmal subarachnoid haemorrhage. J Neurosurg. 2013;119:347–52.
13. Raper DM, Starke RM, Komotar RJ, Allan R, Connollly ES. Seizures after aneurysmal subarachnoid haemorrhage: a systematic review of outcomes. World Neurosurg. 2013;79:682–90.
14. Suehiro E, Sadahiro H, Goto H, Oku F, Oka Y, Fujiyama Y, et al. Importance of early postoperative body temperature management for treatment of subarachnoid haemorrhage. J Stroke Cerebrovasc Dis. 2016;25:1482–8.
15. Zhang G, Zhang JH, Qin X. Fever increased in-hospital mortality after sub-arachnoid haemorrhage. Acta Neurochir Suppl. 2011;110:239–43.
16. Kurtz P, Helbok R, Claassen J, et al. The effect of packed red blood cell transfusion on cerebral oxygenation and metabolism after subarachnoid hemorrhage. Neurocrit Care. 2016;24:118–21.
17. Mutoh T, Kazumata K, Terasaka S, Taki Y, Suzuki A, Ishikawa T. Early intensive versus minimally invasive approach to postoperative hemodynamic management after subarachnoid hemorrhage. Stroke. 2014;45:1280–4.
18. Davison DL, Terek M, Chawla LS. Neurogenic pulmonary edema. Crit Care. 2012;16:212.
19. Kassell NF, Torner JC, Jane JA, Haley EC, Adams HP. The international cooperative study on the timing of aneurysm surgery. Part 2: surgical results. J Neurosurg. 1990;73:37–47.
20. Pasternak JJ, McGregor DG, Lanier WL, Schroeder DR, Rusy DA, Hindman B, Clarke W, Torner J, Todd MM, IHAST Investigators. Effect of nitrous oxide use on long-term neurologic and neuropsychological outcome in patients who received temporary proximal artery occlusion during cerebral aneurysm clipping surgery. Anesthesiology. 2009;110:563–73.
21. Bhatia R, Hashemi P, Razzaq A, Parkin MC, Hopwood SE, Boutelle MG, Strong AJ. Application of rapid-sampling, online microdialysis to the monitoring of brain metabolism during aneurysm surgery. Neurosurgery. 2006;58(4 Suppl 2):ONS-313-20; discussion ONS-321.
22. Bebawy JF, Gupta DK, Bendok BR, Hemmer LB, Zeeni C, Avram MJ, et al. Adenosine-induced flow arrest to facilitate intracranial aneurysm clip ligation: dose-response data and safety profile. Anesth Analg. 2010;110:1406–11.
23. Powers CJ, Wright DR, McDonagh DL, Borel CO, Zomorodi AR, Britz GW. Transient adenosine-induced asystole during the surgical treatment of anterior circulation cerebral aneurysms: technical note. Neurosurgery. 2010;67(2 Suppl Operative):461–70.
24. Hindman BJ, Bayman EO, Pfisterer WK, Torner JC, Todd MM. No association between intraoperative hypothermia or supplemental protective drug and neurologic outcomes in patients undergoing temporary clipping during cerebral aneurysm surgery. Anesthesiology. 2010;112:86–101.
25. Todd MM, Hindman BJ, Clarke WR, Torner JC, Intraoperative Hypothermia For Aneurysm Surgery Trial (IHAST) Investigators. Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med. 2005;352:135–45.
26. Vergouwen MD, Vermeulen M, van Gijn J, Rinkel GJ, Wijdicks EF, Muizelaar JP, et al. Definition of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage as an outcome event in clinical trials and observational studies: proposal of a multidisciplinary research group. Stroke. 2010;41:2391–5.
27. Millikan CH. Cerebral vasospasm and ruptured intracranial aneurysm. Arch Neurol. 1975;32:433–49.
28. Wilson CD, Jai J, Shankar S. Diagnosing vasospasm after subarachnoid hemorrhage: CTA and CTP. Can J Neurol Sci. 2014;41:314–9.
29. Miller C, Armonda R, Participants in the International Multi-Disciplinary Consensus Conference on Multimodality Monitoring. Monitoring of cerebral blood flow and ischemia in the critically ill. Neurocrit Care. 2014;21(S2):121–8.
30. Lindegaard KF, Nornes H, Bakke SJ, Sorteberg W, Nakstad P. Cerebral vasospasm diagnosis by means of angiography and blood velocity measurements. Acta Neurochir (Wien). 1989;100:12–24.
31. Kumar G, Shahripour RB, Harrigan MR. Vasospasm on transcranial Doppler is predictive of delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. J Neurosurg. 2016;124:1257–64.
32. Mir DIA, Gupta A, Dunning A, Puchi L, Robinson CL, Epstein HBAB, Sanelli PC. CT perfusion for detection of delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. AJNR Am J Neuroradiol. 2014;35:866–71.
33. Rots ML, van Putten MJAM, Hoedemaekers CWE, Horn J. Continuous EEG monitoring for early detection of delayed cerebral ischemia in subarachnoid hemorrhage: a pilot study. Neurocrit Care. 2016;24:207–16.
34. Stuart RM, Waziri A, Weintraub D, Schmidt MJ, Fernandez L, Helbok R, Kurtz P, Lee K, Badjatia N, Emerson R, Mayer SA, Connolly ES, Hirsch LJ, Claassen J. Intracortical EEG for the detection of vasospasm in patients with poor-grade subarachnoid hemorrhage. Neurocrit Care. 2010;13:355–8.
35. Patet C, Quintard H, Zerlauth JB, Maibach T, Carteron L, Suys T, et al. Bedside cerebral microdialysis monitoring of delayed cerebral hypoperfusion in comatose patients with poor grade aneurysmal subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry. 2017;88:332–8.

36. Allen GS, Ahn HS, Preziosi TJ, Battye R, Boone SC, Chou SN, et al. Cerebral arterial spasm—a controlled trial of nimodipine in patients with subarachnoid haemorrhage. N Engl J Med. 1983;308:619–24.
37. Hanggi D, Etminan N, Mayer SA, Aldrich EF, Diringer MN, Schmutzhard E, NEWTON investigators. Clinical Trial Protocol: Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Efficacy, and Safety Study Comparing EG-1962 to Standard of Care Oral Nimodipine in Adults with Aneurysmal Subarachnoid Hemorrhage [NEWTON-2 (Nimodipine Microparticles to Enhance Recovery While Reducing Toxicity After Subarachnoid Hemorrhage)]. Neurocrit Care. 2019;30:88–97.
38. MacDonald RL, Higashida RT, Keller E, et al. Randomized trial of clazosentan in patients with aneurysmal subarachnoid hemorrhage: a randomized controlled trial. Stroke. 2005;36:1011–5.
39. Tseng MY, Hutchinson PJ, Richards HK, Czosynka M, Pickard JD, Erber WN, Brown S, Kirkpatrick PJ. Acute systemic erythropoietin therapy to reduce delayed ischemic deficits following aneurysmal subarachnoid hemorrhage: a Phase II randomized, double-blind, placebo-controlled trial: clinical article. J Neurosurg. 2009;111:171–80.
40. Mees SMD, Rinkel GJE, Vandertop WP, Pablo AA, Lavados M, van Kooten F, Kuijsten HAJM, Boiten J, van Oostenbrugge RJ, Salman RA-S, van den Bergh WM. Magnesium for aneurysmal subarachnoid haemorrhage (MASH-2): a randomised placebo-controlled trial. Lancet. 2012;380:44–9.
41. Kirkpatrick PJ, Turner CL, Smith C, Hutchinson PJ, Murray GD, STASH Collaborators. Simvastatin in aneurysmal subarachnoid haemorrhage (STASH): a multicentre randomised phase 3 trial. Lancet Neurol. 2014;13:666–75.
42. Zwienenberg-Lee M, Hartman J, Rudisill N, Madden LK, Smith K, Eskridge J, Newell D, Verweij B, Bullock MR, Baker A, Coplin W, Mericle R, Dai J, Rocke D, Muizelaar JP, Balloon Prophylaxis for Aneurysmal Vasospasm (BPAV) Study Group. Effect of prophylactic transluminal balloon angioplasty on cerebral vasospasm and outcome in patients with Fisher grade III subarachnoid hemorrhage: results of a phase II multicenter, randomized, clinical trial. Stroke. 2008;39:1759–65.
43. Wolf S, Participants in the International Multi-Disciplinary Consensus Conference on the Critical Care Management of Subarachnoid Hemorrhage. Routine management of volume status after aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2011;15:275–80.
44. Lennihan L, Mayer SA, Fink ME, Beckford A, Paik MC, Zhang H, Wu YC, Klebanoff LM, Raps EC, Solomon RA. Effect of hypervolemic therapy on cerebral blood flow after subarachnoid hemorrhage: a randomized controlled trial. Stroke. 2000;31:383–91.
45. Kramer AH, Roberts DJ, Holodinsky J, Todd S, Hill MD, Zygun DA, Faris P, Wong JH. Intraventricular tissue plasminogen activator in subarachnoid hemorrhage patients: a prospective, randomized, placebo-controlled pilot trial. Neurocrit Care. 2014;21:275–84.
46. Al-Tamimi YZ, Bhargava D, Feltbower RG, et al. Lumbar drainage of cerebrospinal fluid after aneurysmal subarachnoid hemorrhage: a prospective, randomized, controlled trial (LUMAS). Stroke. 2012;43:677–82.
47. Francoeur C, Mayer SA. Management of delayed cerebral ischemia after subarachnoid haemorrhage. Crit Care. 2016;20:277–89.
48. Gathier CS, van den Bergh WM, van der Jagt M, et al; HIMALAIA Study Group. Induced Hypertension for delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage: A randomized clinical trial. Stroke. 2018;49:76–83.
49. Haegens NM, Gathier CS, Horn J, Coert BA, Verbaan D, van den Bergh WM. Induced hypertension in preventing cerebral infarction in delayed cerebral ischemia after subarachnoid hemorrhage. Stroke. 2018;49:2630–6.
50. Fraticelli AT, Cholley BP, Losser MR, Saint Maurice JP, Payen D. Milrinone for the treatment of cerebral vasospasm after aneurysmal subarachnoid hemorrhage. Stroke. 2008;39:893–8.
51. Crespy T, Heintzelmann M, Chiron C, Vinclair M, Tahon F, Francony G, Payen JF, et al. Which protocol for milrinone to treat cerebral vasospasm associated with subarachnoid hemorrhage? J Neurosurg Anesthesiol. 2019;31(3):323–9. https://doi.org/10.1097/ANA.0000000000000527.
52. Lannes M, Zeiler F, Guichon C, Teitelbaum J. The use of milrinone in patients with delayed cerebral ischemia following subarachnoid hemorrhage: a systematic review. Can J Neurol Sci. 2017;44:152–60.
53. Diringer MN, Bleck TP, Claude Hemphil J, Menon D, Shutter L, Vespa P, Bruder N, Connolly ES, Citerio G, Gress D, Hanggi D, et al. Critical care management of patients following aneurysmal subarachnoid haemorrhage: recommendations from the neurocritical Care Society's Multidisciplinary Consensus Conference. Neurocrit Care. 2011;15:211–40.

6 Management of Patient with Cervical Spine Injury

Daniel Van Leuven and Ehab Farag

Stem Case Terminology

A 49-year old male with no significant medical history presented with a myelopathy secondary to a large extended C5–C6 disc herniation with compression of the spinal cord. The patient was classified as grade 2 on the Narick's functional scale. The patient was scheduled for a single-level discectomy, decompression, reconstruction, and stabilization. Due to motor weakness, pain in the upper and lower limbs with neck movement, and examination of the patient's magnetic resonance imaging (MRI), the decision was made to safely secure the patient's airway with an awake fiber-optic intubation (FOI). After being premedicated with 2 mg of midazolam and 0.2 mg of glycopyrrolate, the upper airway was anesthetized using nebulized 4% lidocaine, and the patient was intubated smoothly.

After a neurological examination, while the patient was still awake and confirming that there were no changes from baseline, anesthesia was induced with 200 mg of propofol and 50 μg of fentanyl. The anesthesia was maintained using isoflurane (end-tidal concentration 0.5%) and remifentanil infusion (0.05–0.2 μg/kg/min). No muscle relaxants were used to allow for motor-evoked potentials (MEPs) to be monitored. The blood pressure (BP) was kept tightly controlled within 10% of preoperative value during the whole procedure.

After induction of anesthesia, neurophysiologic monitoring was instituted, during that period the head was kept in neutral position with almost no movement. Intraoperative neurophysiologic monitoring (IONM) revealed no lower extremity transcranial electrical motor-evoked potentials (tceMEPs) despite increasing the stimulating voltage while those from upper extremities as well as somatosensory-evoked potential (SSEP) from both upper and lower extremities were intact.

In spite of this disturbing finding, the whole team (surgeon, anesthesiologist, and neurophysiologist) decided to proceed and not to wake up the patient to perform the wake-up test. The decision was based on the fact that the patient had unchanged motor strength in his lower extremities after an awake intubation, the head was kept in neutral position and unmoved after induction anesthesia, and the planned surgery would be anterior cervical approach requiring minimal or no neck movement. Surgery was completed uneventfully. The patient's postoperative neurologic examination after extubation revealed no difference from the baseline examination.

D. Van Leuven · E. Farag (✉)
Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA

Department of General Anesthesia, Anesthesiology Institute, Cleveland Clinic, Cleveland, OH, USA

Department of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, Cleveland, OH, USA
e-mail: FARAGE@ccf.org

© Springer Nature Singapore Pte Ltd. 2020
H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_6

6.1 Preoperative

Question 1:
What would be an appropriate preoperative examination for a patient with cervical myelopathy?

Answer:
A thorough history and physical, including a neurological, examination are important factors for avoiding major complications associated with surgical correction of a patient with cervical myelopathy. A high incidence of this patient population has associated cardiac, pulmonary, and rheumatological conditions that could have an effect on the anesthetic plan. Also, review of relevant images will help ascertain the extent of any spinal cord compression. Assessing the patient's oropharynx, neck mobility, and associated neurological symptoms may be appropriate to help determine if an awake FOI is needed. If so, a detailed discussion regarding an awake intubation should be done to confirm their ability to cooperate for the procedure [1].

Question 2:
Describe the occipitoatlantoaxial unit and what constitutes spinal cord compression?

Answer:
The occipitoatlantoaxial unit is one of the most complex and vital structures of the body. It supports the head and provides essential range of motion and protection of the spinal cord. It consists of the first cervical vertebra (C1), or the atlas, which articulates with the occipital condyles of the skull via two large depressions on its anterior surface. The weight of the skull is transferred to the second cervical vertebra (C2) which is characterized by a prominent odontoid process (dens) from its body. The space at C1 between the posterior aspect of the odontoid process and the anterior aspect of the posterior ring of the atlas provides space for the spinal cord. In a normal spinal column, approximately 20 mm^2 is available for passage of the cord. Spinal cord compression begins to occur when the space is less than 14 mm^2 [2].

6.2 Intraoperative

Question 3:
Describe the movement of the cervical spine during direct laryngoscopy (DL)?

Answer:
The primary force applied by the laryngoscopist is an upward lift. This force can be as high as 50–70 N (40 N is enough to lift 10 lbs). Greater force is used in difficult laryngoscopies. The result is the extension of the occiput on C_1, combined with flexion at the lower vertebrae (the fulcrum is probably at C7–T1). A Mac 3 blade results in near-maximal extension at the occiput and C1 (with the posterior arch of C1 touching the skull) and flexion below C2–C3. There are only minimal differences with the use of either straight or curved blades [3].

Question 4:
What is the best way to secure the upper airway in a patient with cervical myelopathy?

Answer:
Awake FOI is the best way for intubation in the patient with cervical myelopathy for the following reasons:

(a) FOI produces the least amount of cervical vertebral motion during intubation.
(b) Awake intubation maintains the protective stabilizing effect of neck muscles during intubation.
(c) Awake intubation allows for a neurological assessment before induction of anesthesia [4, 5].

Question 5:
What is the safest way for positioning a patient with cervical myelopathy in the prone position for posterior cervical laminectomy with instrumentation?

Answer:
Awake FOI is followed by baseline neurologic assessment, then under light sedation and analgesia, Mayfield head frame is applied unto the

patient's head under local anesthesia. After the awake patient is positioned in the surgical position, the patient's neurologic status will be examined before induction of anesthesia [6].

Question 6:
Is Manual-Inline Stabilization (MILS) safe during intubation in patients with cervical myelopathy?

Answer:
It was found in a recent study that in the presence of cervical instability, impaired glottic visualization and marked increases in pressure application with MILS have the potential to increase pathologic craniocervical motion [7].

Question 7:
Is LMA and ILMA safe for managing the upper airway in patients with cervical myelopathy?

Answer:
Keller et al. [8] concluded that LMA devices exert high pressure against the upper cervical vertebrae during insertion and during inflation while in situ. These pressures could produce posterior displacement of the upper C spine.

Question 8:
Does a Glidescope produce less movement of the cervical spine when compared with DL?

Answer:
Glidescope produced better glottic visualization, but did not significantly decrease the movement of the nonpathologic cervical spine when compared with DL [9].

Question 9:
What are SSEPs and the most common sites of stimulation?

Answer:
SSEPs are cortical or subcortical responses to repetitive electrical stimulation of a mixed peripheral nerve. The posterior column spinal pathways are the primary mediation for SSEPs. The typical stimulation sites include the posterior tibial nerve (ankle), the peroneal nerve (fibular nerve), and the ulnar or median nerves (wrist). The ulnar nerve is the preferred stimulation site for the upper extremity SSEPs because the lower spinal nerve entry between C7 and T1 permits assessment of the entire cervical neural axis [10].

Question 10:
What parameters are measured during SSEPs and what constitutes a significant change from baseline?

Answer:
SSEPs are measured in regard to the signal amplitude (power) and latency (velocity), which are recorded continuously and compared to baseline. Of the two, amplitude is more relevant at detecting spinal cord injury. However, changes in latency are quite common although less significant. Criteria for surgeon notification vary from center to center but generally include an intraoperative unilateral or bilateral amplitude loss of at least 50–60% [11].

Question 11:
What are MEPs?

Answer:
MEPs are neuroelectric signals elicited by the stimulation of the motor cortex via a high-voltage transcranial electrical stimulus. These signals travel down the descending motor pathways which include the corticospinal tract, spinal cord interneurons, anterior horn cells, peripheral nerves, and skeletal muscles inverted by alpha motor neurons. MEPs can be recorded directly either from the spinal cord or from the muscle. Due to the less invasive nature and convenience, it is preferable to record myogenic motor responses (CMAPs) from upper and lower extremity peripheral muscles.

A change in amplitude of >75% from baseline is indicative of spinal cord injury [12].

Question 12:
What are the effects of anesthetics on neurophysiologic signals?

Answer:
In general, all inhalation agents including N_2O produce a dose-related increase in latency and reduction in amplitude of the SSEP and tceMEP. Although neuromuscular relaxants have no adverse effect on SSEPs, neuromuscular blockade will compromise tceMEP and electromyography (EMG) recordings [13].

Question 13:
How can you monitor a specific nerve root?

Answer:
SSEPs are neither sensitive nor specific for the identification of injury to a specific nerve root because of their multiple nerve root mediation. Electromyographic techniques overcame this limitation and can be classified into two categories based on the method of elicitation—mechanical and electrical. Mechanically elicited EMG, also called spontaneous EMG, is useful for dynamic pulses of surgery (e.g., implant placement, nerve root manipulation). Electrically elicited EMG may be useful during static phases of surgery (e.g., testing pedicle screws after placement) [14].

6.3 Postoperative

Question 14:
What is the most common neurological complication from anterior cervical spine surgery?

Answer:
The recurrent laryngeal nerve is the most common nerve injured during anterior cervical spine surgery which is characterized as new onset hoarseness or dysphonia. The etiology of the injury could be from direct damage to the nerve during the neck dissection or from compression from the endotracheal balloon. Prior studies have shown a decrease in recurrent laryngeal nerve injuries after deflation of the cuff and reinflating after retractor blade placement [15].

Question 15:
What are other complications associated with anterior cervical spinal surgery?

Answer:
Dysphagia, postoperative hematoma, dural puncture, esophageal perforation, and worsening of the preexisting myelopathy are complications that can be seen in the postoperative period. Out of all these, postoperative hematoma is a life-threatening condition that needs to be immediately identified and evacuated in order to avoid airway collapse [16].

Multiple Choice Questions

1. All of the following are associated with cervical instability EXCEPT:
   (a) Klippel-Feil syndrome
   (b) Achondroplastic dwarfism
   (c) Rheumatoid arthritis
   (d) Trisomy 21
   Answer: a
   Contrary to other choices, patients with Klippel-Feil syndrome exhibit inflexibility rather than cervical instability. Klippel-Feil syndrome is characterized by congenital fusion of the cervical vertebrae.
2. Which of the following ligaments is MOST important for preventing anterior displacement of the atlas with respect to the axis?
   (a) Atlantooccipital ligament
   (b) Alar ligaments
   (c) Transverse ligament of the atlas
   (d) Accessory atlantoaxial ligament
   Answer: c
   The transverse ligament spans across the inner ring of the atlas (C1) and lies immediately posterior to and against the superiorly projecting odontoid process of the axis (C2), preventing the atlas from moving anterior in relation to the axis. Laxity of this ligament in disease such as rheumatoid arthritis and trisomy 21 can result in atlantoaxial instability requiring special care to be taken to avoid excessive force when managing the airway.
3. What determines spinal cord perfusion?
   (a) Systolic BP: cerebrospinal fluid pressure
   (b) Mean arterial BP: cerebrospinal fluid pressure

(c) Diastolic BP: cerebrospinal fluid pressure
(d) Diastolic BP only

Answer: b

Spinal cord perfusion pressure is the difference between mean arterial pressure (MAP) and cerebrospinal fluid pressure. If perfusion pressure is not maintained, cord ischemia may result. Hence, MAP is closely monitored and managed throughout spinal cord surgery. A minimum MAP of around 85 mmHg is usually chosen at the beginning of the case, used throughout and even sometimes in the postoperative period.

4. What neurological pathway is monitored with MEPs?
   (a) Spinocerebellar tract
   (b) Posterior columns and medial lemniscus
   (c) Spinothalamic tract
   (d) Corticospinal tracts

   Answer: d

   Primary motor neurologic transmission is conducted via the anterior and lateral corticospinal tracts. The other choices are involved in carrying sensory information.

5. What is MOST likely to be preserved with anterior spinal artery syndrome in the following?
   (a) Muscle strength
   (b) Proprioception
   (c) Pain sensation
   (d) Temperature

   Answer: b

   The anterior spinal artery supplies the anterior two thirds of the spinal cord. Anterior spinal artery syndrome can result from retractor placement or hypotension. Motor weakness is the most characteristic manifestation, but injury to the spinothalamic tracts can result in loss of pain and temperature sensation as well. Proprioception is preserved because it is relayed through the posterior columns [6].

6. Which is least likely to affect SSEP amplitudes in the following?
   (a) Ketamine
   (b) Nitrous oxide
   (c) Propofol
   (d) Isoflurane

   Answer: c

   Propofol is least likely to affect intraoperative evoked potential monitoring. Inhaled agents including nitrous oxide decrease SSEP amplitudes, whereas ketamine and etomidate increase SSEP amplitudes.

References

Question 1

1. Kim KA, Wang MY. Anesthetic considerations in the treatment of cervical myelopathy. Spine J. 2006;6:207–2011.

Question 2

2. Farag E. Airway management for the cervical spine surgery. Best Pract Res Clin Anaesthesiol. 2016;30:13–25.

Question 3

3. Sahin A, Salman MA, Erden IA, Aypar U. Upper cervical vertebrae movement during intubating laryngeal mask, fibreoptic and direct laryngoscopy: a video-fluoroscopic study. Eur J Anaesthesiol. 2004;21(10):819–23.

Question 4

4. Farag E. Airway management for the cervical spine surgery. Best Pract Res Clin Anaesthesiol. 2016;30:13–25.
5. Sahin A, Salman MA, Erden IA, Aypar U. Upper cervical vertebrae movement during intubating laryngeal mask, fibreoptic and direct laryngoscopy: a video-fluoroscopic study. Eur J Anaesthesiol. 2004;21(10):819–23.

Question 5

6. Farag E. Airway management for the cervical spine surgery. Best Pract Res Clin Anaesthesiol. 2016;30:13–25.

Question 6

7. Santoni BG, Hindman BJ, Puttlitz CM, Weeks JB, Johnson N, Maktabi MA, Todd MM. Manual in-line stabilization increases pressures applied by the laryngoscope blade during direct laryngoscopy and orotracheal intubation. Anesthesiology. 2009;110:24–31.

Question 7

8. Keller C, Brimacombe J, Keller K. Pressures exerted against the cervical vertebrae by the standard and intubating laryngeal mask airways: a randomized, controlled, cross-over study in fresh cadavers. Anesth Analg. 1999;89:1296–300.

Question 8

9. Robitaille A, Williams SR, Tremblay MH, Guilbert F, Thériault M, Drolet P. Cervical spine motion during tracheal intubation with manual in-line stabilization: direct laryngoscopy versus GlideScope videolaryngoscopy. Anesth Analg. 2008;106:935–41.

Question 9

10. Devlin VJ, Schwartz DM. Intraoperative neurophysiologic monitoring during spinal surgery. J Am Acad Orthop Surg. 2007;15:549–60.

Question 10

11. Devlin VJ, Schwartz DM. Intraoperative neurophysiologic monitoring during spinal surgery. J Am Acad Orthop Surg. 2007;15:549–60.

Question 11

12. Devlin VJ, Schwartz DM. Intraoperative neurophysiologic monitoring during spinal surgery. J Am Acad Orthop Surg. 2007;15:549–60.

Question 12

13. Kawaguchi M, Furya H. Intraoperative spinal cord monitoring of motor function with myogenic motor evoked potentials: a consideration in anesthesia. J Anesth. 2004;18:18–24.

Question 13

14. Devlin VJ, Schwartz DM. Intraoperative neurophysiologic monitoring during spinal surgery. J Am Acad Orthop Surg. 2007;15:549–60.

Question 14

15. Kim KA, Wang MY. Anesthetic considerations in the treatment of cervical myelopathy. Spine J. 2006;6:207–2011.

Question 15

16. Tasiou A, et al. Anterior cervical spine surgery-associated complications in a retrospective case-control study. J Spine Surg. 2017;3:444–59.

Suggested Reading

Apfelbaum RI, Kriskovich MD, Haller JR. On the incidence, cause, and prevention of recurrent laryngeal nerve palsies during anterior cervical spine surgery. Spine. 2000;25(22):2906–12.

Farag E. Airway management for the cervical spine surgery. Best Pract Res Clin Anaesthesiol. 2016;30: 13–25.

Keller C, Brimacombe J, Keller K. Pressures exerted against the cervical vertebrae by the standard and intubating laryngeal mask airways: a randomized, controlled, cross-over study in fresh cadavers. Anesth Analg. 1999;89:1296–300.

Kim KA, Wang MY. Anesthetic considerations in the treatment of cervical myelopathy. Spine J. 2006;6:207–2011.

Robitaille A, Williams SR, Tremblay MH, Guilbert F, Thériault M, Drolet P. Cervical spine motion during tracheal intubation with manual in-line stabilization: direct laryngoscopy versus glide scope videolaryngoscopy. Anesth Analg. 2008;106: 935–41.

Ryan M. Central cord syndrome following assault and subsequent resuscitation. Emerg Med (Fremantle). 2003;15(1):89–91.

Sahin A, Salman MA, Erden IA, Aypar U. Upper cervical vertebrae movement during intubating laryngeal mask, fibre optic and direct laryngoscopy: a video-fluoroscopic study. Eur J Anaesthesiol. 2004;21(10):819–23.

Santoni BG, Hindman BJ, Puttlitz CM, Weeks JB, Johnson N, Maktabi MA, Todd MM. Manual in-line stabilization increases pressures applied by the laryngoscope blade during direct laryngoscopy and orotracheal intubation. Anesthesiology. 2009;110:24–31.

Tasiou A, et al. Anterior cervical spine surgery-associated complications in a retrospective case-control study. J Spine Surg. 2017;3:444–59.

Wattermaker I, Concepcion M, Hibberd P, Lipson S. Upper airway obstruction and perioperative management of the airway in patients managed with posterior operations on the cervical spine for rheumatoid arthritis. J Bone Joint Surg Am. 1994;76(3):360–5.

Yan K, Diggan MF. A case of central cord syndrome caused by intubation: a case report. J Spinal Cord Med. 1997;20(2):230–2.

Management of Patient with Craniosynostosis

7

Rajeev Krishnaney-Davison,
Surendrasingh Chhabada, and Pilar Castro

Stem Case Terminology

The patient is a 7-month-old male, 8.4 kg, coming to the operating room after he was diagnosed with scaphocephaly secondary to sagittal synostosis. His mother noticed his head looked "different" with a "prominent forehead" and took him to see his pediatrician who recognized his head as dysmorphic at his 6-month visit. He was referred to a plastic surgeon who ordered a computed tomography (CT) scan and confirmed the diagnosis of isolated sagittal synostosis. He was a full-term baby, born vaginally without any complications. No prior hospitalizations. No significant past medical history; developmentally he is meeting his milestones and is not taking any other medications other than vitamin D. He has not had any prior anesthetic history, and his family denies any issues with anesthesia.

R. Krishnaney-Davison
Cleveland Clinic, Cleveland, OH, USA

S. Chhabada
Cleveland Clinic, Cleveland, OH, USA

Lerner College of Medicine of CWRU,
Cleveland Clinic, Cleveland, OH, USA

Department of outcomes research,
Cleveland Clinic, Cleveland, OH, USA

P. Castro (✉)
Cleveland Clinic, Cleveland, OH, USA

Lerner College of Medicine of CWRU,
Cleveland Clinic, Cleveland, OH, USA
e-mail: Castrop2@ccf.org

Question 1:
What is craniosynostosis? Describe its incidence and the medical implications.

Answer:
Craniosynostosis occurs when the cranial sutures close prematurely. Its incidence is 1 per 2000 births. When this occurs, there is no space for the brain to continue growing which may cause a dysmorphic appearance and intracranial hypertension and ultimately delay the child's cognitive development [1]. It is a congenital defect where most of the time only one suture is affected. The head assumes different shapes depending on which suture is affected [2]. Craniosynostosis presents in 10–40% of cases as part of a syndrome or genetic disorder such as Crouzon or Apert syndrome. When there is synostosis as part of a syndrome, it usually involves more than one suture. These patients usually present with facial dysmorphism as well as limb deformities. Syndromic patients with synostosis of multiple sutures are at higher risk of developing elevated intracranial pressure (ICP).

Regarding the implications for brain development and the potential for intellectual and learning disabilities, children who undergo surgery for craniosynostosis when they are older than a year showed statistically significantly lower intelligence quotient scores compared to those repaired before a year of age [3]. Some studies [4, 5] also suggest that even though children with sagittal

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_7

synostosis corrected before 1 year of age demonstrate normal intelligence quotients (IQs), they may have a higher incidence (50%) of learning disabilities (spelling and reading) compared to a 5% incidence of learning disabilities in the general population.

Bellew and colleagues [3] in a recent article exploring the importance of the timing of surgery suggest that early surgery for sagittal synostosis may result in improved neurodevelopmental outcomes, especially if surgery is performed when patients are <7 months of age. Their results stress the importance of ensuring early diagnosis and prompt referral of patients in whom craniosynostosis is suspected (Figs. 7.1, 7.2, and 7.3).

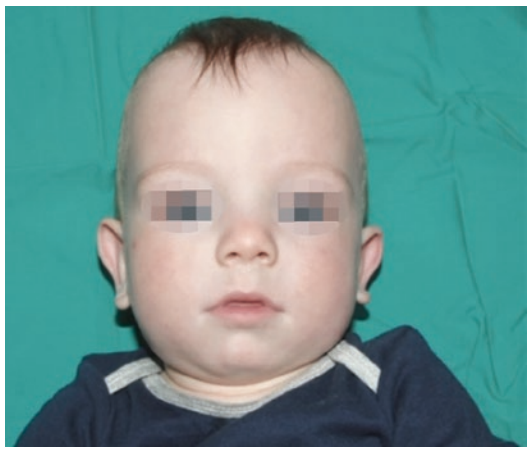


Fig. 7.1 Frontal view, patient with sagittal synostosis

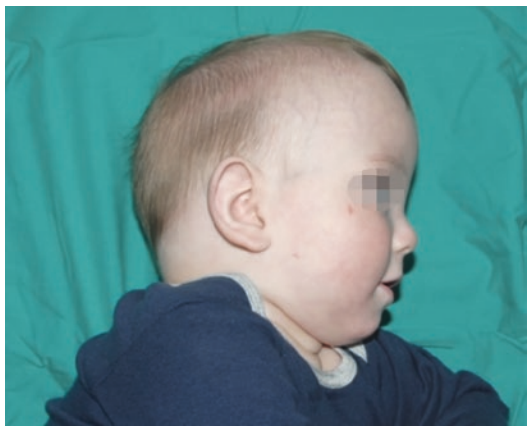


Fig. 7.2 Lateral view, sagittal synostosis, scaphocephaly, long narrow head with frontal bossing

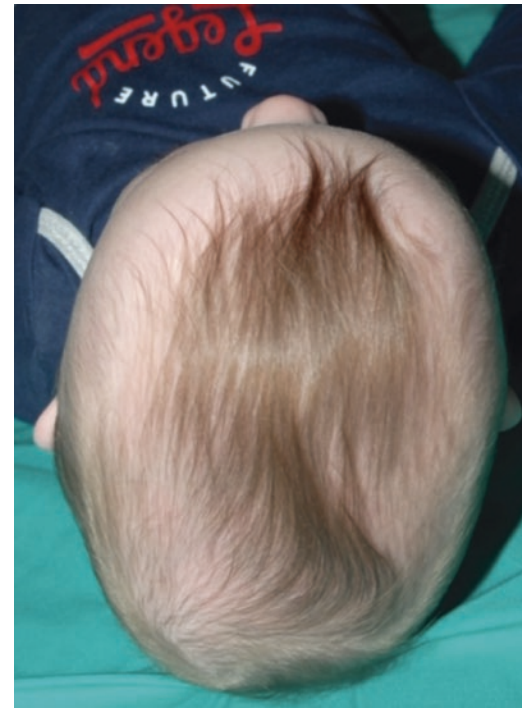


Fig. 7.3 Superior view of patient with sagittal synostosis. (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography. All Rights Reserved)

Question 2:
What are the different types of craniosynostosis?

Answer:
When there is synostosis of a particular suture, there is consequent distortion of the skull shape due to a combination of lack of growth perpendicular to the fused suture, as well as compensatory overgrowth at the non-fused sutures. The most common presentation is when the head may be long and narrow (scaphocephaly, dolichocephaly), followed by triangular at the front (trigonocephaly), broad and flattened (brachycephaly), or skewed (plagiocephaly) (Table 7.1, Fig. 7.4).

Question 3:
What are the most common syndromes associated with craniosynostosis?

Answer:
When cranial deformities exist with facial and extremity deformities, the craniosynostosis is referred to as syndromic, implying a genetic etiol-

Table 7.1 Different types of craniosynostosis defects

Affected suture	Name of defect	Clinical description
Metopic	Trigonocephaly (triangular shaped cranium)	Orbital proptosis, midline ridge, pointed forehead, triangular shape head
Unilateral coronal	Frontal synostotic plagiocephaly (unilateral flat forehead)	Unilateral frontal flattening, anterior position of ear on affected side, nasal root deviated to affected side, prominent brow on unaffected side
Bilateral coronal	Brachycephaly (short cranium)	Orbital hypertelorism, broad, flattened frontal bones, flattened occiput
Sagittal (most common form)	Scaphocephaly (boat-shaped cranium)	Long, narrow forehead, frontal and occipital bossing
Lambdoid	Posterior plagiocephaly (unilateral occipital flattening)	Unilateral occipital flattening, prominent ipsilateral mastoid process

Modified from Surgical treatment of craniosynostosis in infants: open vs closed repair. Erb TO, Meier PM. Surgical treatment of craniosynostosis in infants: open vs closed repair. Curr Opin Anaesthesiol. 2016; 29:345–351

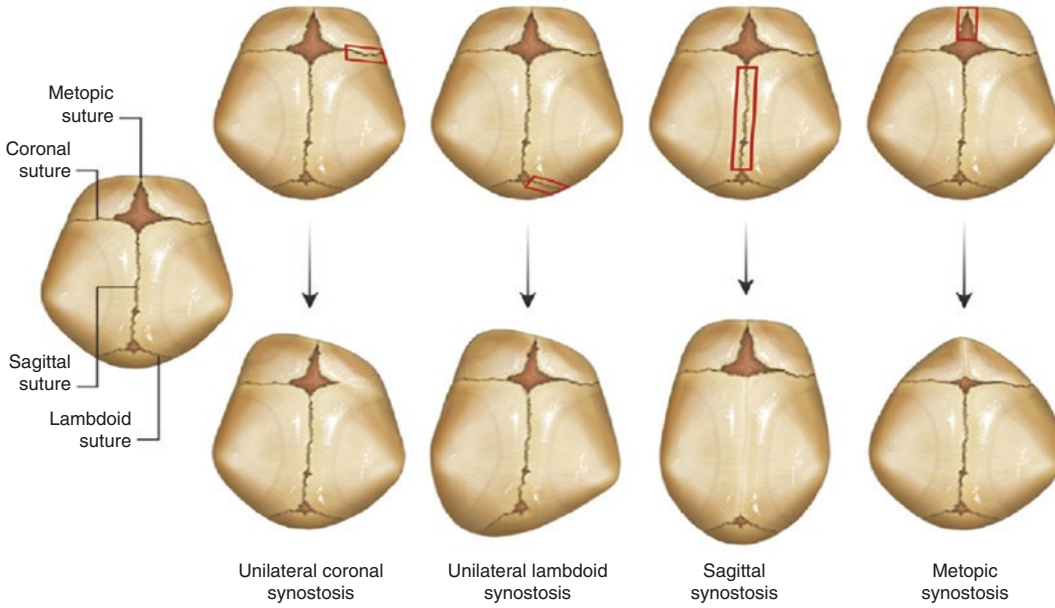


Fig. 7.4 Types of primary craniosynostosis. Reproduced with permission from: Jaskolka MS; Oral Maxillofacial Surg Clin N Am; 29 (2017) 447–463

ogy for the maldevelopment. Syndromic forms typically present in the face, trunk, and extremities and are much less frequent than nonsyndromic types [6]. The incidence of craniosynostosis as a component of a syndrome or genetic disorder is 15–40% of cases [7]. Taking a family history is vital in the preoperative assessment, as the common forms of syndromic craniosynostosis are inherited in an autosomal dominant pattern and include Apert, Crouzon, and Pfeiffer syndromes [6].

A combination of environmental factors and single gene/chromosomal abnormalities can predispose to craniosynostosis. The most commonly associated gene mutations associated with craniosynostosis are FGFR2, FGFR3, TWIST1, and EFNB1 [8]. A heterozygous mutation genotype of FGFR2 is known to cause syndromic craniosynostosis, namely Apert, Crouzon, and Pfeiffer syndromes [8]. Ninety-eight percent of cases of Apert syndrome are caused by missense mutations in the *FGFR2* gene (Ser252Trp or Pro253Arg), and most mutations arise de novo [8]. FGFR3 mutations can cause Muenke syndrome and Crouzon syndrome with acanthosis

nigricans. Saethre-Chotzen syndrome is associated with heterozygous TWIST1 mutations, and craniofrontonasal syndrome is associated with the *EFNB1* gene when there is an X-linked mutation and can occur with males and heterozygous females [8].

Patients with syndromic craniosynostosis are more likely to have multiple suture involvement, which increases the risk of elevated ICP [7]. Ophthalmologic examination is especially important in these patients to assess for signs of increased ICP, for example, papilledema.

Apert, Crouzon, Pfeiffer, and Saethre-Chotzen syndromes are most commonly associated with coronal synostosis. All of these syndromes also include some form of extremity abnormalities and midface hypoplasia (excluding Saethre-Chotzen) [6]. CT scan may reveal Arnold-Chiari syndrome in patients with Crouzon syndrome, and in patients with Apert syndrome, ventriculomegaly due to brain maldevelopment may be seen.

Question 4:
What treatment modalities are there? Endoscopic versus open repair? Advantages and disadvantages.

Answer:
In order to avoid the potential for cognitive impairment, increased ICP and cosmetic consequences, early repair is advocated. Traditional repair involves extensive cranial vault remodeling which can lead to large volumes of blood loss and prolonged intensive care unit (ICU) stays. In the 1990s Barone and Jimenez [9] first described a surgical technique that involved endoscopic assisted repair followed up by postoperative orthotopic molding therapy. This technique is mostly utilized in small infants (younger than 3 months). This is due to the malleability of the cranial bones which allows for the defect to rapidly be corrected and for the craniofacial skeleton to grow normally.

Early reports of endoscopic strip craniectomy (ESC) have shown equally satisfactory cosmetic results compared to open repair [10]; multiple single-center studies have shown that ESC is associated with lower morbidity, mortality, and hospital costs when compared to open cranial vault remodeling [11].

The North American Pediatric Craniofacial Collaborative Group (PCCG) established the Pediatric Craniofacial Surgery Perioperative Registry in 2012 with the aim of evaluating outcomes in children undergoing craniosynostosis repair. The goal of this multicenter study (31 institutions in North America) was to analyze differences in perioperative complications between ESC and open repair in infants undergoing craniosynostosis repair. The cases were collected between June 2012 and September 2015. The variables that the group looked at included: blood utilization, duration of hospitalization, and ICU stay. The study compared unmatched groups (ESC: $N = 310$ vs. open repair: $N = 1071$) and matched groups (ESC: $N = 311$, open repair: $N = 622$); propensity score 2:1 showed significant advantages of EDC compared to open repair. When the matched groups were analyzed, the results showed less utilization of red blood cells (26% vs. 81%, $P < 0.001$) and coagulation (3% vs. 16%, $P < 0.001$) products in the ESC group compared to the open group. Anesthesia duration, surgical duration, ICU stay, and hospital length of stay (LOS) were all significantly lower in the ESC group (all $P < 0.001$) [12]. Interestingly, the incidence of complications such as venous air embolism, hypothermia, and hypotension requiring pressors was equivalent between the two groups.

The same PCCG also analyzed the data for 1223 patients who underwent pediatric complex cranial vault reconstruction surgery (CCVR) during the same time frame [13]. The study showed significant variability in the perioperative management of these patients. The authors reported cardiovascular and respiratory complications, and clinical consequences of large-volume blood loss replacement. The latter is especially relevant for the infant group which experienced more frequent hematologic derangements [13].

7.1 Preoperative

Question 5:
The patient is not a candidate for endoscopic repair and is scheduled for a total cranial vault reconstruction. What preoperative preparation should the patient have? What type of blood work would you order?

Answer:
The care of the patient coming for craniosynostosis surgery requires a multidisciplinary team approach. The anesthesiologist plays an important role in making sure all the important information such as past medical history and anesthetic and surgical history are obtained. A careful discussion with the family to explain the perioperative issues that are common for patients undergoing this procedure is mandatory; there should be time dedicated to addressing any concerns and questions the parents may have.

This patient, as is the case with most patients with nonsyndromic craniosynostosis who are otherwise healthy, does not require any complicated testing [14]. Patients who are syndromic may require further cardiac testing and a careful airway evaluation and planning in case of associated midface defects that may complicate the airway management. Even though it is rare that patients this young exhibit signs of increased ICP, special attention should be paid to any signs such as visual difficulties, nausea, and vomiting [15]. Ophthalmologic examination is important in syndromic patients to look for papilledema.

All patients should have a complete blood cell count (hemoglobin, hematocrit, and platelet count) and a specimen for type and screen ordered; for open procedures, cross-matching of blood is necessary, and the surgery does not start until blood is available in the operating room.

Even for endoscopic procedures, there is potential for unanticipated hemorrhage; having red blood cells available may be warranted especially because these younger patients do not tolerate major blood losses. Coagulation tests are routinely ordered at many centers, (prothrombin time [PT]/international normalized ratio [INR] and partial thromboplastin time [PTT]).

Some centers such as ours have been using erythropoietin (EPO) in the last few years with the idea of increasing the preoperative hematocrit and thus raising the threshold for blood transfusion. This is done in conjunction with the administration of iron and folic acid, starting at least 4 weeks before surgery and guided by the hemato-oncology team. A recent meta-analysis [15] looking at the preoperative use of EPO, reported a decrease in the percentage of patients requiring red blood cell transfusions (54% vs. 98%) and the amount of blood transfused in patients in whom blood products were given (84 vs. 283 mL) compared to patients in whom EPO was not administered preoperatively.

Concerns for the use of EPO have been raised in the adult population. Different studies [15] have reported an increased incidence of venous thrombosis, cancer progression, and cardiovascular complications in the adult population. Thrombotic events are rare in the pediatric population. Naran et al. [16] did not find any thrombotic events in a multicenter study of patients who received EPO preoperatively in craniosynostosis surgery. The concerns from the adult literature and its high cost has made the widespread use of EPO in the pediatric population rare. The pediatric craniofacial surgery reported that EPO use was only reported in three patients [17].

Question 6:
What are the chances of significant perioperative complications in this patient?

Answer:
Morbidity and mortality range from 0 to 40% in pediatric patients undergoing CCVR [18–20]. The PCCG registry recently reported a 15% incidence of perioperative complications in CCVR [21, 22]. Perioperative major complications are as shown in Table 7.2. The study found that intraoperative blood product transfusion of >50 mL/kg was the most significant predictor, increasing the risk of complications by 2.5 times. Other important predictors of perioperative complications were higher ASA physical status (ASA 3 OR 4), surgery duration more than 5 h, absence

Table 7.2 Major perioperative complications recorded in the PCCG database [21]

Neurological	Cardiac	Respiratory	Infectious
Hypoxic brain injury	Sustained hypotension/ hemodynamic instability	Apnea/hypoxia requiring intubation	Central line infection
Hydrocephalus postoperatively	Shock	Failed extubation	Shunt infection
Cerebral salt wasting syndrome	Dysrhythmias	Pulmonary edema	Sepsis
Diabetes insipidus; acute	Hemorrhage—intra or postoperatively	Severe bronchospasm	Wound dehiscence
Dural sinus bleed—severe	Hyperkalemia requiring treatment		Pneumonia—postoperative
Hyponatremia with seizures	Venous air embolism		
Seizure or suspected seizures	Thromboembolism or deep vein thrombosis		
Re-exploration: postoperative			

of intraoperative administration of antifibrinolytics, and diagnosis of craniofacial syndrome [22, 23]. Studies have also shown increased perioperative complications with age less than 9 months and weight less than 10 kg [19, 22]. Since this population is associated with increased blood loss expert consensus recommend waiting for elective CCVR until age is more than 9 months and weight more than 10 kg [22].

Goobie et al. performed a multivariable predictive algorithm for major perioperative complications to better understand the major risk factors that play a significant role in patient outcomes. The risk stratification as shown in Table 7.3 can help differentiate between high- versus low-risk patients. This allows for more selective use of postoperative ICU admission and may help predict total LOS for these patients.

7.2 Intraoperative

Question 7:
What type of monitoring would you consider? What is the value of doing point-of-care test like thromboelastography (TEG) and rotational thromboelastometry (ROTEM) in this population?

Answer:
Besides standard ASA monitoring, there is often a need for invasive monitoring using arterial line, central venous catheter, and precordial Doppler for CCVR. In the presence of ongoing perioperative blood loss, hemodynamic monitoring can be reliably done with the insertion of arterial line. Central venous access is also commonly required to measure volume status using central venous pressure and for safe administration of vasopressors. Venous air embolism is a feared complication during CCVR. Precordial Doppler is a highly sensitive tool to diagnose venous air embolism, and central venous access can be valuable in its management [24]. Esophageal or rectal temperature probes are also inserted to measure core body temperature for the management of intraoperative hypothermia. Foley catheter is inserted to measure urine output. It is important to place these lines and monitors in a timely fashion in order to minimize the induction to incision time and hence hypothermia.

Intraoperative acquired coagulation disorders are difficult to diagnose using standard laboratory tests like platelet count, PT, INR, and PTT [25]. This is because these tests have a prolonged turnaround time. Point-of-care tests such as TEG or ROTEM assess coagulation function in real time.

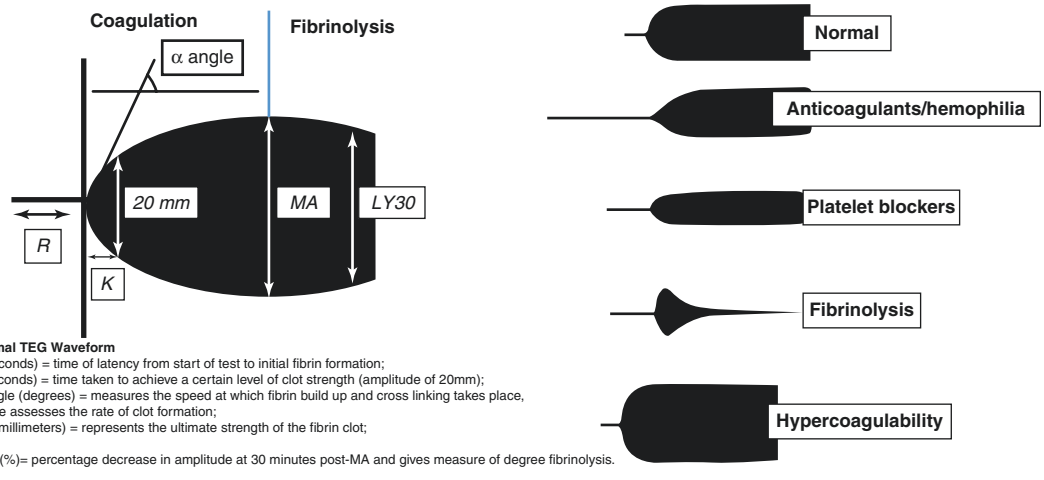
PT and activated partial thromboplastin time (aPTT) provide information on the first phase of coagulation up to fibrin formation, whereas viscoelastic point-of-care testes like TEG/ROTEM

Table 7.3 Multivariable predictive algorithm of a major perioperative complication

ASA physical status	Craniofacial syndrome	Use of antifibrinolytics	Total perioperative blood products >50 mL/kg	Surgery >5 h	Probability of complication (%)
3 or 4	Yes	No	Yes	Yes	58
3 or 4	Yes	Yes	Yes	Yes	46
3 or 4	No	No	Yes	Yes	43
3 or 4	Yes	No	Yes	No	41
3 or 4	Yes	No	No	Yes	38
3 or 4	No	Yes	Yes	Yes	33
3 or 4	Yes	Yes	Yes	No	31
3 or 4	No	No	Yes	No	29
3 or 4	Yes	Yes	No	Yes	28
3 or 4	No	No	No	Yes	26
3 or 4	Yes	No	No	No	24
3 or 4	No	Yes	Yes	No	21
3 or 4	No	Yes	No	Yes	18
3 or 4	Yes	Yes	No	No	17
3 or 4	No	No	No	No	15
3 or 4	No	Yes	No	No	10
1 or 2	Yes	No	Yes	Yes	45
1 or 2	Yes	Yes	Yes	Yes	45
1 or 2	No	No	Yes	Yes	32
1 or 2	Yes	No	Yes	No	31
1 or 2	Yes	No	No	Yes	27
1 or 2	No	Yes	Yes	Yes	24
1 or 2	Yes	Yes	Yes	No	22
1 or 2	No	No	Yes	No	20
1 or 2	Yes	Yes	No	Yes	19
1 or 2	No	No	No	Yes	18
1 or 2	Yes	No	No	No	17
1 or 2	No	Yes	Yes	No	14
1 or 2	No	Yes	No	Yes	12
1 or 2	Yes	Yes	No	No	11
1 or 2	No	No	No	No	10
1 or 2	No	Yes	No	No	5

High risk (>40%): dark grey, moderate risk (20–39%): light grey, low risk (<20%): white shading
Reproduced with permission: S. M. Goobie et al. Br J Anesthesia, 122 (2): 215–223 (2019)

produce information on all phases of coagulation. TEG and ROTEM also help assess platelet function and provide insight into interactions between the cellular and plasma components of whole blood for hemostasis. They are very useful in diagnosing disorders in the fibrinolytic system. Haas et al. in 2014 have shown that ROTEM-guided blood and blood product management decreases the need for transfusion intraoperatively [26]. In this retrospective study, the authors found that there was a complete avoidance of perioperative fresh frozen plasma (FFP) transfusion and also a significant reduction in platelet transfusion when the blood management was guided by ROTEM. Henceforth, the implementation of viscoelastic point of care tests has improved clinical outcomes and decreased transfusion-related costs.



Normal TEG Waveform
R(seconds) = time of latency from start of test to initial fibrin formation;
K(seconds) = time taken to achieve a certain level of clot strength (amplitude of 20mm);
α angle (degrees) = measures the speed at which fibrin build up and cross linking takes place, hence assesses the rate of clot formation;
MA (millimeters) = represents the ultimate strength of the fibrin clot;

LY30(%)= percentage decrease in amplitude at 30 minutes post-MA and gives measure of degree fibrinolysis.

Examples of abnormal TEG tracing

Modified from Thrombelastography (TEG®); practical considerations on its clinical use in trauma resuscitation. Luis Teodero da Luz, Bartolomeu Nascimento, Sandro Rizoli. Scand J Trauma Resusc Emerg Med. 2013; 21: 29.

Question 8:
What blood conservation strategies could be used for this type of procedures?

Answer:
Complex cranial vault remodeling is a high risk procedure associated with intraoperative bleeding which often occurs rapidly during scalp dissection, craniotomy, and bone flap removal. There are various preoperative and intraoperative strategies that are implemented to prevent postoperative anemia.

Preoperatively it is important to optimize the patient's hematocrit before surgery. Recombinant human EPO may be useful and should be considered on a weekly basis for 4–6 weeks with iron and folic acid supplementation [27]. At our institution, this group of patients receive EPO therapy preoperatively for 4–6 weeks as per hematology recommendation with a target hematocrit of 36.

Preoperative autologous blood donation may be offered in older children to decrease the risks associated with allogeneic blood transfusion. However, it is challenging in infants undergoing craniofacial surgery as it is difficult to obtain sufficient blood volume [28, 29]. Some families may elect to arrange for direct donation by family members or friends.

Intraoperative management involves multiple interventions to decrease blood loss and salvage blood using cell saver techniques [30]. Blood loss is decreased by preventing hypothermia-associated coagulation derangement. Forced air warming using underbody Bair-Huggers along with warming the operating room is a useful tool in maintaining normothermia. Skin infiltration of vasoconstrictors like epinephrine (1:200,000) can decrease blood loss with the scalp incision. Our surgical colleagues can also use bone wax, Floseal, Gelfoam, and surgical and fibrin sealant to decrease bleeding during osteotomies. The use of intraoperative blood salvage system has been beneficial in decreasing transfusion requirements in these patients. In the past its use was limited to infants weighing more than 10 kg, but with the recent development of devices like small volume continuous autotransfusion systems (CATS), blood can be salvaged in infants less than 10 kg [31]. Antifibrinolytic therapies, like tranexamic acid (TXA) and aminocaproic acid, have also shown to decrease blood loss in CCVR (see Question 9 for more detail). Restrictive transfusion thresholds like setting a transfusion target of hemoglobin 7 g/dL has been shown to be safe in hemodynamically stable pediatric ICU patients [32]. Implementing postoperative transfusion protocols has also shown to decrease significantly FFP transfusion in CCVR [33].

Hence a multidisciplinary team approach with the participation of hematologists, surgeons, anesthesiologists, and intensivists is vital to prevent and manage postoperative anemia in this patient population.

Question 9:
What is the role of antifibrinolytics for this type of surgery? What are some contraindications for the use of TXA in infants?

Answer:
Craniosynostosis surgical reconstruction in children is associated with major intraoperative blood loss, often requiring the transfusion of packed red blood cells (PRBCs) and other blood products [37]. Surgical blood loss is the leading cause of mortality after these procedures in children [36]. Blood transfusions can be associated with increased mortality and other significant adverse events in pediatric patients such as immunomodulation, alloimmunization, infectious disease, and hemolysis [37, 38], which has led to the study and development of many different strategies to reduce the need for transfusion. The use of TXA in cardiac and pediatric scoliosis correctional surgeries to reduce intraoperative blood loss has been extensively studied and established [36]. Consequently these therapies were also tried and studied in the craniofacial surgery patients.

The PCCG found in a recent study published in 2017 [34] that antifibrinolytics were not administered to 37% of patients undergoing open repair despite favorable data showing decreases in blood loss and transfusion in this patient population [34]. There is evidence from two randomized placebo-controlled prospective trials from two different groups that have shown that TXA decreases blood transfusion and blood loss [35, 36].

Dadure et al. designed a trial which included 39 children undergoing craniosynostosis correction (one patient excluded from the TXA group due to a repeal of parental consent). Patients either received a 15 mg/kg bolus of TXA or 1.5 mL/kg of normal saline over 15 min prior to incision, followed by a continuous infusion of 10 mg/kg/h of TXA or saline (1 mL/kg/h) until skin closure. There was an 85% reduction in the volume of PRBCs transfused in the TXA group compared to those given normal saline placebo intraoperatively (11–1.6 mL/kg) and a 57% reduction in PRBC transfusion throughout the study period (16.6–7.2 mL/kg). Also the percentage of children requiring transfusion intraoperatively was lower in the TXA group compared to placebo (2/19–11% vs. 9/20–45%, $P < 0.05$) and for the entire study period 7/19 (37%) patients in the TXA group compared to 14/20 (70%) in the placebo group ($P < 0.05$) [36]. The study determined that the use of TXA reduced the mean PRBC transfusion volume by 9.4 mL/kg compared to normal saline. There was no significant difference in blood loss between the groups; however, the author notes that estimating blood loss by weighing sponges and measuring suction volume can be imprecise. Furthermore, Goobie et al. on a prospective, double-blind placebo study also found a significantly lower perioperative mean blood loss in their TXA group vs. placebo (65 mL/kg vs. 119 mL/kg, $P < 0.001$) [35]. No adverse events attributed to TXA administration occurred in this study. They found that TXA administration also significantly decreased the perioperative exposure of patients to transfused blood (median, 1 unit vs. 3 units; $P < 0.001$) between both the groups. Of note, all patients were pretreated with EPO and iron supplementation preoperatively, which is often routine in pediatric patients undergoing procedures with the risk of major blood loss.

Contraindications to use of TXA in the pediatric population may include seizure disorder and preexisting prothrombotic state; however, no thrombotic complications have been described in children, and seizures have been seen in animal models and adults, but were not observed in either aforementioned studies [35, 36]. Further studies are needed to assess the most optimal dosing regimen for TXA especially in infants [39].

Epsilon-aminocaproic acid (EACA) is an antifibrinolytic medication with a similar mechanism to TXA (lysine analog that prevents conversion of plasminogen to plasmin). It has been used extensively in children undergoing cardiac and spine surgery and has been shown to reduce transfusion

requirements [37]. Given the theoretical risk of seizures in the pediatric population, EACA may be an alternative to TXA with less possible side effects and cheaper cost [37]. Hsu et al. describe an observational study of data collected from institutional craniofacial perioperative data registries, examining the use of EACA in craniofacial reconstructions and resultant calculated blood loss, intraoperative blood donor exposures, and surgical drain output [37]. Patients less than 24 months old received 100 mg/kg loading dose of EACA followed by an infusion of 40 mg/kg/h. Children older than 24 months received 100 mg/kg loading dose followed by 40, 30, or 20 mg/kg/h dose. Intraoperative blood loss was calculated with the equation estimated red cell mass (ERCM) lost = ERCM preop + ERCM transfused − ERCM postop (where ERCM = estimated blood volume × hematocrit/100). Of 152 subjects, 66 received EACA. EACA was associated with lower calculated blood loss (82 ± 43 mL/kg vs. 106 mL/kg ± 63; $P = 0.01$), and these patients had fewer blood donor exposures intraoperatively (median 2, interquartile range 1–2 vs. median 2, interquartile range 1–3; $P = 0.02$). Patients who received EACA also had lower surgical drain output in the 24 h postoperatively (28 mL/kg vs. 37 mL/kg; $P = 0.001$). In this study, seizures and thrombotic complications were not observed; however, the author notes that antifibrinolytics should be avoided in children with thrombophilic states [37].

Question 10:
What is your choice of induction agent and anesthetic maintenance for this patient?

Answer:
The most common method of induction is inhalational [40]; however, if the patient has risk for elevated ICP, intravenous (IV) induction with any of the IV anesthetics (barring any contraindications) can be performed. Muscle relaxants can be utilized as indicated for tracheal intubation which is typically done with a standard orotracheal tube [40]. Sometimes nasotracheal intubation is employed in patients who are going to be positioned in the sphinx position since this way the endotracheal tube may be more stable than when is placed orally.

Maintenance of anesthesia is typically performed with inhaled volatile anesthetic with air and oxygen, although if elevated ICP is a concern, a TIVA technique may be more ideal. Nitrous oxide is typically contraindicated due to the risk of venous air embolism [40]. Opioid infusions/boluses and other adjuncts such as dexmedetomidine have been used for analgesic purposes as indicated. Remifentanil and IV/laryngotracheal lidocaine may be useful near the end of the procedure to facilitate a smooth emergence and a reduced risk of coughing/gagging that may further increase ICP.

The surgery is half way through, and the patient has lost at least 1/3 of his blood volume … the blood pressure has continued to decline, and the patient remains persistently tachycardic.

Question 11:
When would you consider administering blood products other than red blood cells?

Answer:
Perioperative blood loss and its progression to hypovolemia, anemia, coagulopathy, and hypothermia are the most common complications during CVVR. Also as mentioned in Question 6, the single most important predictor of major complication in patient undergoing CVVR is blood product transfusion >50 mL/kg [41]. It is therefore important to minimize blood loss and judiciously give allogenic blood products.

Current guidelines suggest replacing coagulation factor deficiencies with FFP if there is evidence of ongoing clinical microvascular bleeding and the PT is >1.5 times normal, or INR >2, or PTT >2 times normal. FFP transfusion is also recommended to correct dilutional coagulopathy when more than one blood volume of PRBC is transfused during excessive microvascular bleeding. TEG- or ROTEM-guided transfusion of hemostatic products has also shown to safely decrease transfusion requirements.

Recent studies have shown that whole blood transfusion causes less coagulopathy and does not require FFP administration. Thus it signifi-

cantly reduces total volume of blood product transfusion [42].

In our institute, blood bank aliquots one unit of PRBC and FFP into two smaller bags on the morning of surgery. This helps us in minimizing wastage of blood products and decreasing the donor exposure.

Current guidelines suggest that a preoperative platelet count of 50,000–100,000 cells/μL should be maintained for patients undergoing surgery. Transfusion of one unit of platelet concentrate per 10 kg or 5 mL/kg of apheresis concentrate should raise the platelet count by 20,000–50,000 cells/μL. Transfusion of platelets should be done cautiously as it carries the highest risk of side effects associated with allogeneic blood product transfusion including bacterial contamination [43].

Fibrinogen is the first coagulation factor that depletes to critical low values during massive blood loss. Cryoprecipitate is given if fibrinogen <100 mg/dL with clinical evidence of coagulopathy. A dose of 1 unit per 5 kg usually increases fibrinogen level by 50 mg/dL.

Question 12:
What are the most common intraoperative complications during open craniosynostosis repair?

Answer:
Open craniosynostosis repair is associated with a higher incidence of venous air embolism, blood transfusion, and ICU admission when compared to endoscopic procedures [44]. Infants undergoing open cranial reconstruction procedures may have blood loss in excess of the total blood volume. An estimated percentage of blood volume loss can range from 25 to 500% depending on surgical approach and extent of procedure [45]. Thompson et al. found a 7 mL/kg greater blood loss in open repairs compared to endoscopic-assisted strip craniectomy [44]. Blood loss is the main cause of mortality after major craniofacial procedures in children [45] and results in increased perioperative morbidity and length of hospital stay [46]. Steady venous blood loss is to be prepared for, as large surgical areas and cutting of bone are often necessary. Also, major blood loss can occur due to unintended dural venous sinus tears or disruption of large emissary veins [46].

As the surgical incisions in the scalp and bone are above the level of the heart, there is risk of venous air embolism, and that risk is higher in open repairs [47]. The incidence is as high as 83%; however, most of these events are not hemodynamically significant [44].

Hypothermia is a concern in these lengthy procedures that often involve transfusion of blood products and large volumes of crystalloids/colloids. Incidence of hypothermia appears to be similar between open vs. endoscopic approaches [47]. Hypothermia can lead to worsening coagulopathy and can increase blood loss and the need for transfusion which exposes the child to further risk.

Another potential complication during this type of procedures is electrolyte derangements. Hypocalcemia occurs commonly with massive blood transfusions in children secondary to citrate toxicity. This is especially problematic for the young myocardium that tends to be more dependent on an adequate level of calcium in the plasma to maintain its contractility. Hypocalcemia can manifest as hypotension as well as electrical conduction abnormalities such as prolonged QT. Citrate is metabolized in the liver to bicarbonate. The adult liver is capable of metabolizing approximately 3 g of citrate every 5 min. With massive blood transfusions, the liver fails to make this conversion leading to citrate toxicity and secondary hypocalcemia. It is customary to frequently check plasma calcium levels in infants to prevent this, especially with large transfusions of blood. Hyperkalemia is another potentially lethal electrolyte disturbance that occurs with aggressive blood transfusion; this happens when patients are given units of PRBCs that are old. As the blood ages, the extracellular potassium increases daily due to the lysis of the red cells. Hyperkalemia can result in ECG changes including peaked T waves, small or absent P waves, widening of the QRS, and arrhythmias including ventricular fibrillation and asystole.

In order to prevent this, some institutions have specific blood bank policies where infants receive fresh red cells (<5 days old) [48] as well as blood that is leukocyte reduced and irradiated.

7.3 Postoperative

Question 13:
What are your options for postoperative pain control for this patient?

Answer:
Currently there is a paucity of information describing the different pain therapies utilized after craniosynostosis repair. Most institutions use parenteral opioids in the first 24 h with intravenous acetaminophen and then transition patients to enteral medications [49].

Kattail et al. [50] recently explored this topic retrospectively looking at postoperative pain management in patients with nonsyndromic craniosynostosis. The purpose of their study was to assess the quality of pain management after this type of surgery with the hypothesis that most likely pain is not managed adequately. Their specific aims were to identify perioperative analgesic regimens used in this cohort that included different medications and dosages; to quantify maximum pain scores as well as to identify potential demographic and analgesic regimens that will predict LOS. They retrospectively looked at data from 54 patients at Johns Hopkins hospital who underwent open craniosynostosis repair in a span of 7 years. All patients were managed by the acute pain service postoperatively with a unique mode of analgesia (IV PCA by proxy either by parent or by nurse). Their study demonstrated that pain was not managed adequately in more than 50% of patients who demonstrated moderate or severe pain in the first 48 h postoperatively. They concluded that this finding is probably secondary to the underutilization of multimodal analgesia. The only nonopioid analgesic that was consistently used was acetaminophen. Ketorolac was only used in 11% of patients and dexamethasone in 60% of patients. After their study they implemented a protocol that incorporated both medications and dexmedetomidine intraoperatively and in the first 24 h.

The use of other modalities for pain management different than opioids in this population is an area of recent interest. A group from Johns Hopkins [51] conducted a review of the literature looking for studies that addressed the question "Does Perioperative Steroid Use Improve Clinical Outcomes in Open Repair of Craniosynostosis?" An initial PubMed and Embase search process yielded 149 articles; only three of them were eligible for analysis. All three studies supported the efficacy of perioperative steroid use in the management of postoperative facial edema. In all studies they looked at patients' time to complete eye opening. In one of the studies, a statistically significantly larger group of patients who received steroids recovered with complete eye opening by postoperative day 3 (90%) when compared with the nonsteroid group (10%) [52]. Two of the three studies in the review showed a statistically significant advantage in reducing LOS in the steroid-treated groups. No adverse events were reported. The authors concluded that steroids may be beneficial in this population but due to the scarce information more studies were needed to understand the efficacy and safety in this group.

The other area of recent interest is the use of scalp blocks to reduce perioperative opioid consumption. Only one study from France [53] with 32 patients describes the use of these blocks without any adverse events; the study is mostly descriptive and does not have a control group. It shows a potential advantage on their use, but larger, controlled studies are necessary to explore their safety and efficacy.

Question 14:
Where should this patient recover after surgery? When should the parents expect their child to be discharged home?

Answer:
In our institution all patients undergoing craniosynostosis repair either open or endoscopic are admitted postoperatively to the ICU for the first 24 h for further monitoring and management. This is consistent with data from the PCCG registry [54] that showed that 90% (28/31) of institutions in the infant group and at 92% (22/26) of institutions in the older group admitted patients to the ICU. ICU LOS data were available for more than 90% of patients in both the groups; the median ICU LOS was 2 days for both the groups.

Only 4% (39/872) of infants and 3% (7/279) of older children were not admitted to the ICU.

In regard to hospital LOS, data were available for >95% of all patients in the study. The median hospital LOS was 4 days in infants: 97% stayed more than or equal to 3 days and 80% stayed more than or equal to 4 days. Findings were similar in older children [54].

The same group compared data from the registry between the CVVR and endoscopic group (ESC) and looked at ICU admission rate and LOS data [55]. Data were available for 92% of infants in the open group and 91% of infants in the ESC group. In the ESC group, only 35% of infants (99/283) were admitted to the ICU. Only 8 of 20 institutions admitted all their patients to the ICU. This shows that ICU admission after ESC repair was not routine practice in the majority of centers [55].

In the era of cost efficiency and safety, the question remains about the need for ICU admission for patients undergoing open repair who underwent uneventful anesthetics. A group from British Columbia Children's Hospital (BCCH) examined "the need for routine intensive care admission after surgical repair of nonsyndromic craniosynostosis" [56]. The authors retrospectively reviewed medical records of 114 patients who underwent nonsyndromic craniosynostosis repair from 2011 to 2016 at BCCH of which 80 surgeries were opened and 34 were EAC. Admission from the operating room (i.e., ward or ICU) and transfer to the ICU from the ward were evaluated. Only 6% who had open procedures were initially admitted to the ICU; the reasons for admission were: the suggestion of preoperative elevated ICP and pain control or a significant medical comorbidity. Overall, of the 107 patients admitted directly to the ward (75 who underwent an open surgery, 32 who underwent an EAC), none required ICU transfer. The authors suggested that patients with nonsyndromic craniosynostosis can be managed safely on the regular ward and do not require postoperative ICU admission, potentially making it cost efficient [56]. More is to be said on this topic since more institutions in the United States admit patients after CVVR surgery to the ICU.

Multiple Choice Questions

1. The patient developed sudden onset of bradycardia during the fronto orbital advancement. What will be the next step to manage bradycardia?
   (a) Administration of anticholinergic agent like atropine or glycopyrrolate
   (b) Ask the surgeon to flood the field with normal saline
   (c) Ask the surgeon halt the advancement temporarily
   (d) Give epinephrine
   Answer: c
2. Which of the following is not an independent predictor for perioperative complications in pediatric cranial vault reconstruction?
   (a) Craniofacial syndrome
   (b) Duration of surgery for more than 5 h
   (c) Lack of use of antifibrinolytics
   (d) Intraoperative blood and blood product transfusion <50 mL/kg
   Answer: d
3. Which of the following syndromes is not associated with craniosynostosis?
   (a) Apert syndrome
   (b) Pierre Robin sequence
   (c) Crouzon syndrome
   (d) Pfeiffer syndrome
   Answer: b
4. During the repair, this patient's systolic blood pressure drops from 70 mm of Hg to 30 mm of Hg and end-tidal CO_2 ($EtCO_2$) decrease from 35 to 10. What is the most likely diagnosis?
   (a) Hypovolemia
   (b) Hemorrhage
   (c) Venous air embolism
   (d) Tension pneumothorax
   (e) Too much anesthesia
   Answer: c
5. In regard to Question 4, what will be the next best step in the management of this complication?
   (a) Head up position of patient and OR table
   (b) Application of increase PEEP
   (c) Administration of mannitol
   (d) Informing surgical team and flooding the field with saline
   (e) Aspiration of central line
   Answer: d

References

Question 1

1. Stricker PA, Fiadjoe JE. Anesthesia for craniofacial surgery in infancy. Anesthesiol Clin. 2014;32:215–35.
2. Seruya M, Magge S, Keating R. Diagnosis and surgical options for craniosynostosis. In: Ellenbogen RG, Abdulrauf S, Sekhar L, editors. Principles of neurological surgery. 3rd ed. St Louis: Saunders; 2012. p. 138.
3. Bellew M, Mandela RJ, Chumas PD. Impact of age at surgery on neurodevelopmental outcomes in sagittal synostosis. J Neurosurg Pediatr. 2019:1–8.
4. Magge SN, Westerveld M, Pruzinsky T, Persing JA. Long-term neuropsychological effects of sagittal craniosynostosis on child development. J Craniofac Surg. 2002;13:99–104.
5. Bellew M, Chumas P. Long-term developmental follow-up in children with nonsyndromic craniosynostosis. J Neurosurg Pediatr. 2015;16:445–51.

Question 3

6. Persing JA. MOC-PS(SM) CME article: management considerations in the treatment of craniosynostosis. Plast Reconstr Surg. 2008;121(4 Suppl):1–11.
7. Stricker PA, Fiadjoe JE. Anesthesia for craniofacial surgery in infancy. Anesthesiol Clin. 2014;32(1):215–35.
8. Johnson D, Wilkie AOM. Craniosynostosis. Eur J Hum Genet. 2011;19(4):369–76.

Question 4

9. Barone CM, Jimenez DF. Endoscopic craniectomy for early correction of craniosynostosis. Plast Reconstr Surg. 1999;104:1965–73.
10. Jimenez DF, Barone CM. Multiple-suture nonsyndromic craniosynostosis: early and effective management using endoscopic techniques. J Neurosurg Pediatr. 2010;5:223–31.
11. Meier PM, Goobie SM, DiNardo JA, Proctor MR, Zurakowski D, Soriano SG. Endoscopic strip craniectomy in early infancy: the initial five years of anesthesia experience. Anesth Analg. 2011;112:407–14.
12. Thompson DR, Zurakowski D, Haberkern CM, The Pediatric Craniofacial Collaborative Group. Endoscopic versus open repair for craniosynostosis in infants using propensity score matching to compare outcomes: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesth Analg. 2018;126(3):968–75.
13. Stricker PA, Goobie SM, Cladis FP, et al. Pediatric Craniofacial Collaborative Group. Perioperative outcomes and management in pediatric complex cranial vault reconstruction: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesthesiology. 2017;126:276–87.

Question 5

14. Stricker PA, Fiadjoe JE. Anesthesia for craniofacial surgery in infancy. Anesthesiol Clin. 2014;32:215–35.
15. Aljaaly HA, et al. Effect of erythropoietin on transfusion requirements for craniosynostosis surgery in children. J Craniofac Surg. 2017;28:1315–9.
16. Naran S, Cladis F, Fearon J, et al. Safety of preoperative erythropoietin in surgical calvarial remodeling: an 8-year retrospective review and analysis. Plast Reconstr Surg. 2012;130:305e–10e.
17. Stricker PA, Goobie SM, Cladis FP, et al. Pediatric Craniofacial Collaborative Group. Perioperative outcomes and management in pediatric complex cranial vault reconstruction: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesthesiology. 2017;126:276–87.

Question 6

18. Czerwinski M, Hopper RA, Gruss J, Fearon JA. Major morbidity and mortality rates in craniofacial surgery: an analysis of 8101 major procedures. Plast Reconstr Surg. 2010;126:181–6.
19. Lee HQ, Hutson JM, Wray AC, et al. Analysis of morbidity and mortality in surgical management of craniosynostosis. J Craniofac Surg. 2012;23:1256–61.
20. Lin Y, Pan IW, Mayer RR, Lam S. Complications after craniosynostosis surgery: comparison of the 2012 kids' inpatient database and pediatric NSQIP database. Neurosurg Focus. 2015;39:E11.
21. Goobie SM, Zurakowski D, Proctor M, The Pediatric Craniofacial Collaborative Group. Predictors of clinically significant postoperative events after open craniosynostosis surgery. Anesthesiology. 2015;122:1021–32.
22. Goobie SM, Zurakowski D, Isaac KV, Taicher BM, Fernandez PG, Derderian CK, Hetmaniuk M, Stricker PA, Abruzzese C, Apuya J, Beethe A. Predictors of perioperative complications in paediatric cranial vault reconstruction surgery: a multicentre observational study from the Pediatric Craniofacial Collaborative Group. Br J Anaesth. 2019;122(2):215–23.
23. Fernandez PG, Taicher BM, Goobie SM et al. Predictors of transfusion outcomes in pediatric complex cranial vault reconstruction: a multicentre observational study from the Pediatric Craniofacial Collaborative Group. Can J Anaesth. 2019;14(2).

Question 7

24. Faberowski LW, Black S, Mickle JP. Incidence of venous air embolism during craniectomy for craniosynostosis repair. Anesthesiology. 2000;92:20–3.
25. Goobie SM, Haas T. Bleeding management for pediatric craniotomies and craniofacial surgery. Paediatr Anaesth. 2014;24:678–89.

26. Haas T, Goobie S, Spielmann N, et al. Improvement in patient blood management for pediatric craniosynostosis surgery using a ROTEM-assisted strategy-feasibility and costs. Pediatr Anesth. 2014;24:774–80.

Question 8

27. Shander A, Ozawa S, et al. Erythropoiesis-stimulating agents: friends or foes? Transfusion. 2013;53:1867–72.
28. Hans P, Collin V, Bonhomme V, Damas F, Born JD, Lamy M. Evaluation of acute normovolemic hemodilution for surgical repair of craniosynostosis. J Neurosurg Anesthesiol. 2000;12:33–6.
29. Knuckey MI, Wood EM, Savoia HF. Audit of a paediatric directed donation programme. J Paediatr Child Health. 2003;39:364–7.
30. Pietrini D. Intraoperative management of blood loss during craniosynostosis surgery. Pediatr Anesth. 2013;23:278–80.
31. Dahmani S, Orliaguet GA, Meyer PG, et al. Perioperative blood salvage during surgical correction of craniosynostosis in infants. Br J Anaesth. 2000;85:550–5.
32. Secher EL, Stensballe EJ, Afshari A. Transfusion in critically ill children. Acta Anaesthesiol Scand. 2013;57:684–91.
33. Stricker PA, Fiadjoe JE, Kilbaugh TJ, et al. Effect of transfusion guidelines on postoperative transfusion in children undergoing craniofacial reconstruction surgery. Pediatr Crit Care Med. 2012;13(6):e357–62.

Question 9

34. Thompson DR, Zurakowski D, Haberkern CM, Stricker PA, Meier PM, Bannister C, et al. Endoscopic versus open repair for craniosynostosis in infants using propensity score matching to compare outcomes: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesth Analg. 2018;126(3):968–75.
35. Goobie SM, Meier PM, Pereira LM, McGowan FX, Prescilla RP, Scharp LA, et al. Efficacy of tranexamic acid in pediatric craniosynostosis surgery: a double-blind, placebo-controlled trial. Anesthesiology. 2011;114(4):862–71.
36. Dadure C, Sauter M, Bringuier S, Bigorre M, Raux O, Rochette A, et al. Intraoperative tranexamic acid reduces blood transfusion in children undergoing craniosynostosis surgery: a randomized double-blind study. Anesthesiology. 2011;114(4):856–61.
37. Hsu G, Taylor JA, Fiadjoe JE, Vincent AM, Pruitt EY, Bartlett SP, et al. Aminocaproic acid administration is associated with reduced perioperative blood loss and transfusion in pediatric craniofacial surgery. Acta Anaesthesiol Scand. 2016;60(2):158–65.
38. Blackwood J, Joffe AR, Robertson CMT, Dinu IA, Alton G, Penner K, et al. Association of hemoglobin and transfusion with outcome after operations for hypoplastic left heart. Ann Thorac Surg. 2010;89(5):1378–1384.e2.
39. Erb TO, Meier PM. Surgical treatment of craniosynostosis in infants: open vs closed repair. Curr Opin Anaesthesiol. 2016;29(3):345–51.

Question 10

40. Stricker PA, Fiadjoe JE. Anesthesia for craniofacial surgery in infancy. Anesthesiol Clin. 2014;32:215–35.

Question 11

41. Goobie SM, Zurakowski D, Isaac KV, Taicher BM, Fernandez PG, Derderian CK, Hetmaniuk M, Stricker PA, Abruzzese C, Apuya J, Beethe A. Predictors of perioperative complications in paediatric cranial vault reconstruction surgery: a multicentre observational study from the Pediatric Craniofacial Collaborative Group. Br J Anaesth. 2019;122(2):215–23.
42. Muhly WT, Tan JM, et al. Care standardization reduces blood donor exposures and transfusion in complex cranial vault reconstruction. Hosp Pediatr. 2018;8(10):595–603.
43. Goobie SM, Haas T. Bleeding management for pediatric craniotomies and craniofacial surgery. Paediatr Anaesth. 2014;24(7):678–89.

Question 12

44. Thompson DR, Zurakowski D, Haberkern CM, Stricker PA, Meier PM, Bannister C, et al. Endoscopic versus open repair for craniosynostosis in infants using propensity score matching to compare outcomes: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesth Analg. 2018;126(3):968–75.
45. Dadure C, Sauter M, Bringuier S, Bigorre M, Raux O, Rochette A, et al. Intraoperative tranexamic acid reduces blood transfusion in children undergoing craniosynostosis surgery: a randomized double-blind study. Anesthesiology. 2011;114(4):856–61.
46. Stricker PA, Fiadjoe JE. Anesthesia for craniofacial surgery in infancy. Anesthesiol Clin. 2014;32:215–35.
47. Erb TO, Meier PM. Surgical treatment of craniosynostosis in infants: open vs closed repair. Curr Opin Anaesthesiol. 2016;29(3):345–51.
48. Lavoie J. Blood transfusion risks and alternative strategies in pediatric patients. Pediatr Anesth. 2011;21:14–24.

Question 13

49. Stricker PA, Fiadjoe JE. Anesthesia for craniofacial surgery in infancy. Anesthesiol Clin. 2014;32:215–35.
50. Kattail D, et al. Pain management for nonsyndromic craniosynostosis: adequate analgesia in a pediatric cohort? J Craniofac Surg. 2018;29:1148–53.
51. Wei AT, Madsen C, Al-Sheemy A, Raj Kumar A. Does perioperative steroid use improve clinical outcomes in open repair of craniosynostosis? J Craniofac Surg. 2015;26:226–31.
52. Choi WT, Greensmith AL, Chatdokmaiprai C, et al. Tumescent steroid infiltration reduces postoperative eye closure after craniofacial surgery. Plast Reconstr Surg. 2008;122:30e–2e.
53. Pardey Bracho GF, Pereira De Souza Neto E, Grousson S, et al. Opioid consumption after levobupivacaine scalp nerve block for craniosynostosis surgery. Acta Anaesthesiol Taiwan. 2014; 52:64–9.

Question 14

54. Stricker PA, Goobie SM, Cladis FP, et al. Pediatric Craniofacial Collaborative Group. Perioperative outcomes and management in pediatric complex cranial vault reconstruction: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesthesiology. 2017;126:276–87.
55. Thompson DR, Zurakowski D, Haberkern CM, Stricker PA, Meier PM, Bannister C, et al. Endoscopic versus open repair for craniosynostosis in infants using propensity score matching to compare outcomes: a multicenter study from the Pediatric Craniofacial Collaborative Group. Anesth Analg. 2018;126(3):968–75.
56. Bonfield C, Basem J, Cochrane D, Singhal A, Steinbok P. Examining the need for routine intensive care admission after surgical repair of nonsyndromic craniosynostosis: a preliminary analysis. J Neurosurg Pediatr. 2018;22:616–9.

8 Management of Patient with Craniopharyngioma

M. Srilata

Stem Case Terminology

A 30-year-old female presented with one episode of seizures 2 months back, increased thirst, increased frequency of micturition and blurring of vision for the last 2 months and headache for last 2–3 years. On further evaluation, the patient had stunted growth with short stature, malnourished, primary amenorrhoea and absence of secondary sexual characters. On general examination, height was 136 cm, weight 18 kg and body mass index (BMI) 18 kg/m^2. Her baseline vitals were as noted: HR—73/min, BP—87/45 mmHg and SPO_2—100%. Routine investigations were within normal limits. Endocrine testing revealed serum FSH—0.7 mIU/mL, serum LH—0.1 mIU/mL, prolactin—5.4 ng/mL, GH—0.71 ng/mL, ACTH—39.8 pg/mL, IGF1—<15 ng/mL, serum cortisol—7.6 mcg/dL, serum osmolality—274 mOsm/L, urine osmolality—260 mOsm/L and glycosylated Hb—4.8%. Thyroid profile demonstrated serum total T3—1.4 nmol/L, serum total T4—11.9 mcg/dL, TSH—0.4 mcIU/mL, free T4—1.73 ng/dL and free T3—2.77 pg/mL (after 1 month of thyronorm 50 mcg dose daily). Visual field testing revealed bilateral temporal scotomas. Computed tomography (CT) brain showed signs of well-defined hypodense lesion in the suprasellar region with multiple peripheral calcification. Magnetic resonance imaging (MRI) brain showed well-defined T1 hypointense, T2 flair hyperintense cystic lesion 6 × 3 × 2.8 cm in the suprasellar region extending superiorly into third and fourth ventricles; on contrast—heterogeneous enhancement of cyst wall was seen (Fig. 8.1). Medical management included tab thyronorm 50 mcg OD and tab levetiracetum 500 mg BD. The patient underwent craniotomy and decompression with aspiration of the cystic lesion, and an Ommaya reservoir with a catheter was placed inside the cyst cavity and left. The intraoperative and the immediate postoperative period was uneventful. And there was subjective improvement in the vision in the left eye. In the first and second PO days, she had hypernatremia which was managed with free water administration and monitoring of fluid intake and output. After 14 days of surgery, the patient developed nausea and vomiting with S&S of diabetes insipidus (DI) which was medically managed and deteriorating consciousness (MRI scan showed residual craniopharyngioma with mass effect with ventriculomegaly and Ommaya reservoir in situ) managed with ventriculoperitoneal shunt. Later both Glasgow coma scale (GCS) and DI improved.

M. Srilata (✉)
Department of Anesthesia and Intensive Care,
Nizams Institute of Medical Sciences,
Hyderabad, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_8

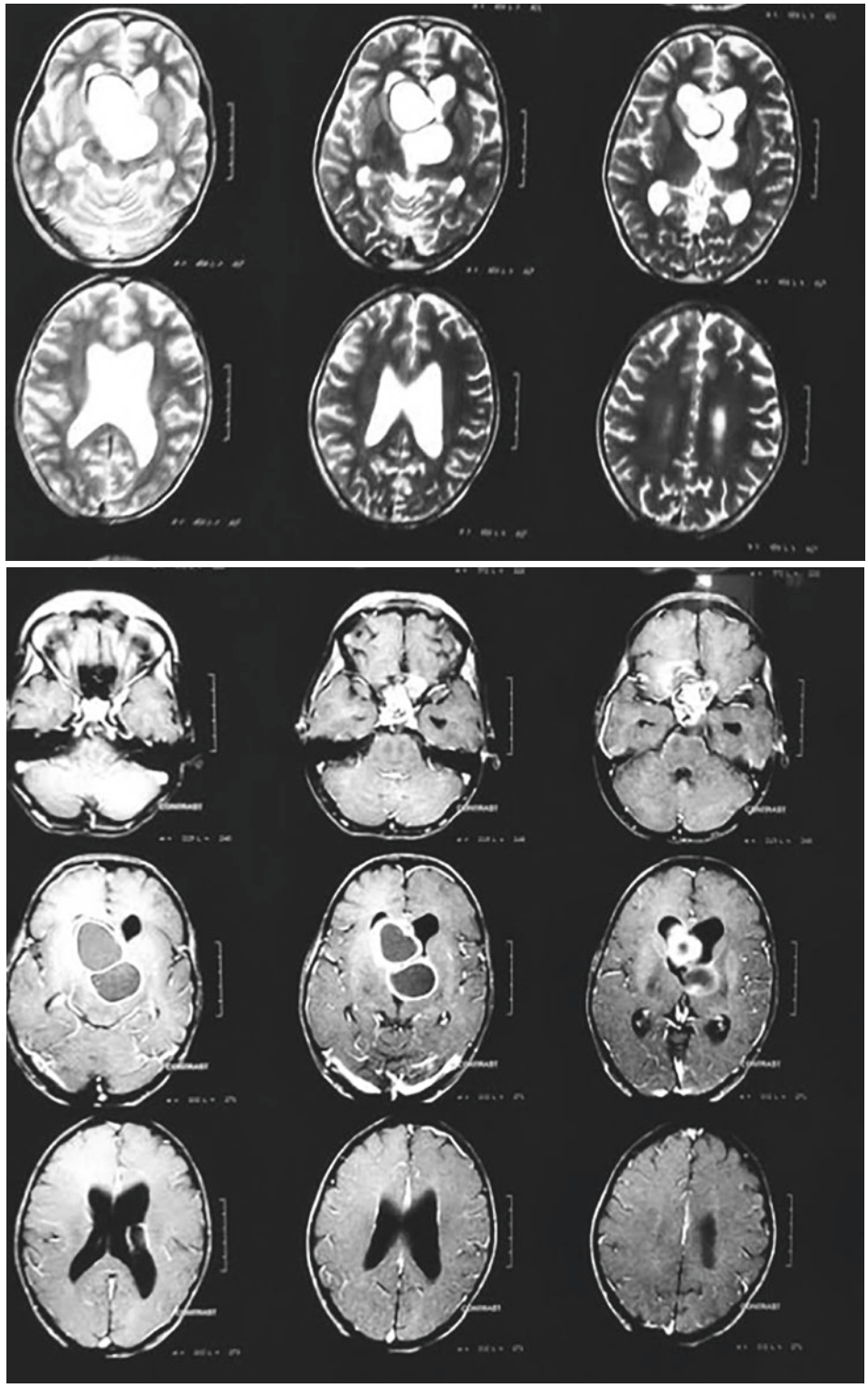


Fig. 8.1 MRI of brain with and without contrast demonstrating well-defined T1 hypointense, T2 flair hyperintense cystic lesion 6 × 3 × 2.8 cm in the suprasellar region extending superiorly into third and fourth ventricles; on contrast—heterogeneous enhancement of cyst wall was seen. Post-op MRI showing residual tumour with Ommaya reservoir in situ

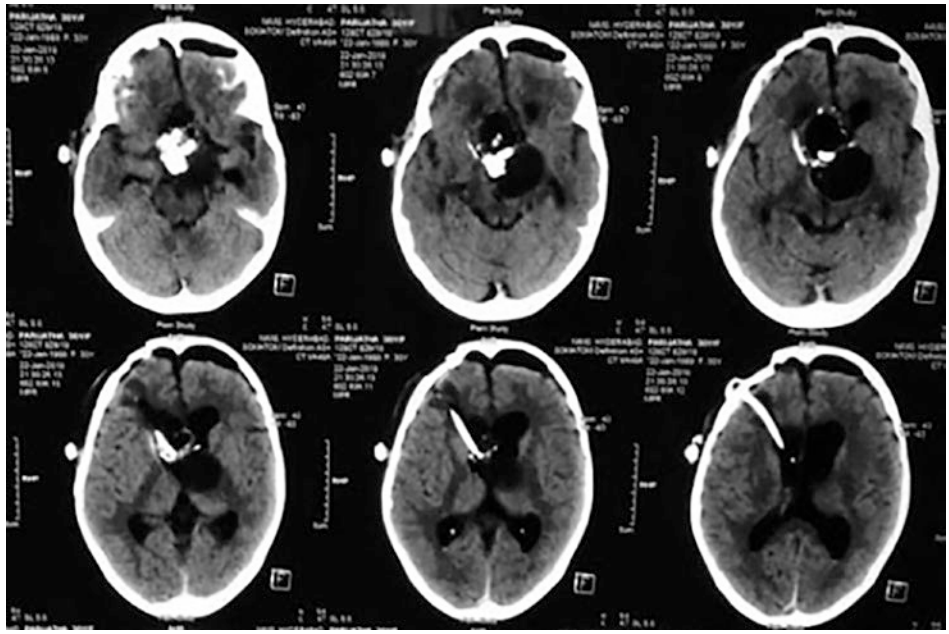


Fig. 8.1 (continued)

8.1 Preoperative

Question 1:
What are the presenting signs and symptoms of patients with craniopharyngiomas?

Answer:
The presenting signs and symptoms and its severity depend on the site, extent and growth potential of the lesion [1, 2]. These are slow-growing tumours, and usually a gap of 1–2 years is seen before their clinical presentation. The central location of these tumours attribute for the neuroendocrine dysfunction, especially hypopituitarism and hypothalamic dysfunction, which is seen in 85–100% of patients. Headache and other S&S of increased intracranial pressure (ICP) is the next common presentation. The size of the tumour and its effect on the ventricular system are responsible for the findings of increased ICP like headache, nausea and vomiting [3]. The details of clinical presentation and its attributes are described in Table 8.1. Compared to adults, headache, nausea/vomiting, papilledema, cranial nerve palsy and hydrocephalus are more frequent among children. Endocrine dysfunction like hypogonadism is common in adolescents and psychiatric disturbances are common in elderly patients [2]. Visual disturbances and hypopituitarism are common in young and middle-aged adults.

The incidence of recurrence is too high for these tumours, both in local and meningeal vicinity, which adds to increased morbidity. Multiple recurrences and post radiotherapy (RT) may present with a malignant change, and this is very rare [4]. These patients may actually present to the ophthalmology outpatient department (OPD) or surgical OPD for either visual disturbances or growth abnormalities.

Question 2:
What preoperative investigations do patients with craniopharyngioma need?

Answer:
These patients are thoroughly evaluated for the type, site and extent of the tumour spread.

A. Endocrine evaluation includes the battery of tests for both anterior and posterior pituitary [2, 5] (Table 8.2).
B. MRI with or without contrast enhancement is the diagnostic modality for screening craniopharyngiomas and helps in planning the surgi-

Table 8.1 Clinical presentation in craniopharyngioma

Structures involved	Results	Clinical presentation
Pituitary	Hypopituitarism—growth hormone deficiency, corticotrophin, thyrotrophin and gonadotrophin deficiencies, prolactin deficiency, DI Hyperpituitarism	Short stature, decreased muscle development, decreased bone mineral density, impotence, oligomenorrhea, amenorrhea, erectile dysfunction, decreased libido, hypothyroidism, polyuria, polydipsia, decreased stamina, weight loss, nausea, vomiting, headache and orthostatic hypotension, precocious puberty in children, SIADH
Hypothalamus and thalamus	Hypothalamic dysfunction	Obesity (hyperphagia), lethargy (decreased functional activity), adipsia or hypodipsia (deficient thirst), temperature dysregulation, abnormalities in sleep wakefulness (excessive daytime somnolence or insomnia), behavioural changes
Mass effect or compression of the ventricular system—third ventricle, foramen of Monroe or aqueduct of Sylvius	S&S of raised ICP	Headache, vomiting and bradycardia, papilledema, decreased consciousness, coma
Optic pathway—due to compression or mass effect	Visual field defects	Bitemporal hemianopsia, homonymous anopia, decreased central vision scotoma, optic atrophy with papilledema
Motor		Hemi or mono paresis
Brain parenchyma	Anterior, middle, or posterior cranial fossa	Seizures, cognitive dysfunction, psychiatric disturbances like hallucinations, emotional lability and paranoid delusions, apathy and incontinence
Rupture of the cyst	Chemical meningitis	Headache, neck stiffness, seizures
Vessel compression or involvement of the midbrain	Midbrain infarction Occlusion of the posterior inferior cerebellar artery	Weber's syndrome—ipsilateral third cranial nerve palsy with contralateral hemiplegia Wallenberg syndrome
Parasellar extension and involving cavernous sinus	Local invasion	Cranial nerve palsies, diplopia, paresis of the ocular muscles
Nasopharynx, paranasal area, and ethmoid sinus involvement	Obstructive or compressive or bleeding symptoms	Nasal obstruction, epistaxis, anosmia
CP angle	Site of tumour	Hearing loss
Brain stem	Local invasion of the brain stem—rarely seen	S&S of brains stem dysfunction

cal approach. T1-weighted images demonstrate hyperintensity for the cystic component and iso-intensity for the solid component, with enhancement of the rim and the tumour nodule. In T2-weighted images, both the cystic and solid component demonstrate hyperintensity.

C. Computed tomography of the brain is an alternative screening tool for its diagnosis. Craniopharyngiomas are heterogeneous tumours, cystic component being hypodense and solid component being isodense with variable enhancement (with contrast). Presence of calcification (90%) is suggestive of diagnosis of craniopharyngioma [6].

D. Plain skull X-rays show pathological changes in most of the adults and almost all children. Noted changes include any calcifications, enlargement of the sella, erosion of the sella, clinoid and dorsum, and any signs of increased ICP.

E. Ophthalmological assessment should include visual acuity, confrontation visual field testing, Goldman field testing, Amsler grid for central visual field and retinoscopy for papilloedema [7].

Table 8.2 Battery of tests for endocrine evaluation in craniopharyngioma

Anterior pituitary evaluation	Normal levels			Comments	Posterior pituitary evaluation	Normal levels	Comments
Adrenocorticotropic hormone	8–100 pg/mL			<3 µg/dL—suggests hypoadrenalism 3–7 µg/dL—requires stimulation testing	Vasopressin (ADH)	1–5 pg/mL	Urine osmolality <700 mOsm/kg in the presence of hypernatremia (>145 mmol/dL)/hyperosmolality (>295 mOsm/kg)—suggestive of DI >50% increase in urine osmolality to desmopressin—confirms central DI (renal response)
Cortisol	>18 µg/dL suggests adrenocortical sufficiency				Serum electrolytes	Serum sodium: 135–145 mmol/L Serum potassium: 3.5–5 mmol/L	
Prolactin	Females: 25–396 mU/L Males: 5–178 mU/L			<150 ng/mL—large sellar tumours (>1 cm) due to stalk effect >150–200 ng/mL—prolactin secreting tumours	Serum osmolality	275–295 mosm/kg	
GH	<6 ng/mL			<3 ng/mL—suggestive of GH deficiency (GH stimulation testing)	Urine osmolality	500–800 mOsm/kg of H_2O	
FSH and LH (mIU/mL)	Female: Follicular phase Mid-cycle Luteal phase Postmenopausal Male: Child (1 year to puberty)	FSH 3–16 12–27 2–16 40–185 3–16 2.5	LH 3–45 45–300 3–45 49–128 5–23 –	Low testosterone (<250–300 ng/dL) without elevated gonadotrophin (LH)—suggestive of central hypogonadism in men Oligomenorrhea/amenorrhea with low estradiol and normal gonadotrophin levels—suggestive in women	Oxytocin	Released in spurts	
Testosterone	270–1070 ng/dL						
TSH	0.4–4 mIU/L			Low free T4 without elevated TSH—suggestive of central hypothyroidism			
Tri-iodothyronine	80–180 ng/dL						
Free T4	0.7–1.9 ng/dL						

Question 3:
What other conditions should be considered in the differential diagnosis?

Answer:
The common geographical sites suprasellar, sellar and parasellar. The differential diagnosis include [1]:

- Sarcoid, sellar tumour, pituitary adenoma
- Aneurysm, arachnoid cyst
- Teratoma/dermoid, epidermoid cyst, tuberculosis
- Rathke's cleft cyst, choristoma, choroid glioma
- Hypothalamic glioma, teratoma, hamartoma of the tuber cinereum, Langerhan's cell histiocytosis
- Meningioma, metastasis
- Optic chiasm glioma
- Lymphocytic hypophysitis, lipoma
- Non-Hodgkin's lymphoma
- Germinoma
- Infundibuloma
- Suprasellar abscess

Question 4:
Describe the history and epidemiology of craniopharyngiomas.

Answer:
History: Craniopharyngiomas were first identified as a mass of squamous epithelial cells along the pars distalis and pars tuberalis of the pituitary by Friedrich Albert von Zenker in 1857 [8]. Later, histological origin of these tumours from hypophyseal duct or Rathke's pouch was first postulated by Mott and Barret in 1899, and later the same was confirmed by Erdheim in 1904. The widely used term "Craniopharyngioma" for these tumours was introduced by Cushing in 1932.

Incidence and Prevalence: Craniopharyngiomas are rare and benign epithelial tumours emanating along the path of craniopharyngeal duct. The incidence of these tumours varies from 0.13 to 2 per 1 lakh population per year with a point prevalence of approximately 1–3 per 1 lakh population [9]. There is no predilection to race or gender. The age of presentation is bimodal, children 5–14 years and elderly 65–74 years of age [10]. They represent about 2–6% of all paediatric primary intracranial tumours and around 50% of all sellar/parasellar tumours. Apart from the sellar region, it may present in other parts of CNS or nasopharynx. It can have multiple origins at the time of presentation. Congenital craniopharyngioma has been described in the literature. It was diagnosed in the antenatal period and later was radically excised after birth [11].

Question 5:
Briefly describe the anatomy of the craniopharyngeal duct and its adjacent structures with their physiologic functions.

Answer:
Craniopharyngeal duct is a rare, well-corticated canal from the sellar floor through the midline of the sphenoid bone to the anterosuperior part of the nasopharynx (adenohypophyseal stalk). During development, at 6th–7th weeks of gestation, the cartilaginous sphenoid skull base develops and obliterates the stalk.

Pituitary gland is the master of all glands and regulates all other endocrine organs [12, 13]. It is located in the sella turcica of the sphenoid bone at the base of the skull. This provides a path for the excision of the pathological lesions via the nasal cavity (transnasal transphenoidal approach). The optic chiasma is superiorly placed to the gland and further superiorly is the hypothalamus. Laterally lies the cavernous sinus with carotid arteries and cranial third, fourth and fifth nerves and posteriorly the clivus. The pituitary stalk is anterior to the optic chiasma.

Pituitary gland has three lobes: anterior lobe (adenohypophysis), intermediate lobe and posterior lobe (neurohypophysis). The release of hormones from these lobes is regulated by the hypothalamus via the hypothalamo-pituitary axis via the hormonal (anterior lobe) or nervous signals (posterior lobe) [13]. The list of hormones is tabulated (Table 8.2).

Question 6:
How do you classify craniopharyngiomas?

Answer:
Based on the embryology and histology, they are commonly classified into two types [14]:

1. Adamantinomatous tumours: (a) They arise from the epithelial remnants of the Rathke pouch or the craniopharyngeal duct, (b) the location of the tumour is explained by this embryogenesis and (c) common in children. The incidence of recurrence is high, and they are locally invasive tumours [15].
2. Squamous papillary: (a) These result from the metaplasia of squamous epithelial cells at the junction of the pituitary stalk and pars distalis and (b) more common in adults.
3. Transitional or mixed types.

Question 7:
What are the common sites of craniopharyngioma?

Answer:
According to the location of the tumour, they may be sellar, suprasellar, parasellar, retrosellar and infrasellar or multicompartmental. They are rarely malignant, but have the propensity for local invasion. A recent classification of craniopharyngiomas was based on the site of tumour origin and tumour–meningeal relationship: (a) infrasellar/infradiaphragmatic, common in children (b) suprasellar, subarachnoid extraventricular; common in adults and rarely seen in children and (c) suprasellar subpial types, seen in both adults and children [16].

They are avascular tumours, either displace or encase the vessels of circle of Willis, depending upon the site, growth and invasiveness of the tumour. Sellar tumours may present with sellar enlargement due to erosion of the floor of the sella.

Question 8:
What are the treatment options for patients with craniopharyngiomas?

Answer:
The main stay of therapeutic management is to cure the disease with the preservation and restoration of the functional activity [17, 18].

1. Medical management: Hormonal replacement therapy is instituted for any endocrine abnormalities present.
2. Surgical approach—biopsy, subtotal or total excision of the tumour. Total excision is attempted wherever possible to prevent recurrence of the tumour.
   (a) Small tumours restricted to sella—endoscopic transnasal transphenoidal approach; but rarely done in children (because of the developing sinuses, anatomy and small nares compared to adults); increased chances of CSF leak but decreased risk of visual injury.
   (b) Large tumours far beyond sella—craniotomy and radical excision or extended or far extended endoscopic transphenoidal approach
   (c) Keyhole or minimally invasive approaches via supraorbital incision—advantages include decreased dural leak and cosmetic incision (Fig. 8.2).
3. RT—after biopsy, subtotal excision or in recurrent tumours.
4. Intracystic RT—recurrent cystic tumours.
5. Chemotherapy—with bleomycin.
6. Aspiration—purely cystic mass.
7. Emergency Ommaya reservoir or biventricular shunt in children with giant tumours.
8. Stereotactic radiosurgery—for recurrent solid tumours.

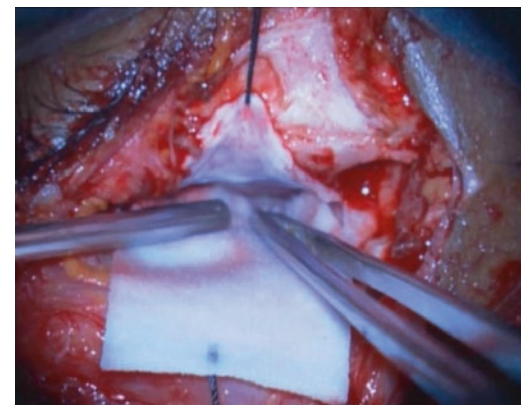


Fig. 8.2 Supraorbital keyhole subfrontal approach for excision of suprasellar cystic craniopharyngioma

The most common indication for surgery is local invasion or compression effect of the tumour leading to symptomatology.

8.2 Intraoperative

Question 9:
What are the anaesthetic concerns in the management of patients with craniopharyngiomas?

Answer:
Anaesthetic concerns include:

(a) Endocrine evaluation: This is done to identify abnormalities in endocrine function like thyroid function tests, growth hormone, cortisol levels, sex hormones, ACTH and prolactin [1]. Hypoadrenalism, DI and hypothyroidism have shown to have significant morbidity and mortality and should be normalised prior to any elective surgery. In cases of emergency, both hypoadrenalism and DI should be evaluated and treatment started prior to surgery.

Older children and adults peak cortisol levels in the morning around 8.00 am. Hence, sampling for cortisol assay is preferred in the morning. Presence of eosinophils in a peripheral blood smear is an indirect clue pointing towards cortisol deficiency. Patients with low cortisol levels are supplemented with steroids and optimised before elective surgery [2]. Replacement is done with prednisone single morning oral dose of 3–4 mg or hydrocortisone 15–25 mg orally in 2–3 divided doses. In children, hydrocortisone is given in an oral dose of 10–15 mg/m^2/day, in either two or three divided doses. Only 50–90% of the oral dose is absorbed; hence, oral dose should be approximately 1.5–2 times the daily production rate of cortisol. Adequacy of replacement is assessed by clinical criteria. In critically ill and hemodynamically unstable patients, urgent replacement is done with hydrocortisone intravenously at a dose of 100 mg in three divided doses. All patients with confirmed central hypopituitarism should be warned about the sick day stress glucocorticoid replacement for added intercurrent infection and prior to surgery. Almost 2–3 times the maintenance dose is required to combat the adrenocorticoid requirement. On the other hand, overdosage with glucocorticoid replacement and its side effects like central adiposity, dyslipidaemia and cardiovascular mortality should be avoided.

Free T4 levels are the main target to treat hypothyroidism. Thyroxine tablets should be supplemented to normalise the free T4 levels at least to upper level of the normal values or till the symptoms are normalised. The dose recommended for children 6–10 years of age is 4–5 μg/kg/day PO and according to body surface area; it is approximately 50 μg/m^2 per day (or approximately half that used to treat primary hypothyroidism). The adequacy of the dose can be readily determined by measuring the serum level of free T4. TSH levels should not be monitored as the patients are TSH-deficient.

In the case of concomitant hypopituitarism with corticotropin deficiency or any other causes of suspected adrenal insufficiency, glucocorticoid replacement should always precede thyroid hormone replacement. This reduces the risk of adrenal crisis resulting from increased demands from enhanced metabolism from thyroid hormone replacement.

DI is a common finding and treated with fluid management, vasopressin or desmopressin [19]. Desmopressin is safely used in a dose of 0.05 mg per oral (PO) twice daily in children. Though it is 20 times less potent than nasal form, the safety and flexibility of dosing have replaced the nasal form of desmopressin. Lysine vasopressin can also be used in a dose of 2.5–10 units intramusculary (IM)/subcutaneous (SC)/intranasally twice or thrice daily [20]. Management of DI requires meticulous monitoring of fluid intake, urine output, serum sodium levels and body weight, especially in patients with deficient thirst to guide fluid and desmopressin administration.

Other neuroendocrine replacements include growth hormone and sex steroids

though not much of anaesthetic relevance. Growth hormone replacement is considered in paediatric patients to improve the linear growth and also in normal adult patients to improve the exercise capacity, quality of life and body composition. Adequacy of GH replacement is assessed with clinical criteria and insulin-like growth factor-1 (IGF-1) levels. During GH and glucocorticoid replacement therapy, blood sugars should be monitored as obese patients are at increased risk of developing diabetes mellitus. If the patient has concomitant hypothyroidism, it should be assessed and treated first before testing for GH deficiency and initiation of its management.

Sex steroid replacement for men with testosterone and for women with oestrogen containing OC pills is considered, especially in premenopausal adults. Gonadotrophin replacement may be considered in patients with infertility.

Overall, the morbidity and mortality along with cardiovascular and cerebrovascular mortality are more with craniopharyngiomas. Adequate optimization of the neuroendocrine dysfunction and obesity management improves the outcome and overcomes the mortality and morbidity risk.

(b) Interpretation of CT and MRI findings—provides an idea about the extent and involvement of adjacent structures, correlation with the clinical findings and careful understanding and meticulous management of both intraoperative and postoperative complications.

(c) Airway in paediatrics is completely different from adults. Short stature and obese children pose challenges in airway management. Proper airway assessment is mandatory in special category of cases with hypothalamic involvement [21].

(d) The circle of Willis and its arterial components, the adjacent carotid and basilar arteries and their perforating branches are usually stretched around the suprasellar extensions of the craniopharyngioma tumour. Though the tumour is avascular, vicinity of the tumour to these adjoining vessels may present with vascular damage and increased chances of bleeding. This requires meticulous and vigilant management during acute and sudden blood loss [22]. Understanding the tumour anatomy helps in gentle and meticulous dissection and avoids major catastrophe.

(e) Obese children may have associated respiratory problems and obstructive sleep apnoea (OSA). These patients should be identified preoperatively and categorised as high-risk candidates. Patients with sleep apnoea may benefit from CPAP therapy. Bariatric surgery is an option especially in patients with BMI exceeding 40 kg/m^2 or >35 kg/m^2 with serious comorbidities.

(f) Risk stratification: Age more than 5 years, tumour size less than 4 cm, complete surgical removal, lack of calcification, Caucasian race, absence of hydrocephalus (need for CSF shunting) and absence of severe endocrinological dysfunction are the conditional criteria required for a favourable prognosis.

Another important grading to judge the severity of the lesion and surgical decision in children speaks of three grades: Type 0—no hypothalamic involvement, Type 1—distorts or elevates the hypothalamus and Type 2—hypothalamus is not visible (infiltrating/invoking) in imaging [23].

These grading systems give an overall picture of the incidence of PO morbidity, the plan of surgery, anticipated problems and anaesthetic plan and management accordingly.

(g) Volume status and electrolyte disturbances are monitored and corrected especially in children with S&S of increased ICP and receiving mannitol [24]. Patients with preoperative DI, due to nocturnal enuresis, may present with hypovolaemia in the morning of surgery. These children should be cautiously handled for hemodynamic instability at the time of induction.

Other minor concerns include:

1. Children and their parents are counselled regarding the diagnosis, the extent of the lesion, anaesthesia technique, surgical approach, positioning during surgery,

possible complications, and PO intensive care stay.
2. All the children are advised nil orally at least for 6 h for solids and 2 h for clear liquids as per American Society of Anesthesiologists guidelines.
3. Patients on replacement hormonal therapy should receive their morning doses of drugs. Children on antiepileptic agents for seizure management are continued on the day of surgery. This may have an effect on the neuromuscular blocking effect of non-depolarising muscle relaxants [25].
4. Neurocognitive testing is important in children showing deterioration in school performance [26].
5. Premedication with sedatives is not mandatory, especially in children with S&S of increased ICP. Anxious children without any signs of increased ICP may be advised mild sedatives like trichlorofos 100–125 mg/kg or alprazolam 0.25 mg under vigilant monitoring.
6. Informed consent is mandatory.
7. Pre-emptive analgesia with tab paracetamol or any nonsteroidal anti-inflammatory drugs (NSAIDs) and carbohydrate drinks 2 h before surgery may be helpful for implementing ERAS in straightforward Type 0 tumours or patients with favourable prognosis.

Question 10:
Describe briefly the anaesthesia management and positioning of patients undergoing surgery for craniopharyngioma.

Answer:
After proper identification of the patient and rechecking the medications and neurological status, children are shifted to the operation theatre in a trolley. Balanced anaesthesia is a requisite, as for any craniotomy. The aim is to maintain cerebral perfusion pressure, avoid any increase in ICP or any variations in mean arterial pressure [27]. Intravenous induction is ideal, but inhalational induction with sevoflurane is preferred in un-cooperative children and with difficult intravenous (IV) access [24]. Multimodal analgesia is provided with IV fentanyl, paracetamol and scalp block. Maintenance of anaesthesia is accomplished with inhalational agents or total IV anaesthesia with intermittent or continuous infusion of a short-acting opioid (like fentanyl or remifentanil) and neuromuscular blocking agent (atracurium). Inhalational anaesthetics like isoflurane are administered at 0.8–1.2 minimum alveolar concentration to avoid cerebral vasodilation and further aggravation of ICP. Anaesthetics like propofol or dexmedetomidine infusions may be used as anaesthetic adjuvants [28].

A motionless and blood less surgical field is essential for clear and clean plane of dissection, identification of vital structures and excision of the tumour mass [28]. Maintaining the arachnoid layer around the tumour during tumour dissection and excision helps in preserving the neurovascular structures around the craniopharyngioma. Mannitol (0.25–1 g/kg) and other ICP lowering interventions are carried out for children with increased ICP. Sometimes, emergent decompressive craniotomy is required for sudden and acute presentation of patients with tumours obstructing at the level of fourth ventricle and aqueduct of Sylvius.

Airway management is crucial in paediatrics, more so in short stature and obese children. Intubation may require bougie, video laryngoscope, fibre-optic bronchoscope and other airway equipment for handling a difficult paediatric airway. Opioids are administered in low doses or avoided, especially in patients with OSA.

Surgical Position: The surgical approach dictates the position of the patient [28]. Supine position with slight head tilt and lateroflexion (malar prominence should be at the highest level) is the most commonly advocated one. The Mayfield frame is used to fix the head with paediatric pins or head is supported in a horse shoe frame. Application of skull pins in paediatric patients carries the danger of intracranial haematoma, dural tear and skull fracture. Careful positioning is done keeping in view of any airway compromise, venous congestion of the neck, IV access, padding of pressure points and protection of the eyes. Gross rotation of the head or neck flexion is avoided for any increase in venous pressure and for any inward migration of the endotracheal tube.

Question 11:
Describe the anaesthesia concerns in patients undergoing trans sphenoidal resection of sellar craniopharyngiomas?

Answer:
The most common approach used nowadays is endoscopic endonasal approach. There are many advantages of this approach over craniotomy. They are cosmetic reasons, lesser incidence of injury to optic chiasm and frontal lobes, lesser incidence of DI, shorter duration of surgical intervention, minimal pain scores, shorter hospital stay and decreased morbidity [29].

The specific anaesthesia concerns include:

(a) Route of entry via the nasal cavity with an endoscope invokes sympathetic response and sometimes results in exaggerated hemodynamic response and its consequences. Balanced anaesthesia with the use of depth of anaesthesia monitoring and adequate analgesia combats this response. Other options include inhalational anaesthesia, propofol or dexmedetomidine infusion, labetalol or NTG infusion and high dose of opioids. Regional anaesthesia with infraorbital block, maxillary block or sphenopalatine ganglion block will supplement general anaesthesia and overall decreases the dose of inhalational and IV anaesthetic drugs. Endoscopic endonasal approach has the least hemodynamic response compared to the traditional approach.
(b) Throat pack is an essential component. This prevents any seepage of blood from the site of tumour excision and nasal cavity into the throat. The throat should be properly packed with a saline-soaked roll of gauze. This should be properly tagged, labelled and removed at the end of surgery before extubation. There are reports of missed gauze rolls leading to obstructive breathing pattern and even cardiac arrest [30].
(c) All the patients should be counselled regarding the surgical route and postoperative nasal obstruction due to nasal packing. Patients are taught about mouth breathing in the postoperative period, especially in patients with bilateral nasal packing. Negative pressure pulmonary oedema is a major concern in these patients [31].
(d) Obese patients especially with OSA may have a problem in the immediate postoperative period at the time of extubation in patients with bilateral nasal packing. Opioids are avoided or administered at very low doses. NSAIDs or regional anaesthesia is supplemented for analgesia.

Question 12:
What are the monitoring modalities for the intraoperative management of craniopharyngioma? Also describe the vascular access and fluid management in brief.

Answer:
Routine monitoring includes oxygen saturation by pulse oximetry, heart rate, electrocardiography, capnography and temperature. Surgery for craniopharyngioma may be associated with sudden blood loss, sometimes hypothalamic and rarely brain stem stimulation. The potential for any vascular injury warrants placement of an arterial cannula for continuous vigilance and timely action. Systolic pressure variation monitoring guides us in identifying and treating volume deficit. It also assists in frequent sampling of blood gases, electrolytes, glucose and osmolality, especially for the treatment of DI.

DI is a common intraoperative complication of craniopharyngioma. Apart from urine output, central venous pressure (CVP) monitoring is required for the diagnosis and management of DI. This also helps in rapid replenishment of acute blood losses and for the administration of vasoactive drugs.

Vascular Access and Fluid of Choice: Two large bore cannula would suffice for any craniotomy in paediatric patients. This would take care of any unexpected and sudden blood loss. Central venous catheter may be required depending upon the size of the tumour and extent of the radical excision. This is beneficial especially in patients suspected of developing DI or already established DI. Arterial pressure with systolic

pressure variation monitoring is an important requisite for the chances of blood loss, and hemodynamic instability during surgery is increased with radical excision of the tumour. Normovolaemia is the accepted criteria for perioperative fluid management in neurosurgery. Normal saline is the fluid of choice for all intracranial neurosurgical procedures as it is slightly hyperosmolar and attenuates cerebral oedema [32]. Balanced salt solutions have replaced normal saline in many of the centres for they have shown to have better control over the acid–base balance and electrolyte status. Hypoglycaemia is a common presentation in paediatric patients undergoing major surgery, and on the other hand, hyperglycaemia exacerbates neurologic injury if ischemia occurs. Frequent monitoring of blood glucose and timely and appropriate management of glucose disturbances is essential.

Question 13:
What are the intraoperative concerns in a patient undergoing surgery for craniopharyngioma?

Answer:
The intraoperative concerns include:

1. Injury to adjacent neural structures: Manipulation or any injury to the optic nerve and optic chiasm may result in deterioration of the vision.
2. Steroid replacement is an essential component for major surgery in these patients. These children require an initial dose of 0.5–1 mg/kg of hydrocortisone every 6 h at least for 72 h.
3. Because of the close vicinity of the ICA and other vessels of the circle of Willis and due to the local invasion of the tumour, bleeding is a major concern. Controlling the depth of anaesthesia with lower side of the normal blood pressure is important to minimise the blood loss. Estimation of the blood volume and calculation of maximum allowable blood loss is essential and should be determined in advance for effective management of blood loss and its transfusion in paediatrics. Since the tumour is avascular, pharmacological agents like tranexamic acid may not be useful. Sometimes, uncontrolled bleeding may result in cardiac arrest and increased mortality [28].
4. DI is the most anticipated intraoperative complication. This occurs due to injury to the pituitary stalk or hypothalamus, resulting in decreased antidiuretic secretion and diminished ability to concentrate urine. The incidence following transcranial excision is around 60–70%. It is characterised by increased output (≥4 mL/kg/h in 24 h) of dilute urine (<300 mOs/kg). Volume replacement is the main line of treatment with continuous monitoring of CVP, acid base, osmolality, electrolyte changes and glucose. If it is associated with hypernatremia (>150 mg/dL), a hypo-osmolar fluid is preferred. To avoid rapid correction of sodium levels and its deleterious effects, the fall in sodium levels should be targeted at 0.5 mmol/L/h. Continuous infusion of arginine vasopressin with deficit-directed fluid management is useful in the intraoperative management of DI [33] (Fig. 8.3).

   During the initial therapy, one should monitor for fluid retention and hyponatremia. Overall, monitoring of fluid intake, output, thirst, specific gravity, serum sodium and 24 h urinary volumes helps in early identification and timely management of DI.
5. Hypothalamic disturbances may result in loss of temperature homeostasis. Stimulation of the anteromedial hypothalamus may induce ST-T changes, which may be misleading towards cardiac ischemia [34].
6. Injury to mammillothalamic tract, thalamus and basal forebrain may result in children undergoing radical excision of the tumour [35].
7. Brain stem injury is rare but may occur in cases with widespread invasion [36]. Sometimes, the patient may require intensive care unit (ICU) admission in a comatose state.
8. Hypotension, not responding to vasoactive drugs, may be seen in patients with severe hypoadrenalism. Hydrocortisone in a dose of 0.5–1 mg/kg may be beneficial.

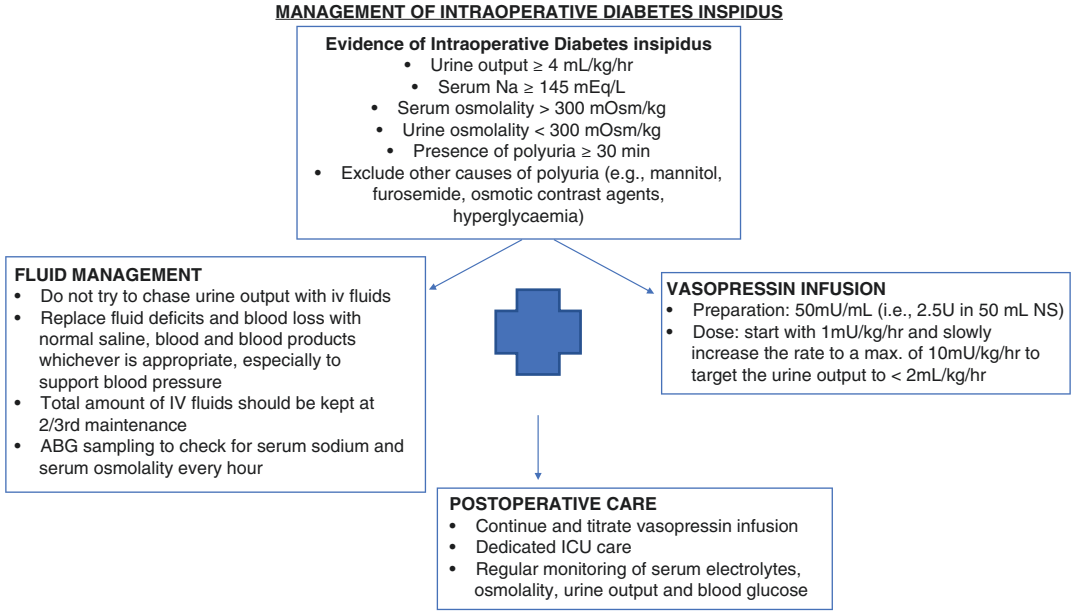


Fig. 8.3 Algorithm for the management of diabetes insipidus

9. As the conventional craniotomy involves frontal lobe retraction and manipulation, seizures are common in the postoperative period. These patients are administered antiepileptics like IV phenytoin 10 mg/kg as a loading dose for prophylaxis soon after excision of the tumour in the intraoperative period and are continued in the PO period. Patients with symptomatology of seizures and on antiseizure treatment will receive their maintenance dose of antiepileptic drug in the intraoperative period.
10. CSF leakage: more commonly seen in children undergoing trans-sphenoidal approach [37].

Question 14:
Will you tracheally extubate the patients at the end of surgery?

Answer:
The duration of surgery depends on the extent of the lesion, surgical plan, surgical expertise and surgical field conditions. The patients with an uneventful intraoperative period may be extubated on table. Difficult extubation is anticipated in obese patients with OSA.

8.3 Postoperative

Question 15:
What are the different postoperative concerns and complications? How should one anticipate and manage the same?

Answer:
The postoperative concerns are enumerated as below:

1. Pain: Postoperative pain is a major concern. Analgesic priming with injection fentanyl, injection paracetamol, scalp block and infiltration analgesia are helpful in combating postoperative pain. Sphenopalatine ganglion block, maxillary block and infraorbital block are helpful.
2. Fluid management: Normovolaemia should be maintained with the use of normal saline. Balanced salt solution is an alternative option.
3. The intraoperative problems like DI may carry onto the PO period. The incidence is around 70–90%. Details are already described in the intraoperative concerns [34]. Other symptoms of DI like loss of thirst is

unmasked in the postoperative period and hence pose a high risk for hypernatremia. Nasal desmopressin is effective in the dose of DI present in the preoperative period. DI may improve after surgery but other endocrine abnormalities rarely improve.

4. Other features of hypopituitarism, like anterior and posterior pituitary dysfunction, may be seen. The incidence is around 50–100%. After 48–72 h of supraphysiologic doses of steroid replacement, the dose is maintained or tapered down to physiologic doses of hydrocortisone depending on the daily morning cortisol levels [38]. Some of the patients receive steroids for long term in order to balance the hypothalamo-pituitary axis.
5. In patients undergoing radical surgery, hypothalamic dysfunction like hyper- or hypothermia, behavioural and memory changes may be evident. These subset of patients with loss of temperature homeostasis and somnolence have a very bad prognosis [34, 39].
6. Postoperative seizures are common following craniotomy surgery and respond promptly to antiseizure treatment. They rarely occur following transphenoidal surgery.
7. Obese patients with established diagnosis of OSA may have difficulty in weaning from ventilation and, in due course, may develop respiratory infections and become ventilator dependent. Careful and timely weaning of these patients is important to avoid these complications.
8. Patients with severe dyselectrolytaemia, haemodynamic instability, hypothalamic injury, changes in osmolality and acid base may require postoperative elective respiratory support.
9. Residual tumour: MRI scan is repeated in the postoperative period to evaluate the extent of lesion which may be responsible for the delayed appearance of symptoms. Most of the patients with residual tumour are effectively treated with RT. RT is like a double edge sword. RT following surgery is very effective in regression of the tumour, but at the same time, it may have its effect on intelligence quotient and growth. Delayed RT is preferred in paediatric patients to avoid this effect.
10. Follow-up of the neurocognitive function in the PO period is essential to understand the quality of life in children, especially with preoperative changes, and following subtotal resection and RT [40].
11. Rarely, patients may develop radiation-induced gliomas, most common site being the temporal lobe. Other side effects of RT are endocrine dysfunction, optic neuritis, dementia and radiation necrosis.
12. Some patients may present with S&S of obstructive hydrocephalus; respond to surgical bypass procedures like ventriculoperitoneal shunt.
13. An adequate and balanced intake of salt and water is necessary. Low protein and low salt diet would be helpful to decrease urine volume.
14. All these patients require regular lifelong assessment, almost every 6–12 months and treatment for endocrine deficits. These deficits may be the result of tumour recurrence, progression of the tumour, surgery or radiation therapy.

Multiple Choice Questions

1. Glucocorticoid replacement is done prior to thyroid replacement to avoid
   (a) Adrenal crisis
   (b) Thyroid crisis
   (c) Inadequacy of treatment
   (d) DI
   Answer: a

   In the case of concomitant hypopituitarism with corticotropin deficiency or any other causes of suspected adrenal insufficiency, glucocorticoid replacement should always precede thyroid hormone replacement. This reduces the risk of adrenal crisis resulting from increased demands from enhanced metabolism from thyroid hormone replacement.
2. Adequacy of thyroid replacement in craniopharyngioma patients with thyroid dysfunction is assessed by

(a) TSH levels
(b) Free T4 levels
(c) Free T3 levels
(d) Thyroid binding globulin

Answer: b

Thyroxine tablets should be supplemented to normalise the free T4 levels at least to upper level of the normal values or till the symptoms are normalised. The dose recommended for children 6–10 years of age is 4–5 μg/kg/day PO, and according to body surface area, it is approximately 50 μg/m^2 per day (or approximately half that used to treat primary hypothyroidism). The adequacy of the dose can be readily determined by measuring the serum level of free T4. TSH levels should not be monitored as the patients are TSH-deficient.

3. The aim of surgical management in craniopharyngioma is:
   (a) Maintain the blood–brain barrier
   (b) Maintain the ICP
   (c) Maintain the integrity of the arachnoid layer
   (d) Maintain muscle relaxation

   Answer: c

   Maintaining the arachnoid layer around the tumour during tumour dissection and excision helps in preserving the neurovascular structures around the craniopharyngioma.

4. Central DI is characterised by
   (a) Urine osmolality >300 mOsm/kg in the presence of hypernatremia (>145 mmol/dL)/hyperosmolality (>295 mOsm/kg)
   (b) Urine osmolality <300 mOsm/kg in the presence of hypernatremia (>145 mmol/dL)/hyperosmolality (>295 mOsm/kg)
   (c) Urine osmolality <300 mOsm/kg in the presence of hyponatremia (<135 mmol/dL)/hyperosmolality (>295 mOsm/kg)
   (d) Urine osmolality <300 mOsm/kg in the presence of hypernatremia (>145 mmol/dL)/hyposmolality (<275 mOsm/kg)

   Answer: b

   DI is the most anticipated intraoperative complication. This occurs due to injury to the pituitary stalk or hypothalamus, resulting in decreased anti-diuretic secretion and diminished ability to concentrate urine. The incidence following transcranial excision is around 60–70%. It is characterised by increased output (≥4 mL/kg/h in 24 h) of dilute urine (<300 mOsm/kg).

5. Adequacy of GH replacement is guided by
   (a) Melatonin levels
   (b) IGF-1 levels
   (c) Melatonin levels and clinical criteria
   (d) IGF-1 levels and clinical criteria

   Answer: d

   The actions of growth hormone is mediated by IGF-1; hence, the adequacy of GH replacement is best assessed by IGF-1 levels and clinical criteria.

6. Response to desmopressin treatment for central DI is assessed by:
   (a) >50% decrease in urine osmolality
   (b) >50% increase in serum osmolality
   (c) >50% increase in urine osmolality
   (d) >50% increase in serum osmolality

   Answer: c

   DI is characterised by urine osmolality <300 mOsm/kg in the presence of hypernatremia (>145 mmol/dL)/hyperosmolality (>295 mOsm/kg); >50% increase in urine osmolality to desmopressin suggest central DI. This is called renal response.

7. Favourable prognosis in patients undergoing surgery for craniopharyngioma is stratified by
   (a) Age more than 5 years and hypothalamic involvement
   (b) Age less than 5 years and absence of endocrinological dysfunction
   (c) Tumour size less than 4 cm and absence of endocrinological dysfunction
   (d) Tumour size more than 5 cm and complete surgical excision of the tumour

   Answer: c

   Risk stratification: Age more than 5 years, tumour size less than 4 cm, complete surgical removal and absence of severe endocrinological dysfunction are the conditional criteria required for a favourable prognosis.

   Another important grading to judge the severity of the lesion and surgical decision in children speaks of three grades: Type 0—no hypothalamic involvement, Type 1—distorts

or elevates the hypothalamus and Type 2—hypothalamus is not visible

8. In hemodynamically unstable paediatric patients with craniopharyngioma, steroid replacement is done with
   (a) Injection dexamethasone 1–5 mg/m^2/day, in either two or three divided doses
   (b) Injection hydrocortisone 10–15 mg/m^2/day, in either two or three divided doses
   (c) Injection dexamethasone 10–15 mg/m^2/day, in either two or three divided doses
   (d) Injection hydrocortisone 1–5 mg/m^2/day, in either two or three divided doses

   Answer: b

   Hypoadrenalism is the main cause for glucocorticoid deficiency and its consequences; replacement is mandatory in emergency situations and adequate replacement is guided by clinical criteria.

References

1. Lania A, Spada A, Lasio G. Diagnosis and management of craniopharyngiomas: key current topics. Springer International Publishing; 2016.
2. Evans JJ, Kenning TJ. Craniopharyngiomas: comprehensive diagnosis, treatment and outcome. Elsevier Science; 2014.
3. Zoicas F, Schöfl C. Craniopharyngioma in adults. Front Endocrinol. 2012;3:46.
4. Nelson GA, Bastian FO, Schlitt M, White RL. Malignant transformation in craniopharyngioma. Neurosurgery. 1988;22(2):427–9. PubMed PMID: 3352897.
5. Wills MR, Havard B. Laboratory investigation of endocrine disorders. Elsevier Science; 2013.
6. Curran JG, O'Connor E. Imaging of craniopharyngioma. Childs Nerv Syst. 2005;21(8–9):635–9.
7. Defoort-Dhellemmes S, Moritz F, Bouacha I, Vinchon M. Craniopharyngioma: ophthalmological aspects at diagnosis. J Pediatr Endocrinol Metab. 2006;19:321–4.
8. Barkhoudarian G, Laws ER. Craniopharyngioma: history. Pituitary. 2013;16(1):1–8.
9. Müller HL. Craniopharyngioma. Endocr Rev. 2014;35(3):513–43.
10. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM. The descriptive epidemiology of craniopharyngioma. J Neurosurg. 1998;89(4):547–51.
11. Kageji T, Miyamoto T, Kotani Y, Kaji T, Bando Y, Mizobuchi Y, et al. Congenital craniopharyngioma treated by radical surgery: case report and review of the literature. Childs Nerv Syst. 2017;33(2):357–62.
12. ElSayed SA, Bhimji SS. Physiology, pituitary gland. StatPearls [Internet]: StatPearls Publishing; 2018.
13. Amar AP, Weiss MH. Pituitary anatomy and physiology. Neurosurg Clin. 2003;14(1):11–23.
14. Fernandez-Miranda JC, Gardner PA, Snyderman CH, Devaney KO, Strojan P, Suárez C, et al. Craniopharyngioma: a pathologic, clinical, and surgical review. Head Neck. 2012;34(7):1036–44.
15. Pekmezci M, Louie J, Gupta N, Bloomer MM, Tihan T. Clinicopathological characteristics of adamantinomatous and papillary craniopharyngiomas: University of California, San Francisco experience 1985–2005. Neurosurgery. 2010;67(5):1341–9.
16. Müller HL. Preoperative staging in childhood craniopharyngioma: standardization as a first step towards improved outcome. Springer; 2016.
17. Bhatoe HS. Evolution of concepts in the management of craniopharyngiomas: lessons learnt from Prof. SN Bhagwati's article published in 1993. Neurol India. 2018;66(3):613.
18. Varlotto J, DiMaio C, Grassberger C, Tangel M, Mackley H, Pavelic M, et al. Multi-modality management of craniopharyngioma: a review of various treatments and their outcomes. Neuro-Oncol Pract. 2015;3(3):173–87.
19. Bajwa SJS, Kaur G. Endocrinopathies: the current and changing perspectives in anesthesia practice. Indian J Endocrinol Metab. 2015;19(4):462.
20. Mishra G, Chandrashekhar SR. Management of diabetes insipidus in children. Indian J Endocrinol Metab. 2011;15(Suppl3):S180.
21. Vinchon M, Weill J, Delestret I, Dhellemmes P. Craniopharyngioma and hypothalamic obesity in children. Childs Nerv Syst. 2009;25(3):347.
22. Tomita T, Bowman RM. Craniopharyngiomas in children: surgical experience at Children's Memorial Hospital. Childs Nerv Syst. 2005;21(8–9):729–46.
23. Vinken PJ, Bruyn GW. Handbook of clinical neurology. Elsevier; 2002.
24. Rath GP, Dash HH. Anaesthesia for neurosurgical procedures in paediatric patients. Indian J Anaesth. 2012;56(5):502.
25. Furay C, Howell T. Paediatric neuroanaesthesia. Contin Educ Anaesth Crit Care Pain. 2010;10(6):172–6.
26. Sands SA, Milner JS, Goldberg J, Mukhi V, Moliterno JA, Maxfield C, et al. Quality of life and behavioral follow-up study of pediatric survivors of craniopharyngioma. J Neurosurg Pediatr. 2005;103(4):302–11.
27. Prabhakar H. Paediatric neuroanaesthesia: Oxford University Press; 2018.
28. Cottrell JE, Young WL. Cottrell and Young's neuroanesthesia. Elsevier Health Sciences; 2016.
29. Prabhakar H. Essentials of neuroanesthesia. Elsevier Science; 2017.
30. To E, Tsang W, Yiu F, Chan M. A missing throat pack. Anaesthesia. 2001;56(4):383–4.
31. Bhaskar B, Fraser JF. Negative pressure pulmonary edema revisited: pathophysiology and review of management. Saudi J Anaesth. 2011;5(3):308.

32. Tommasino C, Picozzi V. Volume and electrolyte management. Best Pract Res Clin Anaesthesiol. 2007;21(4):497–516. PubMed PMID: 18286834.
33. Wise-Faberowski L, Soriano SG, Ferrari L, McManus ML, Wolfsdorf JI, Majzoub J, et al. Perioperative management of diabetes insipidus in children. J Neurosurg Anesthesiol. 2004;16(1):14–9. PubMed PMID: 00008506-200401000-00004.
34. Cohen M, Bartels U, Branson H, Kulkarni AV, Hamilton J. Trends in treatment and outcomes of pediatric craniopharyngioma, 1975-2011. Neuro Oncol. 2013;15(6):767–74. PubMed PMID: 23486689.
35. Iizuka O, Suzuki K, Mori E. Severe amnesic syndrome and collecting behavior after surgery for craniopharyngioma. Cogn Behav Neurol. 2007;20(2):126–30. PubMed PMID: 17558257.
36. Grover WD, Rorke LB. Invasive craniopharyngioma. J Neurol Neurosurg Psychiatry. 1968;31(6):580–2. PubMed PMID: 5709844.
37. Jane JA Jr, Prevedello DM, Alden TD, Laws ER Jr. The transsphenoidal resection of pediatric craniopharyngiomas: a case series. J Neurosurg Pediatr. 2010;5(1):49–60. PubMed PMID: 20043736.
38. Coté CJ, Lerman J, Anderson BJ. A practice of anesthesia for infants and children: expert consult. Online and Print: Elsevier/Saunders; 2013.
39. Muller HL. Childhood craniopharyngioma: current controversies on management in diagnostics, treatment and follow-up. Expert Rev Neurother. 2010;10(4):515–24. PubMed PMID: 20367205.
40. Sands SA, Milner JS, Goldberg J, Mukhi V, Moliterno JA, Maxfield C, et al. Quality of life and behavioral follow-up study of pediatric survivors of craniopharyngioma. J Neurosurg. 2005;103(4 Suppl):302–11. PubMed PMID: 16270681.

9 Management of Patient with Acromegaly

Lee C. Chang

Stem Case Terminology

A 49-year-old man presents for endonasal transphenoidal resection of a pituitary mass. His PMHx is significant for acromegaly, hypertension, uncontrolled diabetes mellitus, obstructive sleep apnea (OSA), and C3–5 cervical spine stenosis. He is 72″ and 102 kg with a Grade 4 Mallampati score and an otherwise reassuring airway and physical exam. The patient reports having a good exercise tolerance.

Question 1:
What is the etiology and pathophysiology of acromegaly? How is the disorder diagnosed?

Answer:
Acromegaly is characterized by excessive levels of growth hormone (GH) most often due to a GH-secreting pituitary adenoma, with the majority being classified as macroadenomas at the time of diagnosis. Approximately 5% of cases are a result of tumors found in the adrenals, lungs, and pancreas that secrete GH. The total prevalence of the disorder is very low, with an estimated 28–137 cases per million [1]. The disorder is diagnosed equally among both men and women, with the mean age of diagnosis being in the early to mid-40s [2]. GH stimulates the secretion of insulin-like growth factor-1 (IGF-1) from the liver which is responsible for most clinical manifestations seen with acromegaly. Interestingly, the use of minoxidil has been associated with the condition pseudoacromegaly, which has the clinical features of acromegaly but normal GH and IGF-1 levels.

Although acral enlargement and maxillofacial changes account for the most common presenting clinical features, acromegaly is often diagnosed following a different presenting complaint, such as amenorrhea, visual field defects, sleep apnea, or carpal tunnel syndrome. Approximately a third of patients have no complaints associated with acromegaly at the time of diagnosis [3, 4]. Often, the first diagnostic measure is the observation of growth charts that show a change from the normal height and weight curves. Diagnosis can be verified by measuring for appropriate normal age- and sex-based GH and IGF-1 levels, conducting a GH suppression test, and magnetic resonance imaging (MRI) studies.

Question 2:
What treatment options are available for acromegaly?

Answer:
The treatment options of acromegaly include surgery, pharmacotherapy, and radiotherapy all

L. C. Chang (✉)
Department of Anesthesiology, Baylor College of Medicine, Houston, TX, USA
e-mail: lcchang@bcm.edu

© Springer Nature Singapore Pte Ltd. 2020
H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_9

with the goal of lowering GH and IGF-1 hypersecretion and improving morbidity. The initial management is typically transsphenoidal surgery for resection of the hyperfunctioning adenoma with follow-up assessment of GH levels. Some surgeons will place a lumbar intrathecal catheter to allow for the removal of cerebrospinal fluid (CSF) in order to have better visualization of the tumor. Patients who continue to have elevated levels due to residual tumor or show recurrence visualized on MRI may need additional surgical procedures [5]. Major complications from the surgery can include mortality, visual impairment, and meningitis, occurring cumulatively less than 2%. Other complications are CSF leak, permanent anterior lobe deficits, and diabetes insipidus [6]. The mainstay medical treatment for acromegaly is somatostatin receptor ligands which can result in hormone suppression while therapy is continued. Derived from the hypothalamus, somatostatin is an endogenous peptide that regulates neuroendocrine secretion [7]. Approximately 50% of patients treated with somatostatin receptor ligands will have a moderate decrease in the volume of the pituitary tumor, usually occurring within 3 months of initiating therapy [5]. Ongoing drug expenses and drug intolerance due to side effects are the limitations of medical treatment. Additional methods of medical therapy includes dopamine receptor agonists and GH-receptor antagonists, which lowers IGF-1 levels by blocking the GH receptors. Based on the etiology and comorbidities, some acromegalic patients are selected to first begin medical treatment as the primary therapy or as a pretreatment prior to surgery. Pretreatment may reduce both surgical complications and hospitalization stay [8]. Conventional radiotherapy is considered for patients who continue to have elevated GH and IGF-1 levels despite surgery and/or medical therapy. Survival for patients with acromegaly is reduced by an average of 10 years compared to patients without acromegaly, irrespective of management [9].

9.1 Preoperative

Question 3:
What preoperative assessment should be done for patients with pituitary adenomas prior to surgery?

Answer:
Patients with pituitary tumors may have different endocrine disorders and require an extensive preoperative assessment. Collaboration and discussion between the anesthesiologist, neurosurgeon, and endocrinologist is often required prior to the procedure. Prolactinomas are the most common of functioning tumors and account for 30% of all pituitary tumors. While the symptoms of hyperprolactinemia in men are relatively nonspecific, for women symptoms include galactorrhea, infertility, amenorrhea, and loss of libido [10]. In addition to acromegaly from GH-secreting tumors, Cushing's disease may result from adrenocorticotropic hormone (ACTH)-secreting tumors as well as thyrotropic disease from thyroid-stimulating hormone (TSH) secretion [11]. The mass effect of the pituitary tumor may also result in chronic headaches as well as vision loss from compression of the optic chiasm. Approximately 55% of acromegalic patients report having headaches and 18% will have visual field defects. Although rare, the possibility of increased intracranial pressure (ICP) increases as the adenoma increases in size, and these patients may present with nausea/vomiting, papilledema, and worsening headache. The increased ICP may also result from the tumor causing obstruction of the third ventricle [12].

Patients should have a complete blood count to rule out the possibility of anemia, which may be present in men who may have low testosterone [13]. In addition, a metabolic panel should be completed to assess the possibility of hyponatremia, hypercalcemia, and hyperglycemia which may be present. Diabetes insipidus may result in hyponatremia with patients who have posterior pituitary dysfunction [12]. Several hormonal serum tests should be conducted to determine if the pituitary adenoma is considered functioning or non-functioning.

Question 4:
What metabolic issues should be anticipated for patients with acromegaly?

Answer:
Both adrenal insufficiency and central hypothyroidism may result in patients with the disorder due to compression of the pituitary gland [14]. Acromegalic patients are glucose intolerant due to the elevated GH levels causing resistance to the effects of insulin. Diabetes mellitus is present in up to 27.5% of the patients at the time of diagnosis for acromegaly [15]. Higher intraoperative glucose levels have been found to be significantly higher compared to patients without acromegaly [16]. This is especially important in the patients undergoing certain neurological procedures as hyperglycemia is a risk factor for worsening cerebral ischemia [17]. There have been some studies that there is an increased mortality associated with acromegaly with the presence of diabetes. Following treatment of acromegaly, improvements of the metabolic profile is noted [18].

Question 5:
What cardiovascular involvement should be evaluated for acromegalic patients?

Answer:
Cardiovascular disease accounts for nearly 60% of the deaths with this disease. Chronic GH hypersecretion acts as a vascular growth factor that can stimulate collagen deposits as well as lead to an expansion of plasma volume [19]. Preexisting hypertension is a common finding, with a prevalence reaching up to 50%, associated with increased left ventricular mass or left ventricular wall thickness and likely due to an increase in sodium retention and plasma volume. Cardiac tissue is often involved with acromegalics which may result in the development of congestive cardiac failure, with the most common finding being biventricular cardiac hypertrophy [20]. Based on autopsy data, there is a disproportionate amount of cardiomegaly in comparison to other organ hypertrophy and a higher incidence of small vessel disease [21]. Electrocardiography changes, such as bundle branch blocks, atrial fibrillation, and supraventricular tachycardia have also been noted in acromegalic patients, and there is an increased incidence of both ventricular and supraventricular ectopy with physical exertion and stress [22]. Interestingly, the level of GH concentration and the degree of cardiac enlargement do not seem to be related [23]. However, the duration of the disorder and the age of the patient do correlate with the degree of the cardiac hypertrophy [24].

Current recommendations include an annual echocardiography, electrocardiography, and echo Doppler of peripheral arterial and venous system for patients with acromegaly [25]. Despite the preexisting cardiovascular involvement, a retrospective study found no significant evidence of any differences in regard to major hemodynamic effects when comparing patients with acromegaly to a control group. There was also no significant difference in the use of vasoactive drugs between the two groups intraoperatively [26].

Question 6:
What risk factors are there for developing left ventricular hypertrophy?

Answer:
Age, hypertension, disease activity, and duration are suggested risk factors for patients with acromegaly to develop left ventricular hypertrophy. Studies have found that age is an independent predictor for hypertrophy, and those older than 50 years of age to have a significantly higher likelihood [27, 28]. Patients with left ventricular hypertrophy are more prone to having cardiac valve abnormalities as well which should be ruled out [29].

9.2 Intraoperative

Question 7:
What monitors are indicated for this patient? Are there any concerns about placing an arterial line?

Answer:
When deciding if an arterial line should be placed, it should be noted that patients with acro-

megaly may already have some compression and impaired circulation of the ulnar artery due to a higher incidence of carpal ligament hypertrophy. Approximately up to 50% of acromegalic patients may have ulnar artery circulation that is impaired in either one or both hands. If necessary, an arterial line may need to be placed in an alternative location, such as the dorsalis pedis artery [30]. Technically, the placement of arterial lines and peripheral IVs may also be more challenging due to thickening of the skin that is often seen with the disorder. Excessive sweating and oily skin may also result in additional measures needed to secure monitors attached and lines placed [31]. The need for placement of a central venous catheter is dependent on the patient's preexisting cardiovascular disease.

Question 8:
What concerns do you have with the patient's airway? Is a reliable airway exam a good indication of an easy airway? What is your plan on securing an airway?

Answer:
The potential airway sequelae of acromegaly include mandibular prognathism, overgrowth of the lips, nose, tongue, pharyngeal tissue, and epiglottis. Maxillary and mandibular widening associated with jaw malocclusion may also contribute to the difficulty of securing an airway. The incidence of difficult intubation for acromegalic patients is 10% with a high incidence (26%) of grade III view with the initial laryngoscopy. Assessment of the airway can prove deceptively reassuring as up to 20% of Mallampati 1–2 scores have been noted to be "difficult intubations" (more than two attempts, blade change, or use of a bougie). Neck extension and thyromental distance has not been found to be related to difficult laryngoscopy [32]. A recent study found increased IGF-1 levels to be an independent risk factor for predicting difficult intubation in patients with acromegaly [33]. For patients with difficulties in either ventilation or intubation, an awake intubation with sedation and topical anesthesia is the safest way to proceed. However, even a fiber-optic approach may prove difficult, or for acromegalic patients due to problems with advancing, either the fiber-optic or the endotracheal tube as a result of the distorted anatomy and alternative methods, such as video laryngoscopy, should be available [34]. Given the altered airway anatomy and large tongue often seen with this disorder, the use of an intubating laryngeal mask airway may be difficult.

Question 9:
Do you have any concerns when positioning the patient?

Answer:
Approximately 75% of patients with acromegaly will have some form of arthropathy which can range from osteoarthritis to fractures and often develops early in the course of the disorder [35]. In addition, soft tissue swelling and bony overgrowth may result in higher risk of nerve damage if improper positioning and padding is present. The enlargement of the hands and feet must be considered when they are secured so that repositioning of the operating room table will not result in injury. Acromegalic patients may also be more prone to vertebral fractures [36]. Given these risk factors associated with acromegaly, it is critical that the patients are positioned properly on the operating table.

Question 10:
Would you administer long-acting opioids and benzodiazepines to patients with acromegaly intraoperatively?

Answer:
Sleep apnea syndrome is a common disorder found with acromegalic patients and can be divided into obstructive, central, or mixed. OSA due to polypoid masses in the pharynx is the prevalent form and can be observed in up to 70% of patients with acromegaly, more often in men. The cause of central OSA may be a result of the increased GH levels, resulting in an increase in the ventilatory response to carbon dioxide, resulting in respiratory arrest [37]. In addition, laryngeal stenosis and cricoid narrowing are often

present [38]. Short-acting opiates and the avoidance of benzodiazepines should be considered in patients with a known diagnosis of OSA or with a high suspicion of the disease. All patients with acromegaly should be asked about risk factors for OSA, such as snoring, excessive daytime somnolence, or observed periods of apnea while sleeping, and polysomnography should be included in the work-up of patients diagnosed with acromegaly. It is believed that up to 90% of patients with acromegaly who snore will have sleep apnea [39]. Although there is some improvement of sleep apnea with patients who have been treated for acromegaly, it still persists following therapy [40].

9.3 Postoperative

Question 11
Following transsphenoidal surgery, would you recommend the use of continuous positive airway pressure (CPAP) for the patient with the history of OSA?

Answer:
OSA may worsen following transsphenoidal surgery due to the placement of nasal packing and increased edema of the nose and oral airway. However, the use of CPAP after transsphenoidal surgery carries the risk of potentially developing pneumocephalus and meningitis and has generally been thought to be contraindicated [41]. There is currently no consensus on appropriate management for patients with OSA following transsphenoidal surgery [42]. For patients with OSA who do have postoperative hypoxemia, conservative treatment with an oxygen face mask with the use of an oral airway should first be considered.

Question 12:
What postoperative concerns do you have following pituitary surgery?

Answer:
Headache is the most common complaint patients have following transsphenoidal surgery and should be treated appropriately, again with the avoidance of opioids if possible in patients with OSA. Nausea and vomiting are complications often seen in patients undergoing neurosurgical procedures, and pharmacologic prophylaxis should be administered to diminish any effect it may have on ICP. Cranial nerve dysfunction should be followed immediately in the postoperative period, and any changes need to be followed up with additional diagnostic tests. CSF leakage is another concern for patients who demonstrate continuous fluid leakage associated with headaches [43]. Diabetes insipidus and syndrome of inappropriate antidiuretic hormone secretion are also common complications following surgery and should be considered if patients exhibit abnormal sodium levels [44].

Multiple Choice Questions:

1. What is the mainstay medical therapy for patients with acromegaly?
   (a) Dopamine agonists
   (b) Somatostatin analogues
   (c) IGF-1 antagonists
   (d) GH antagonists
   Answer: b
2. What is the most common form of ventricular hypertrophy?
   (a) Biventricular hypertrophy
   (b) Left ventricular hypertrophy
   (c) Right ventricular hypertrophy
   Answer: a
3. Which of the following is not a risk factor for developing left ventricular hypertrophy?
   (a) Hypertension
   (b) Age
   (c) Disease duration
   (d) Gender
   Answer: d
4. What percentage of patients with acromegaly have some form of arthropathy that should be taken into consideration when positioning?
   (a) 5%
   (b) 25%
   (c) 50%
   (d) 75%
   Answer: d

5. Which of the following is more common for acromegalic patients that increases the risk of placing an arterial line in the radial artery?
   (a) Radial artery thrombosis
   (b) Brachial artery occlusion
   (c) Ulnar artery occlusion
   (d) Radial artery pseudoaneurysm
   Answer: c

References

Question 1

1. Lavrentaki A, Paluzzi A, Wass JA, et al. Epidemiology of acromegaly: review of population studies. Pituitary. 2017;20:4–9.
2. Ezzat S, Forster MJ, Berchtold P, Redelmeier DA, Boerlin V, Harris AG. Acromegaly: clinical and biochemical features in 500 patients. Medicine (Baltimore). 1994;73:233–40.
3. Nabarro JD. Acromegaly. Clin Endocrinol (Oxf). 1987;26:481–512.
4. Alexander L, Appleton D, Hall R, Ross WM, Wilkinson R. Epidemiology of acromegaly in the Newcastle region. Clin Endocrinol (Oxf). 1980;12:71–9.

Question 2

5. Melmed S, Casanueva FF, Cavagnini F, Chanson P, Frohman L, Grossman A, Ho D, Kleinberg D, Lamberts S, Laws E, et al. Guidelines for acromegaly management. J Clin Endocrinol Metab. 2002;87:4054–8.
6. Ciric L, Ragin A, Baumgartner C, et al. Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. Neurosurgery. 1997;40:225–37.
7. Chanson P. Predicting the effects of long-term medical treatment in acromegaly. At what cost? For what benefits? Eur J Endocrinol. 1997;136(4):359–61.
8. Ferone D, Colao A, van der Lely A, et al. Pharmacotherapy or surgery as primary treatment for acromegaly? Drugs Aging. 2000;17(2):81–92.
9. Rajasoorya C, Holdaway IM, Wrightson P, et al. Determinants of clinical outcome and survival in acromegaly. Clin Endocrinol. 1994;41(1):95–102.

Question 3

10. Schlechte JA. Clinical practice: prolactinoma. N Engl J Med. 2003;349:2035–41.
11. Abraham M. Perioperative management of patients with pituitary tumors. J Neuroanethesiol Crit Care. 2016;3:211–8.
12. Nemergut EC, Dumont AS, Barry UT, Laws ER. Perioperative management of patients undergoing transsphenoidal pituitary surgery. Anesth Analg. 2005;101:1170–81.
13. Ellegala DB, Alden TD, Couture DE, et al. Anemia, testosterone, and pituitary adenoma in men. J Neurosurg. 2003;98:974–7.

Question 4

14. Katznelson L, Atkinson JL, Cook DM. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. Endocr Pract. 2011;17(Suppl 4):1–44.
15. Petrossians P, Daly AF, Natchev E, et al. Acromegaly at diagnosis in 3173 patients from the Liège Acromegaly Survey (LAS) Database. Endocr Relat Cancer. 2017;24:505–18.
16. Seidman PA, Kofke WA, Policare R, Young M. Anaesthetic complications of acromegaly. Br J Anaesth. 2000;84:179–82.
17. Kruyt ND, Biessels GJ, Devries JH, Roos YB. Hyperglycemia in acute ischemic stroke: pathophysiology and clinical management. Nat Rev Neurol. 2010;6(3):145–55.
18. Mercado M, Ramirez-Renteria C. Metabolic complications of acromegaly. Front Horm Res. 2018;49:20–8.

Question 5

19. Goldberg MD, Vadera N, Yandrapalli S, Frishman WH. Acromegalic cardiomyopathy. An overview of risk factors, clinical manifestations, and therapeutic options. Cardiol Rev. 2019;26:307–11.
20. Agastas L, Muri M, Clark N. Heart disease in acromegalics. Endocrinol Metab Clin North Am. 1991;20:619.
21. Lie JT. Pathology of the heart in acromegaly: anatomic findings in 27 autopsied patients. Am Heart J. 1980;100:41–52.
22. Kahaly G, Olshausen KV, Mohr-Kahaly S, et al. Arrhythmia profile in acromegaly. Eur Heart J. 1992;13:51–6.
23. Rossi L, Thiene G, Caregaro L, Giordano R, Lauro S. Dysrhythmias blood glucose and fluid balance and sudden death in acromegalic heart disease. Chest. 1977;72:495–8.
24. Vitale G, Galderisi M, Pivonello R, et al. Prevalence and determinants of left ventricular hypertrophy in acromegaly: impact of different methods of indexing left ventricular mass. Clin Endocrinol (Oxf). 2004;60:343–9.
25. Melmed S, Casanueva FF, Klibanski A, et al. A consensus on the diagnosis and treatment of acromegaly complications. Pituitary. 2013;16(3):294–302.
26. Seidman PA, Kofke WA, Policare R, Young M. Anaesthetic complications of acromegaly. Br J Anaesth. 2000;84:179–82.

Question 6

27. Guo X, Gao L, Zhang S, et al. Cardiovascular system changes and related risk factors in acromegaly patients: a case-control study. Int J Endocrinol. 2015;2015:573643.
28. Colao A, Pivonello R, Grasso LF, et al. Determinants of cardiac disease in newly diagnosed patients with acromegaly: results of a 10 year survey study. Eur J Endocrinol. 2011;165:713–21.
29. Colao A, Spinelli L, Marzullo P, et al. High prevalence of cardiac valve disease in acromegaly: an observational, analytical, case-control study. J Clin Endocrinol Metab. 2003;88:3196–201.

Question 7

30. Campkin TV. Radial artery cannulation. Potential hazard in patients with acromegaly. Anaesthesia. 1980;35(10):1008–9.
31. Ben-Shlomo A, Melmed S. Skin manifestations in acromegaly. Clin Dermatol. 2006;24:256–9.

Question 8

32. Schmitt H, Buchfelder M, Radespiel-Troger M, Fahlbusch R. Difficult intubation in acromegalic patients: incidence and predictability. Anesthesiology. 2000;93:110–4.
33. Zhang Y, Guo X, Pei L, et al. High levels of IGF-1 predict difficult intubation of patients with acromegaly. Endocrine. 2017;57:326–34.
34. Hakala P, Randell T, Valli H. Laryngoscopy and fiberoptic intubation in acromegalic patients. Br J Anaesth. 1998;80(3):345–7.

Question 9

35. Killinger Z, Payer J, Lazurova I, Imrich R, Homerova Z, Kuzma M, Rovensky J. Arthropathy in acromegaly. Rheum Dis Clin North Am. 2010;36(4):713–20.
36. Wassenaar MJ, Biermasz NR, Hamdy NA, et al. High prevalence of vertebral fractures despite normal bone mineral density in patients with long-term controlled acromegaly. Eur J Endocrinol. 2011;164:475–83.

Question 10

37. Fatti LM, Scacchi M, Pincelli AI, et al. Prevalence and pathogenesis of sleep apnea and lung disease in acromegaly. Pituitary. 2001;4:259–62.
38. Kitahata LM. Airway difficulties associated with anaesthesia in acromegaly: three case reports. Br J Anaesth. 1971;43:1187–90.
39. Attal P, Chanson P. Endocrine aspects of obstructive sleep apnea. J Clin Endocrinol Metab. 2010;95:483–95.
40. Davi MV, Dalle Carbonare L, Giustina A, et al. Sleep Apnoea syndrome is highly prevalent in acromegaly and only partially reversible after biochemical control of the disease. Eur J Endocrinol. 2008;159(5):533–40.

Question 11

41. Rahimi E, Mariappan R, Tharmaradinam S, et al. Perioperative management and complications in patients with obstructive sleep apnea undergoing transsphenoidal surgery: our institutional experience. J Anaesthesiol Clin Pharmacol. 2014;30(3):351–4.
42. Venkatraghavan L, Perks A. Postoperative management of obstructive sleep apnea after transsphenoidal pituitary surgery. J Neurosurg Anesthesiol. 2009;21:179–80.

Question 12

43. Nemergut EC, Dumont AS, Barry UT, Laws ER. Perioperative management of patients undergoing transsphenoidal pituitary surgery. Anesth Analg. 2005;101:1170–81.
44. Jane JA Jr, Laws ER Jr. The surgical management of pituitary adenomas in a series of 3,093 patients. J Am Coll Surg. 2001;193:651–9.

10 Anesthetic Management of Patients with Craniovertebral Junction Anomalies

Archana Mane and Yarnell Lafortune

Stem Case Terminology

A 2-year-old female presents for surgical correction of a cleft palate. A diagnosis of Kippel-Feil syndrome (KFS) is made in this child. Associated pathology, need for a thorough preoperative assessment, strategy for intraoperative management of the airway and potential issues in the post-operative period are discussed.

Cervical X-ray revealed fusion of C2-C3 vertebrae.

This patient presented an anesthetic challenge for the anesthesiologist.

Question 1:
What is the differential diagnosis?

Answer:
A triad of short neck, low hairline, and limited range of neck movement places KFS as a likely diagnosis. Other diagnoses to consider include Noonan and Turner syndromes, ankylosing spondylitis, and juvenile idiopathic arthritis.

A. Mane (✉)
Department of Anesthesiology, Albany Medical Center, Albany, NY, USA
e-mail: Manea@amc.edu

Y. Lafortune
University of Maryland Upper Chesapeake Health, Bel Air, MD, USA

Albany Medical Center, Albany, NY, USA
e-mail: laforty@amc.edu

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_10

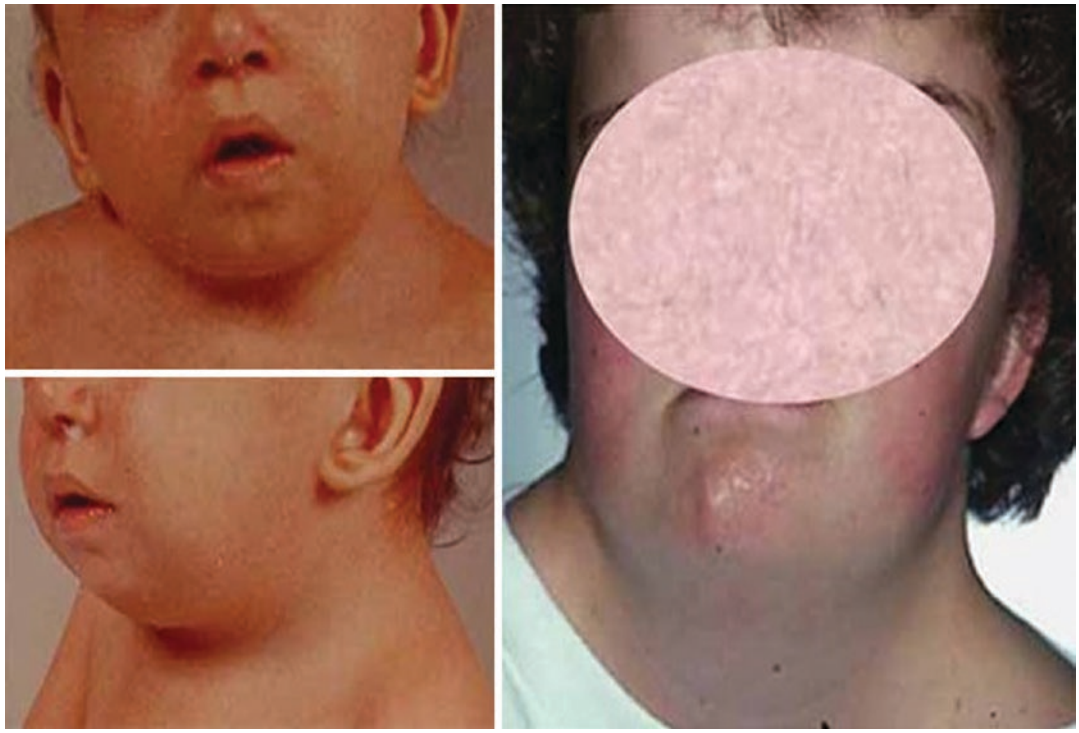


Photo 10.1 Short neck in a child with Noonan syndrome. Elements of Morphology, National Human Genome Research Institute. Use of illustrations from Genetics Home Reference. Your Guide to Understanding Genetics Conditions

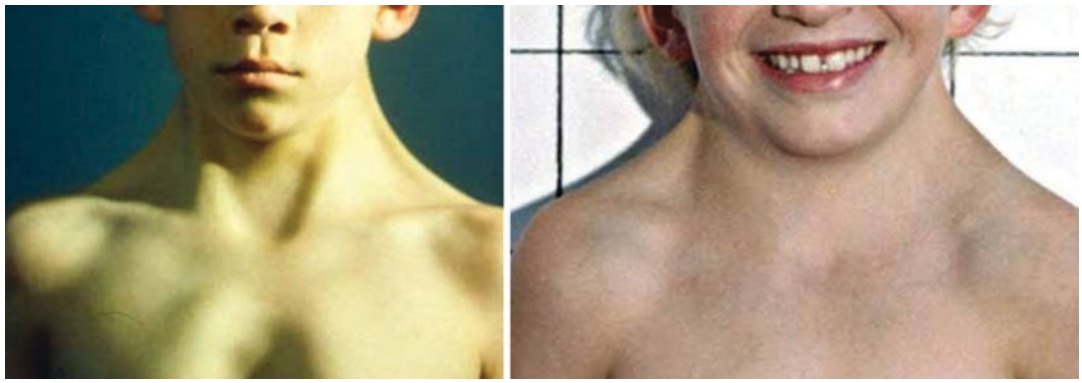


Photo 10.2 Webbed neck in a child with Turner syndrome. Elements of Morphology, National Human Genome Research Institute. Use of illustrations from Genetics Home Reference. Your Guide to Understanding Genetics Conditions

Question 2:
What is KFS?

Answer:
KFS was first reported in 1912 by Maurice Klippel and Andre Feil. It is a rare disorder characterized by the congenital fusion of the first two or more cervical vertebrae. The fused vertebrae can cause nerve damage and pain in the head, neck, or back.

Question 3:
What are the features of patients with KFS?

Answer:
In KFS, classically there is a triad of a short neck, a low posterior hairline, and limited range of neck movements especially of lateral bending. However, it has been found that fewer than 50% of cases have all three elements [1].

In a study performed on 31 patients by Samartzis et al. in 2016, no evidence of any of the clinical triad findings was shown in 35.5% of patients, whereas 38.7, 16.2, and 9.7% were determined to have one, two, or all three criteria, respectively. Limited cervical ROM was the most common finding (64.5% of patients) [2]. Therefore, clinicians should not look solely for the triad for the diagnosis of KFS. However, a high suspicion for KFS is warranted when findings such as congenital scoliosis are present.

A wide variety of additional anomalies affecting different organ systems are associated with KFS. They include but are not limited to: skeletal system abnormalities such as scoliosis and/or kyphosis (50–60%), Sprengel deformity (congenital elevated scapula) (30%), cervical stenosis and torticollis, urinary system abnormalities (35%), loss of hearing (30%), facial asymmetry and flattening of neck (20%), synkinesis or mirror movements (20%), and congenital heart disease (4.2–14%) [3, 4].

Brain stem anomalies, congenital adrenal aplasia, ptosis, lateral rectus muscle paralysis, facial nerve paralysis, syndactilia, and diffuse or focal hypoplasia in the upper extremities may also be seen [5].

Palatal deformities such as clefts are known to be associated with cervical anomalies [6].

Photo 10.3 A child with a severe cervical fusion in KFS. syndromespedia.compicture

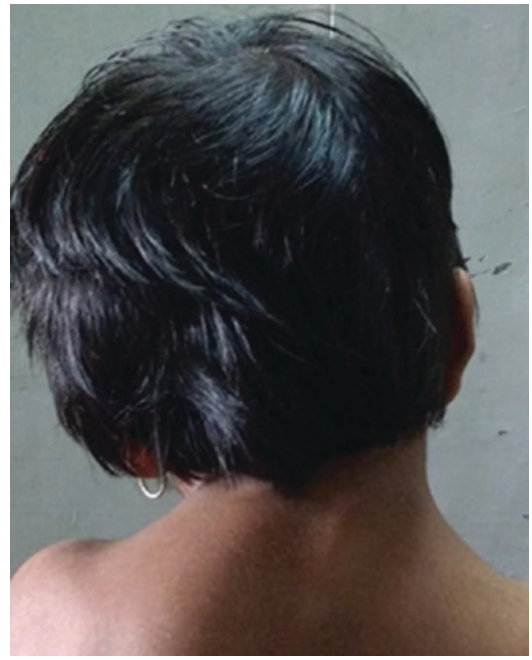


Photo 10.4 Clinical image showing cervical scoliosis to the right, low posterior hair line, and shortened neck. Alapati A, Susheel, Zachariah K, Ravikanth R. Diagnosis and management of Klippel-Feil syndrome. Apollo Med [serial online]. 2018 [cited 2019 Jan 26];15:38–40. http://www.apollomedecine.org/text.asp?2018/15/1/38/229052

Question 4:
What is the incidence and etiology of this disease?

Answer:
KFS occurs in one of every 42,000 births. There is a predominance in females (60%) [1, 6–8].

The etiology is not well understood. There is a genetic component to this disease. There are three main genes that have been linked to KFS: GDF6, GDF3, and MEOX1. The mutation of these genes affects bone development. GDF6 (growth differentiation factor) is located on chromosome 8 and is critical to the healthy formation of cartilage and joints. GDF3 plays an important role in bone formation. During the embryonic stage of human development, MEOX1 plays an integral part in the process of separating the vertebrae. Mutations in the GDF6 and GDF3 genes follow an autosomal dominant pattern. As such, a single copy of the mutated gene is sufficient to

cause the disorder. Conversely, the MEOX1 gene follows an autosomal recessive pattern, requiring two copies of the gene to carry the mutation [9].

Patients with KFS may be polysyndromic. In this situation, KFS results from mutations involved in the genes of the primary syndrome such as Goldenhar syndrome, Wildervanck syndrome, or hemifacial microsomia among others. The prevalence of Goldenhar-associated conditions in patients with congenital spine deformities is 2% [10].

Maternal factors during pregnancy such as diabetes, alcohol, and tobacco use have been implicated in the etiology of KFS [11].

Question 5:
How is KFS classified?

Answer:
Classification of KFS has changed over time. The original classification of the disease was by Klippel and Andre Feil.

Samartzis et al. classified the disease based on the significance of X-ray findings and the impact on clinical symptoms.

- Type I—Single-level fusion
- Type II—Multiple, noncontiguous fusion
- Type III—Multiple, contiguous fused segments

Those with a type I deformity had more axial symptoms while those with type II and type III deformities were the patients who developed myelopathy and radiculopathy [12].

10.1 Preoperative

Question 6:
What are the preoperative tests that should be performed on patients with KFS?

Answer:
Preoperative assessment in patients with craniovertebral anomalies should be directed at evaluating degree of cervical instability present, preexisting neurologic impairment, and evaluation of airway.

X-ray: Anteroposterior (AP), lateral, and odontoid views of the cervical spine. Images will show the fusion of vertebral bodies and facets, and other anomalies such as spina bifida or hemivertebrae. In addition, flexion/extension views are warranted if instability of the craniocervical junction is suspected or if two fused segments are separated by an open segment (making the lesion unstable). Plain films of the total spine should also be obtained to detect any other spinal anomalies.

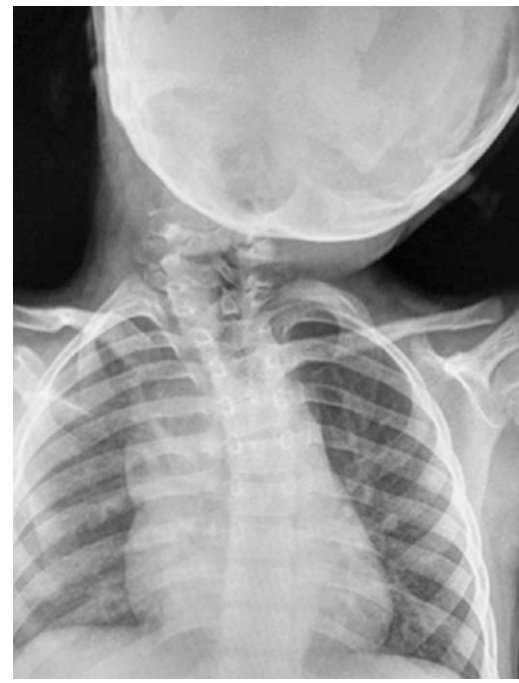


Photo 10.5 Plain radiograph demonstrating the fusion of cervical vertebrae with cervico-dorsal scoliosis. Alapati A, Susheel, Zachariah K, Ravikanth R. Diagnosis and management of Klippel-Feil syndrome. Apollo Med [serial online]. 2018 [cited 2019 Jan 26];15:38–40. http://www.apollomedecine.org/text.asp?2018/15/1/38/229052

Computed tomography (CT) scan: A 3-D image better defines areas of fusion and aids the surgical plan.

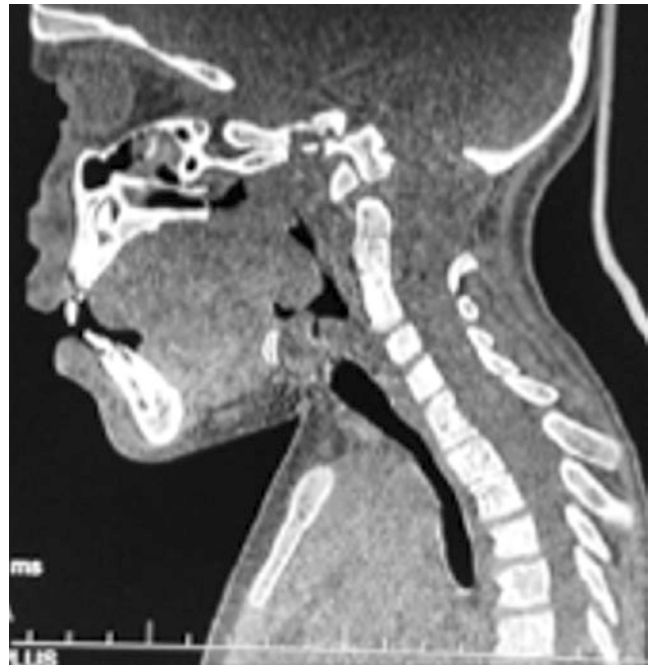


Photo 10.6 Sagittal CT image of the cervical spine showing fusion of C2 and C3 vertebrae. Alapati A, Susheel, Zachariah K, Ravikanth R. Diagnosis and management of Klippel-Feil syndrome. Apollo Med [serial online]. 2018 [cited 2019 Jan 26];15:38–40. http://www.apollomedecine.org/text.asp?2018/15/1/38/229052

Magnetic resonance imaging: MRI is indicated for patients with neurologic deficits. MRI will provide better insight regarding the spinal cord, disc space, nerve rootlets, ligaments and soft tissue, and can illustrate other spinal cord abnormalities such as Chiari malformations and syringomyelia [13].

EOS: EOS imaging is an X-ray imaging system that takes a full body picture in an upright posture showing the child's natural, weight-bearing posture and allowing the clinician to see the interaction between the joints and the rest of the musculoskeletal system, particularly the spine, hips, and legs. It has the additional advantage being a fast study using low dose radiation as compared to a CT scan [14].

Cardiac evaluation: Physical exam is to detect murmurs and echocardiography is to diagnose cardiac function and associated cardiac defects, VSD being the commonest [15].

Audiology testing: Studies have reported the incidence of deafness in patients with KPS to be high. In a study done by McGaughran et al., 35 out of 44 patients with KFS showed abnormalities on audiological testing [16]. Deafness may be conductive, sensorineural, or a mixed type.

Audiology testing is therefore necessary in patients who present with the clinical triad of KFS or exhibit any features or suspicions of having the disease.

Renal ultrasound: Renal ultrasound is used as a screening tool to evaluate the presence of genitourinary anomalies, which may include renal or ureteral agenesis among others [17].

Ultrasound: This study may be done during pregnancy to detect anomalies suspicious of KFS in the developing fetus [18].

10.2 Intraoperative

Question 7:
How would you proceed in your preparation to successfully intubate this child?

Answer:
Golden rules for the anticipated difficult intubation include:

1. All airway equipment should be available in the operating room.
2. Presence of additional anesthesia staff for assistance.
3. Clear communication with the parent/child and surgeon about the initial and alternate plan for airway management, including a tracheostomy.

The ability to induce smoothly is important in order to prevent sudden neck movements; a small sedative pre-medication such as oral midazolam in a dose of 0.3–0.5 mg/kg may be used. Having a dry visual field with the use of antimuscarinics would prove to be helpful in a difficult airway scenario. The principle of managing the difficult airway in this age group is to maintain spontaneous ventilation until the airway is secure. The use of an inhalational technique with sevoflurane in 100% oxygen is favored in pediatric practice. Laryngoscopy is performed when an adequate depth of anesthesia is achieved. The child may then be intubated with a glidescope, fiberoptic bronchoscope (FOB), or a combination of both [19].

The nasal route may be necessary if access to the airway through the mouth is impossible [20].

An awake intubation with a FOB should be considered when the anesthesia provider is concerned of losing the airway during an inhalational induction (obstruction, inability to ventilate by mask) [21, 22].

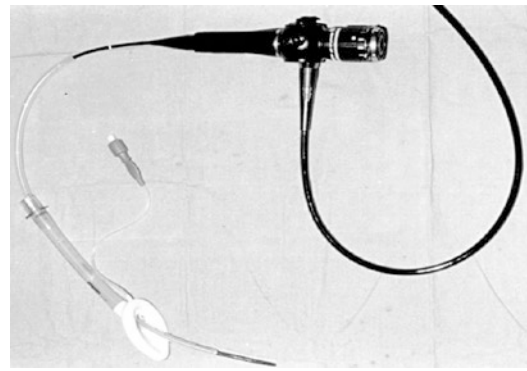
Dexmedetomidine has become an increasingly popular and useful drug to provide sedation and maintain spontaneous ventilation. Its use in pediatrics has increased over the last decade for sedation cases, intubations, and as an adjunct for intraoperative anesthesia. For anesthetic induction, 1 μg/kg dexmedetomidine may be loaded intravenously, followed by an infusion rate of 0.7 μg/kg/h with incremental inhalation of sevoflurane maintaining spontaneous ventilation [23].

Alternately, high doses of dexmedetomidine have been used. Green et al. described using a bolus dose of 2 μg/kg IV (administered over 10 min) followed by an infusion of 2 μg/kg/h. Prior to direct laryngoscopy, ketamine 1 mg/kg IV was administered and good relaxation of the mouth was noted. This alternative technique of adding ketamine avoids apnea and airway obstruction which can be seen if dexmedetomidine is not enough to adequately anesthetize the child when the airway is accessed and agents such as propofol and inhalational agents may be needed [24].

Once an adequate depth of anesthesia is achieved under dexmedetomidine, a glidescope or a flexible FOB could be used to instrument the airway.

The intubating laryngeal mask airway has been effectively used as an aid for fiberoptic intubation [25]. Its rigid curved structure is designed to facilitate tracheal intubation. The LMA can be used in an awake child after administering local anesthesia to the mouth and pharynx or in the anesthetized child with known or suspected difficult airway.

It would be advisable to ensure the ability to mask ventilate the child prior to giving paralytic agents [26].



Additional difficulty in airway access may be complicated by presence of mandibular and facial deformities, torticollis, and presence of anatomical abnormalities such as cleft palates, and congenital scoliosis of the neck and other portions of the spine (most common 60%) [27, 28].

Question 8:
Describe other intraoperative considerations in the anesthetic management of patients with craniovertebral anomalies.

Answer:
- Patient positioning.
- Neurological monitoring.
- Blood loss.
- Respiratory involvement such as presence of associated weakness and dysfunction of respiratory muscles, including the diaphragm, making extubation in the OR difficult, compression of medulla due to bony anomalies resulting in poor gag and cough reflex resulting in frequent aspiration and pulmonary infection [29].

Patient positioning: Surgical approaches to correct craniovertebral anomalies may be done with the patient in a prone or sitting position. Positioning of the patient can therefore be dangerous and must be done very carefully [29, 30].

When surgery is performed in the sitting position, the patient's head is secured in a three pin head holder. Legs are placed in thigh high compression stockings to limit pooling of blood. Elbows need to be supported by pillows or pads, and the legs freed of pressure at the level of common peroneal nerve just distal and lateral to the head of fibula. Meticulous care should be taken to avoid sudden neck movements.

Perioperative visual loss has been reported up to an incidence of 0.2%. Multiple factors have been proposed as risk factors for perioperative ION, including long duration in the prone position, excessive blood loss, hypotension, anemia, hypoxia, excessive fluid replacement, use of vasoconstricting agents, elevated venous pressure, and head positioning [31].

Excessive pressure on the abdomen could impede ventilation, compress the vena cava, and increase epidural venous pressure and bleeding. There may be congestion of the face and tongue, and pressure sores on malar prominences owing to the horseshoe headrest. Extreme flexion of the neck may cause endobronchial intubation because of a short trachea and intraoral kinking of the endotracheal tube (ETT); here armored ETTs are preferred. Excessive flexion or extension of head may cause brainstem compression in patients with Arnold–Chiari malformation [32].

Neurological monitoring: Spinal surgery at any level is associated with a higher risk of spinal cord injury.

"Real time" intraoperative neural monitoring (IONM) utilizing somatosensory evoked potentials along with MEP and EMG should be routine as discussed in an extensive review done by Epstein in 2013. SSEP monitoring as the sole method is inadequate.

Quadriparesis/quadriplegia following a single level anterior cervical diskectomy and fusion (ACDF) is the most common cause for malpractice suits. Typical allegations in these suits included negligent surgery, lack of informed consent, failure to diagnose/treat, and failure to brace. Added to this list, perhaps, the fifth common reason for a lawsuit is failure to monitor with MEP [33].

In CVJ surgery, the risk of neurological injuries is related both to positioning of the patient and then to the surgical procedure. A 2019 study by Sala et al. found a 100% sensitivity with MEPs for detecting injuries to the cervical spine related to neck positioning [34]. These authors also recommend the use of multimodal IONM for detecting intraoperative and neurologic

injuries from positioning. Continuous IONM also permits real-time assessment of the functional integrity of the spinal tracts, which provides useful feedback during surgical maneuvers.

The monitoring team must be well trained, be able to provide the surgeon feedback in real time, and coordinate activities with those of the surgical and anesthesia teams [35, 36].

Blood loss: Blood loss in spine surgery has a significant impact on patient morbidity, length of surgery, and total cost. In addition to maintaining patients' hemodynamics, the control of blood loss is essential in attaining adequate visualization of the surgical field. Vigilance is essential to determine adequate fluid resuscitation in order to maintain cerebral perfusion and management of blood loss with adequate blood transfusions in spite of the drawbacks of transfusion (i.e., immunotolerance and immunosuppression, which in turn predispose to nosocomial and postoperative infections) [37].

The incidence of pulmonary complications was significantly more in adults patients who received blood transfusion during the intraoperative period 15.7%. Blood transfusion is considered to be an independent risk factor for the development of postoperative pulmonary complications (PPCs) [38]. Incidence of TRALI in the pediatric population is not well defined and information is obtained only from reports that have been published. The overall incidence of TRALI in this latter group of patients is estimated at 1.8 per 100,000 transfusions [39].

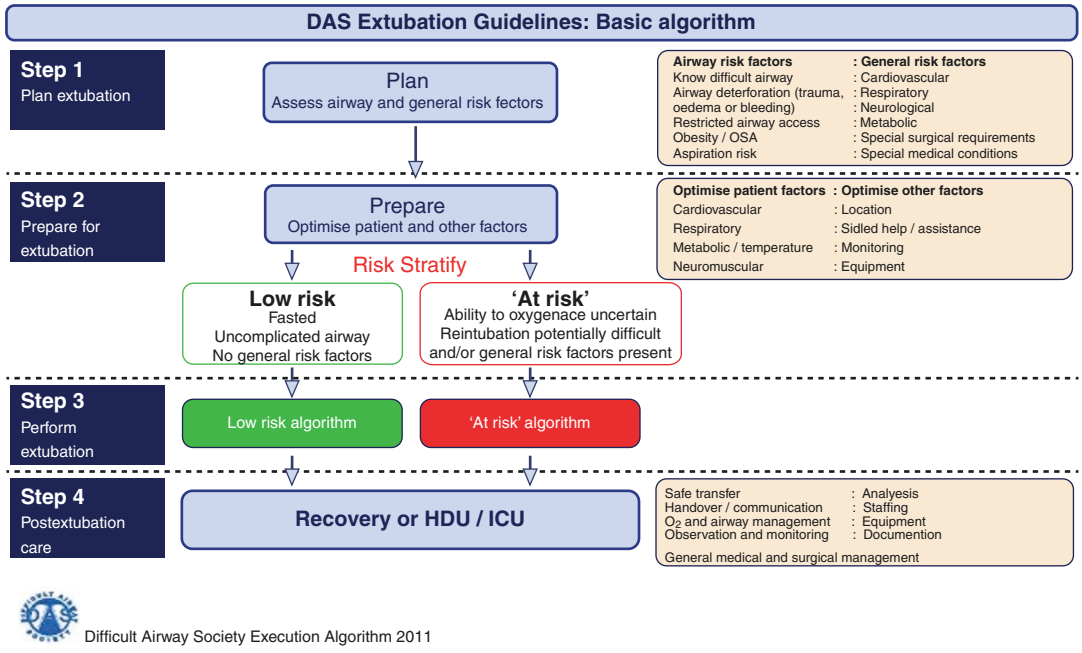
10.3 Postoperative

Emergence and extubation: Planning for tracheal extubation is a critical component of a successful airway management strategy. Pharyngeal edema, vocal cord paralysis, and hematoma formation are known causes of airway obstruction after cervical spine surgery frequently associated with difficult airway management. Use of intraoperative steroids, full reversal of the muscle relaxant, and placement of a nasopharyngeal airway to reduce upper airway obstruction after extubation should be considered if possible. Extubation should be performed in an area where the patient can be reintubated if necessary and where all essential fiberoptic equipment and specialized personnel are available. In the high-risk patient, ENT support for emergency tracheostomy may be needed. A carefully positioned tube changer introduced through the ETT can be used to allow reintubation. This may serve as a bridge device when successful extubation is uncertain; however, its use may promote obstruction and airway irritation in an already severely narrowed airway. The anesthesiologist however must be vigilant for the presence of respiratory weakness and weakened cough reflex when determining the possibility of extubation [40].

Postponing extubation for a few hours, or in some cases for a few days, may be the most appropriate course of action [41].

Patients are best extubated when they are fully awake, reversed and breathing adequately and moving deliberately, early after surgery. The efficacy and safety of 3 mg/kg of sugammadex was reported in a study of 26 infants who had a deep neuromuscular block (TOF, 0) at the end of surgery received 3 mg/kg sugammadex. The mean recovery time of the T4/T1 ratio of 0.9 was 112 s. No clinical evidence of recurarization or residual curarization was observed [42].

Compared with placebo or neostigmine, sugammadex can reverse rocuronium-induced neuromuscular blockade more rapidly with lower incidence of bradycardia. No significant differences were found in the incidences of other adverse events [43].



Since the introduction of the Difficult Airway Society difficult intubation guidelines, the concept of a stepwise approach has been widely accepted. This approach has been used to aid decision-making and safe management of extubation [44].

A reliable method of assessing readiness for weaning and predicting extubation success is not evident from the pediatric literature. Several indices have been developed in an attempt to predict weaning and extubation success but the available literature would suggest they offer no improvement over clinical judgment. Upper airway obstruction is the single most common cause of extubation failure [45]. Laham et al. report that physician judgment to determine extubation readiness led to a first planned extubation success rate of 91% [46].

Patients who do not meet the criteria for extubation in the operating room are ventilated in the intensive care unit (ICU). Rates of reintubation in the operating room and post-anesthesia care unit have been shown to be between 0.1 and 0.45%. Conditions such as obesity, obstructive sleep apnea, major head/neck and upper airway surgery, and obstetric and cervical spine procedures contribute significantly to extubation failure and are frequently associated with difficult airway management. Airway patency, edema, soft tissue collapse, and laryngospasm are among the most frequent mechanisms of upper airway obstruction. Therefore adequate planning requires identification of patients who have or may develop a difficult airway, recognition of patients at increased risk of post-extubation airway compromise, and understanding the causes and underlying mechanisms of extubation failure.

Adult dosage range of 0.2 to 0.7 μg/kg/h may also be used in children. Dexmedetomidine may be initiated with a loading dose of 1 μg/kg given over 10 min, but some pediatric centers reduce or omit the loading dose in an effort to avoid bradycardia and hypotension. The infusion should be titrated to patient response, with a suggested maximum dose of 2 μg/kg/h dexmedetomidine. The use of the drug has been shown to reduce duration of mechanical ventilation and lowering the risk of delirium in ICU ventilated adult patients as compared to midazolam when utilized to sedate patients [47].

Patients for whom reintubation is likely to be difficult may benefit from continuous airway access. Sizes of the CAEC are based on the size of the existing ETT. Sizes 8 (internal diameter [ID] 1.6 mm), 11 (2.3 mm ID), and 14 (3.0 mm ID) CAECs were used for ETT sizes 3.5–4.5, 5.0–6.0, and 6.5–7.0 mm ID, respectively. Sizes may not be readily available. Most of the morbidity attributed to their use is associated with oxygenation and inappropriate positioning [48].

Treatment modalities for patients with KFS and other cranial-cervical abnormalities: Treatment of patients with KFS calls for a multidisciplinary approach which is typically conservative and patient driven. Soft collars and braces are used to stabilize the cervical region. In addition, physical therapy, use of orthotics, and prosthetics play an important role in patient care whether they undergo surgery or not [49, 50].

In the presence of cord compromise or new-onset neurologic changes surgery and immobilization is warranted. Neurosurgery with spinal decompression and untethering of the spinal cord, and lysis of adhesions with electrophysiologic monitoring. Postoperatively, patients wear a halo vest for approximately 3 months, followed by a soft cervical collar for 3 months.

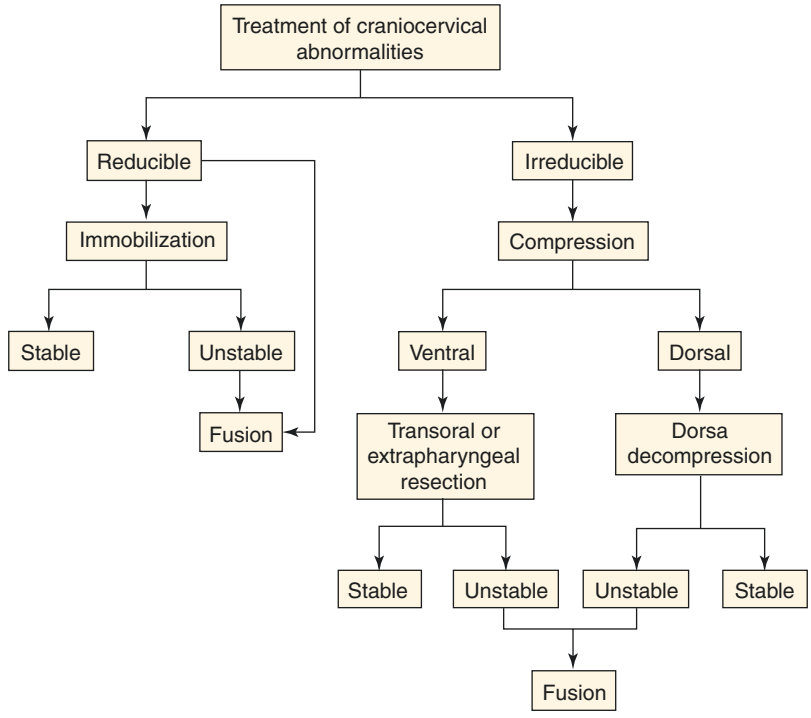
Arnold–Chiari malformation and myelomeningocele repair. Orthopedic surgery may be consulted for scoliosis repair and spinal stenosis decompression. Cosmetic scapuloplasty for Sprengel deformity.

Oral and maxillofacial surgery for cleft palate and associated craniofacial deformities [51].

In patients where alignment cannot be fully restored by traction or when improving the alignment alone does not fully decompress the neural elements, osseous decompression at the site of the cervical lesion and untethering of intradural adhesions as well as adhesions between the thecal sac and extraspinal structures are performed. Finally, if instability is suspected, internal fixation and arthrodesis is required [52]. The early operative procedures were posterior decompression of the cervicomedullary junction for correction of craniocervical stenosis with and without fusion for silization.

In recent years, anterior, transpalatine-transoral and extrapharyngeal approaches are used by surgeons depending on the exact location of the lesion. The operation or combination of operations must be selected on an individual basis to correct the pathologic process responsible for the neurologic deficit [53].

Alapati A, Susheel, Zachariah K, Ravikanth R. Diagnosis and management of Klippel–Feil syndrome. Apollo Med. 2018;15:38–40.



Additional surgeries for Arnold–Chiari malformation and myelomeningocele repair may be needed as well as orthopedic surgery may be consulted for scoliosis repair and spinal stenosis decompression. Cleft palate repair is another common surgery in children with KFS.

Multiple Choice Questions

1. A 12-year-old female presents with headache and neck pain that has been increasing in severity over the past month. There have not been any associated symptoms of nausea, vomiting, or visual changes. MRI of the brain revealed downward displacement of cerebellar tonsils. What is the most likely diagnosis?
(a) Migraine headaches
(b) Chiari malformation
(c) Meningioma
(d) Meningitis
Answer: b

It results from anatomical abnormalities of the posterior fossa leading to caudal displacement of the cerebellar vermis through

the foramen magnum. (Smiths) Classification is based on morphology of the malformation as evidenced radiographically or on autopsy (see Table).

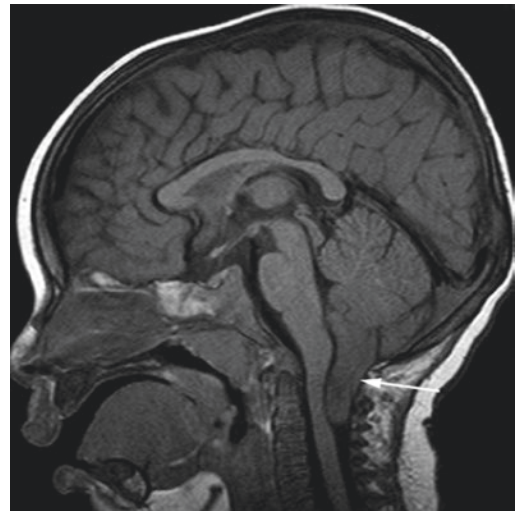
Chiari malformations
Chiari Type I Tonsillar herniation >5 mm below the plane of the foramen magnum No associated brainstem herniation or supratentorial anomalies Low frequency of hydrocephalus *Most common and less severe* 1:1000 births Most common presentation is suboccipital headaches and/or neck pain
Chiari Type II Caudal herniation of the vermis, brainstem, and fourth ventricle Associated with myelomeningocele and multiple brain anomalies High frequency of hydrocephalus and syringohydromyelia
Chiari Type III Occipital encephalocele containing dysmorphic cerebellar and brainstem tissue
Chiari Type IV Hypoplasia or aplasia of the cerebellum

Adapted from Smith's anesthesia for children and infants, 8th ed. Chapter 22

There are two main mechanisms that result in the presentation of neurological signs and symptoms. One mechanism is that the downward displacement of the cerebellar tonsils can compress against the foramen magnum and spinal canal. Secondly, via the development of a syrinx from obstruction of cerebrospinal fluid (CSF) outflow [54].

Diagnosis is made primarily by history, physical examination, and MRI.

Chiari I malformation showing descent of the cerebellar tonsils



A sagittal T1-weighted MRI of the brain shows the low-lying and elongated cerebellar tonsils (arrow), which are displaced below the level of the foramen magnum.

MRI: magnetic resonance imaging.

Courtesy of Eric D Schwartz, MD. UpToDate®

Adapted from UpToDate [55].

2. What are the treatment options for this patient?
   (a) Nonsteroidal anti-inflammatory drugs (NSAIDs)
   (b) Cervical collar
   (c) Surgical decompression
   (d) All of the above

Answer: d

Management options for patients with Chiari malformation are dependent upon the presenting symptoms. A patient presenting with headache and neck pain may benefit from the use of NSAIDs, muscle relaxants, and the temporary use of a cervical collar.

However, with more severe symptoms such as gait abnormalities, medical management will not offer resolution. The main treatment for Chiari malformation is surgical with the goal of re-establishing the CSF flow across the craniovertebral junction and decompressing the nervous system elements [56–58].

Patients with Chiari malformation typically present for decompressive suboccipital craniectomy with duraplasty. The procedure is performed in the prone position with intraoperative neuromonitoring. Positioning is important as excessive flexion can result in brainstem compression. The potential anesthetic complications include vocal cord paralysis, stridor, respiratory distress, apnea, abnormal swallowing, recurrent aspiration pneumonia, possible increase in intracranial pressure, unstable blood pressure, weakness, and paralysis [59].

3. Which of the following syndromes are associated with craniovertebral junction anomalies?
   (a) Trisomy 13
   (b) Trisomy 18
   (c) Trisomy 21
   (d) None of the above

   Answer: c

   Trisomy 21 also referred to as Down's syndrome is a multisystemic chromosomal disorder. The table below lists some of the many clinical manifestations. About 10–30% of people with Down's syndrome have atlantoaxial instability, which is defined as increased mobility of the cervical spine at C1 and C2; this can lead to subluxation of the cervical spine. Most are asymptomatic; however, 10% of individuals with atlantoaxial instability have neck pain, torticollis, gait changes, changes in bowel or bladder control, or other signs of paralysis or weakness [60–62].

Organ system	Clinical manifestation
Airway	High arched narrow palate, subglottic stenosis, macroglossia, **atlantoaxial subluxation**, narrow tracheal lumen
Central nervous system	Mental retardation, altered response to opioids, hypotonia
Cardiovascular system	Congenital heart disease (tetralogy of fallot, ventricular septal defect, endocardial cushion defects, patent ductus arteriosus), predisposition to pulmonary hypertension, bradycardia with inhaled induction, difficult intravenous catheter placement
Endocrine/ hematologic	Hypothyroidism, immunosuppression
Gastrointestinal	Duodenal atresia, Hirschsprung disease, gastroesophageal reflux
Pulmonary	Obstructive sleep apnea

Gregory GA, Andropoulos DB. Gregory's pediatric anesthesia. 5th ed. [63]

4. Which of the following are acquired anomalies of the craniovertebral junction?
   (a) KFS
   (b) Trisomy 21
   (c) Rheumatoid arthritis
   (d) All of the above

   Answer: c

   Acquired anomalies of the craniovertebral junction can occur secondary to trauma to the bones or the supporting ligaments of

the craniovertebral junction. Other etiologies include inflammatory conditions such as rheumatoid arthritis and ankylosing spondylitis. Malignancies such as chondrosarcoma, multiple myeloma, and metastatic deposits can also affect the craniovertebral junction. KFS and Trisomy 21 are congenital anomalies of the craniovertebral junction [64].

References

1. Pledger SR. Cervical spine disease. Ortho secrets. 3rd ed. 2003.
2. Samartzis D, Kalluri P, Herman J, Lubicky JP, Shen FH. "Clinical triad" findings in pediatric Klippel-Feil patients Scoliosis. Spinal Disord. 2016;11:15. https://doi.org/10.1186/s13013-016-0075-x. Published online 2016 Jun 27. PMCID: PMC4922059.
3. Agarwal AK, Goel M, Bajpai J, Shukla S, Sachdeva N, et al. J Orthop Case Rep. 2014;4(3):53–5. PMCID: PMC4719329 PMID: 27298984.
4. Zaki SA, Shenoy P, Shanbag P. Klippel Feil syndrome with isolated hypokinesia of the left ventricle: a rare association. Ann Pediatr Cardiol. 2010;3(1):92. https://doi.org/10.4103/0974-2069.64354. PMCID: PMC2921529 PMID: 20814486.
5. Mahiroğullari M, Ozkan H, Yildirim N, Cilli F, Güdemez E. Klippel-Feil syndrome and associated congenital abnormalities: evaluation of 23 cases. Acta Orthop Traumatol Turc. 2006;40(3):234–9. PMID: 16905897.
6. Srivastava M, Aggarwal A, Batra P, Datana S, Kumar P, Macrcusson KA. Association of cervical vertrebra anomalies with cleft lip and palate. J Cleft Lip Palate Craniofac Anomalies. 2014;1(1):43–7.
7. Klippel-Feil syndrome. Genetics home reference. June 2015. http://ghr.nlm.nih.gov/condition/klippel-feil-syndrome.
8. Kaplan KM, Spivak JM, Bendo JA. Embryology of the spine and associated congenital abnormalities. Spine J. 2005;5:564–76. Review Article
9. Tassabehji M, Fang ZM, Hilton EN, McGaughran J, Zhao Z, de Bock CE, Howard E, Malass M, Donnai D, Diwan A, Manson FD, Murrell D, Clarke RA. Mutations in GDF6 are associated with vertebral segmentation defects in Klippel-Feil syndromes. Hum Mutat. 2008;29:1017–27. https://doi.org/10.1002/humu.20741.
10. Tsirikos AI, McMaster MJ. Goldenhar-associated conditions (hemifacial microsomia) and congenital deformities of the spine. Spine. 2006;31(13):E400–7. https://doi.org/10.1097/01.brs.0000219876.45640.2a.
11. Giampietro PF, Raggio CL, Blank RD, McCarty C, Broeckel U, Pickart MA. Clinical, genetic and environmental factors associated with congenital vertebral malformations. Mol Syndromol. 2013;4(1–2):94–105. https://doi.org/10.1159/000345329. Published online 2012 Nov 15. PMCID: PMC3638777 PMID: 23653580.
12. Samartzis DD, Herman J, Lubicky JP, Shen FH. Classification of congenitally fused cervical patterns in Klippel-Feil patients: epidemiology and role in the development of cervical spine-related symptoms. Spine. 2006;31(21):E798–804**. [**PubMed**].**
13. Menger RP, Notaranni C. Klippel Feil syndrome. STATPEARLS(Internet). Last Update: October 27, 2018.
14. Wybier M, Bossard P. Musculoskeletal imaging in progress: the EOS imaging system. Joint Bone Spine. 2013;80(3):238–43. https://doi.org/10.1016/j.jbspin.2012.09.018. Epub 2012 Nov 22. PMID: 23177915.
15. Masuda H, Arikawa K, Yuda T, Taira A. Total anomalous pulmonary venous connection associated with Klippel-Feil syndrome: a case report. [Article in Japanese]. Kyobu Geka. 1991;44(5):417–20.
16. McGaughran JM, Kuna P, Das V. Audiological abnormalities in the Klippel-Feil syndrome. Arch Dis Child. 1998;79:352–5.
17. Vaidyanathan S, Hughes PL, Soni BM, Singh G, Sett P. Klippel-Feil syndrome—the risk of cervical spinal cord injury: a case report. BMC Fam Pract. 2002;3:6. https://doi.org/10.1186/1471-2296-3-6. © Published: 11 April 2002.
18. www.thefetus.net
19. Adewale L. Review article: anatomy and assessment of the pediatric airway. Pediatr Anesth. 2009;19(Suppl.1):1–8. Robert W M Walker Management of the difficult airway in children J R Soc Med. 2001 Jul; 94(7): 341–344. PMCID: PMC128159821.
20. Walker RW, Ellwood J. The management of difficult intubation in children. Pediatr Anesth. 2009;19(Suppl 1):77–87. https://doi.org/10.1111/j.1460-9592.2009.03014.x.
21. Chura M, Odo N, Foley E, Bora V. Cervical deformity and potential difficult airway management in Klippel–Feil syndrome. Anesthesiology. 2018;V128(5):1007.
22. Ramkumar V. Preparation of the patient and the airway for awake intubation. Indian J Anaesth. 2011;55(5):442–7. https://doi.org/10.4103/0019-5049.89863. PMCID: PMC3237141 PMID: 22174458.
23. The use of dexmedetomidine and Airwayscope in airway ...—NCBI https://www.ncbi.nlm.nih.gov/pubmed/25098144 by A Furuya—2014 fetanyl. Dexmedetomidine infusion was also useful to maintain adequate spontaneous breathing and to achieve awaking before extubation.
24. Green M, Chatterjee D, Meyers M. High dose dexmedetomidine and ketamine for managing difficult pediatric airways. J Anesth Clin Res. 2016;7:652. https://doi.org/10.4172/2155-6148.1000652.
25. Walker RWM. Consultant Paediatric Anaesthetist, Royal Manchester Children's Hospital, Pendlebury, Manchester M27 4HA.

26. Walker RWM. Management of the difficult airway in children. FRCA J R Soc Med. 2001;94(7):341–4.
27. Ramesh S, Jayanthi R. Supraglottic airway devices in children. Indian J Anaesth. 2011;55(5):476–82.
28. Raj D, Luginbuehl I. Managing the difficult airway in the syndromic child. Contin Educ Anaesth Crit Care Pain. 2015;15(1):7–13.
29. Desalu I, Adeyemo WL, Akintimoye MO, Adepoju AA. Airway and respiratory complications in children undergoing cleft lip and palate repair. Ghana Med J. 2010;44(1):16–20. PMCID: PMC2956308 PMID: 21326986.
30. Tracy MR, Dormans JP, Kusumi K. Klippel-Feil syndrome: clinical features and current understanding of etiology. Clin Orthop Relat Res. 2004;424:183–90.
31. Mascarenhas O. Anaesthesia management in craniovertebral junction anomalies. J Craniovertebr Junct Spine. 2016;7(4):193–6.
32. https://www.openanesthesia.org/unilateral_blindness_etiology/
33. Jain VK, Behari S. Management of congenital atlanto -axial dislocation: some lessons learnt. Neurol India. 2002;50:386–97.
34. Epstein NE. Surg Neurol Int. 2013;4(Suppl 5):S383–91. Published online 2013 Oct 29. https://doi.org/10.4103/2152-7806.120782.
35. Sala F, Meneghelli P. Intraoperative neurophysiological monitoring for craniovertebral junction surgery. Acta Neurochir Suppl. 2019;125:369–80. https://doi.org/10.1007/978-3-319-62515-7_53.
36. Stecker MM. A review of intraoperative monitoring for spinal surgery. Surg Neurol Int. 2012;3(Suppl 3):S174–87. Published online 2012 Jul 17. https://doi.org/10.4103/2152-7806.98579. PMCID: PMC3422092 PMID: 22905324.
37. Hill GE, Frawley WH, Griffith KE, Forestner JE, Minei JP. Allogeneic blood transfusion increases the risk of post-operative bacterial infection: a meta-analysis. J Trauma. 2003;54:908–14. [PubMed].
38. Mascarenhas O. Anaesthesia management in craniovertebral junctional anomalies. J Craniovertebr Junct Spine. 2016;7(4):193–6. https://doi.org/10.4103/0974-8237.193256.
39. Gauvin F, Robillard P, Hume H, Grenier D, Whyte RK, Webert KE, Fergusson D, Lau W, Froese N, Delage G. Transfusion-related acute lung injury in the Canadian paediatric population. 2012;17(5):235–9. PMCID: PMC3381913 PMID: 23633895.
40. Rosomoff HL. Occult respiratory and autonomic dysfunction in craniovertebral anomalies and upper cervical spinal disease. Spine (Phila Pa 1976). 1986;11(4):345–7.
41. Hase Y, Kamekura N, Fujisawa T, Fukushima K. Repeated anesthetic management for a patient with Klippel-Feil syndrome. Anesth Prog. 2014;61(3):103–6.
42. Ozmete O, Bali C, Cok OY, Turk HE, Ozyilkan NB, Civi S, Aribogan A. Sugammadex given for rocuronium-induced neuromuscular blockade in infants: a retrospective study. J Clin Anesth. 2016;35:497–501.
43. Liu G, Wang R, Yan Y, Fan L, Xue J, Wang T. The and safety of sugammadex for reversing postoperative residual neuromuscular blockade in pediatric patients: a systematic review. Sci Rep. 2017;7(1):5724. https://doi.org/10.1038/s41598-017-06159-2.
44. Newth CJ, Venkataraman S, Willson DF, Meert KL, Harrison R, Dean JM, Pollack M, Zimmerman J, Anand KJ, Carcillo JA, Nicholson CE, Eunice Shriver Kennedy National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Weaning and extubation readiness in pediatric patients. Pediatr Crit Care Med. 2009;10(1):1–11. https://doi.org/10.1097/PCC.0b013e318193724d.
45. Laham JL, Breheny PJ, Rush A. Do clinical parameters predict first planned extubation outcome in the pediatric intensive care unit? J Intensive Care Med. 2015;30(2):89–96. https://doi.org/10.1177/0885066613494338. Epub 2013 Jun 27.
46. Cavallone LF, Vannucci A. Review article: extubation of the difficult airway and extubation failure. Anesth Analg. 2013;116(2):368–83. https://doi.org/10.1213/ANE.0b013e31827ab572. Epub 2013 Jan PMID: 23302983.
47. Buck ML. Dexmedetomidine use in pediatric intensive care and procedural sedation. J Pediatr Pharmacol Ther. 2010;15(1):17–29. PMCID: PMC3017406 PMID.
48. Faberowski L, Nargozian C. Utility of airway exchange catheters in pediatric patients with a known difficult airway. Pediatr Crit Care Med. 2005;6(4):454–6.
49. Dokai T, Nagashima H, Nanjo Y, Tanida A, Teshima R. Posterior occipitocervical fixation under skull-femoral traction for the treatment of basilar impression in a child with Klippel-Feil syndrome. J Bone Joint Surg Br. 2011;93(11):1571–4.
50. Menezes A, Lindley T. Craniovertebral abnormalities and their neurosurgical management. Last modified 13 Mar 2015, Chapter 181.
51. Craniocervical junction abnormalities, MERCK manual. By Michael Rubin, MDCM, Photo courtesy of Depuy/Synthes. Ref -Clinical Gate, Filed under Neurosurgery.
52. Morota N. Pediatric craniovertebral junction surgery. Neurol Med Chir (Tokyo). 2017;57(9):435–60 . Published online 2017 Aug 1. PMCID: PMC5638788 PMID: 28768919. https://doi.org/10.2176/nmc.ra.2017-0032.
53. Dickman CA, Spetzler RF, Sonntag VKH. In: Bambakidis N, Dickman C, Spetzler R, et al., editors. Surgery of the craniovertebral junction. 2nd ed. New York: Thieme; 2012. https://doi.org/10.1055/b-002-85485.
54. Dlouhy BJ, Dawson JD, Menezes AH. Intradural pathology and pathophysiology associated with Chiari I malformation in children and adults with

and without syringomyelia. J Neurosurg Pediatr. 2017;20(6):526–41.
55. https://www.uptodate.com/contents/image?imageKey=NEURO%2F68681&topicKey=NEURO%2F13507&search=chiari%20malformation&source=outline_link&selectedTitle=1~118. Accessed 8 Jan 2019.
56. Hidalgo JA, Varacallo M. Arnold Chiari malformation. Treasure Island, FL: StatPearls Publishing; 2018.
57. Lin W, Duan G, Xie J, Shao J, Wang Z, Jiao B. Comparison of results between posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation type I: a systematic review and meta-analysis. World Neurosurg. 2018;110:460–474.e5.
58. Giammattei L, Borsotti F, Parker F, Messerer M. Chiari I malformation: surgical technique, indications and limits. Acta Neurochir. 2018;160(1):213–7.
59. Smith's anesthesia for children and infants. 8th ed. Chapter 22. Pages 734.
60. Mundakel GT, et al. Down syndrome. Medscape. https://emedicine.medscape.com/article/943216-overview. Accessed 8 Jan 2019.
61. Rogers PT, Roizen NJ, Capone GT. Down syndrome. In: Capute AJ, Accardo PJ, editors. Developmental disabilities in infancy and childhood. 2nd ed; 1996. p. 221–4.
62. Pueschel SM, Scola FH. Atlantoaxial instability in individuals with Down syndrome: epidemiologic, radiographic, and clinical studies. Pediatrics. 1987;80:555–60.
63. Gregory GA, Andropoulos DB. Gregory's pediatric anesthesia. 5th ed. Hoboken, NJ: Wiley-Blackwell.
64. Craniovertebral junction anomalies. https://www.amboss.com/us/knowledge/Craniovertebral_junction_anomalies. Accessed 10 Jan 2019.

Management of Patient with Hydrocephalus

11

Farzana Afroze and Helena Oechsner

Stem Case Terminology

A 13-year-old child is presented to the ER with altered mental status. He has been complaining of nausea and vomiting on and off for few days. Diagnostic workup showed malfunctioning ventriculoperitoneal (VP) shunt with enlarged ventricles. He is scheduled for an emergent revision of his ventricular shunt.

He was born at 35 weeks of gestation with congenital hydrocephalus and spina bifida with open defect. He underwent closure of his neural tube defect and ventricular peritoneal shunt as an infant.

Since then he had to have two other revisions for failure of his shunt and VP shunt infection.

His past medical history includes spina bifida, depression, obesity, gastroesophageal reflux disease (GERD), neurogenic bladder and two episodes of pyelonephritis and difficult peripheral venous access.

Not on any home medications. No known drug allergy.

He weighs 87 kg, he is wheelchair bound, now in bed, somnolent and has 24G PIV in his left forearm. Vital signs WNL, no recent labs available.

Airway evaluation is difficult due to lack of cooperation.

Heart and lung auscultation revel distant breath sounds and regular sinus rhythm without a murmur.

11.1 Preoperative

Question 1:
What is hydrocephalus?

Answer:
Hydrocephalus is defined as a condition caused by abnormal accumulation of cerebrospinal fluid (CSF) within the brain resulting in enlarged cerebral ventricles, due to a disruption of CSF formation, absorption, or flow. It can occur in both children and adults but is more common in the pediatric population. Hydrocephalus is the most commonly treated disease by pediatric neurosurgeons in the USA with a prevalence of roughly 1 in 1000 live births, which accounts for roughly $2 billion in health expenditures in the USA every year. The incidence and prevalence of hydrocephalus in adults are not known as it is secondary to other pathogenesis, such as intracranial hemorrhage, tumor, head trauma, and infection. The literature on the incidence of pediatric hydrocephalus is divided: some report a decreased incidence in developed countries secondary to reduced rates of congenital malformation and infections, while others indicate an increased rate of hydrocephalus because of

F. Afroze (✉) · H. Oechsner
Albany Medical Center, Albany, NY, USA
e-mail: AfrozeF@amc.edu; OechsnH@amc.edu

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_11

improved survival of premature infants with a corresponding increase in the incidence of intraventricular hemorrhage (IVH).

Question 2:
What is the pathogenesis of developing hydrocephalus?

Answer:
CSF is secreted by the choroid plexus located within the cerebral ventricles which flows freely to surround the brain and the spinal cord in the subarachnoid space. The CSF production rate is considered to be 0.3–0.4 mL/min, which translates into an hourly production rate of roughly 20 mL/h. Hourly CSF production in infants and children from external ventricular drain has been documented and suggests that CSF outputs increase logarithmically with increase in age and body weight, which further suggests that the CSF production increases proportionally with the growth of the brain. The output increases rapidly in infancy and by 2 years of age, output is approximately two-thirds of adult levels. The total CSF volume in infants is approximately 50 mL, while in adults it is 125–150 mL. The overall total volume of CSF is smaller in children due to the smaller subarachnoid space, but larger on an mL/kg basis.

CSF is reabsorbed into the cerebral venous system through the arachnoid granulations of the subarachnoid space. According to this model, hydrocephalus can result from physical or functional obstruction of CSF flow within the ventricular system, the subarachnoid space or venous sinuses as well as excess production or defective absorption of CSF. When the rate of production is increased, the corresponding increase in CSF pressure typically results in increased absorption and therefore increased production of CSF rarely results in hydrocephalus. Within the ventricular system, an obstructive malformation can cause physical blockage of CSF flow and outside the ventricular system, inflammation and scarring of the subarachnoid space, or elevated pressures within the venous sinuses can impair translocation of CSF into the systemic circulation.

The Monro–Kellie doctrine describes the relationship between the volume of the intracranial components and intracranial pressure (ICP). The cranial vault is a "rigid" structure, with a finite amount of space within. The three components that occupy the intracranial space are: (1) brain bulk and interstitial fluid (80%), (2) CSF (10%), and (3) blood (10%). Under the Monro–Kellie hypothesis, the sum of the intracranial components is constant and an increase in any one of the intracranial constituents or in the presence of a mass lesion, e.g., tumor or hematoma, would increase ICP and decrease the volume of another component.

- *Intracranial volume (constant) = brain volume + CSF volume + blood volume + mass lesion.*

Due to the existing physiological buffer, some compensation is possible—an increase in the volume of one of the components would therefore involve a decrease in the volume of one or both components. Typically, when there in an increase in any one of the intracranial components, compensation occurs by increasing CSF reabsorption or moving CSF and blood into the spinal canal or extracranial vasculature, respectively. When these compensatory mechanisms are exhausted, ICP rises dramatically leading to life threatening herniation syndrome. Infants and children under the age of 2 are an exception to this rule, due to unfused suture lines and fontanelles, and a slow increase in intracranial volume can be compensated for more readily until even these compensatory mechanisms are exhausted.

Question 3:
What are the different types and etiology of hydrocephalus?

Answer:
There are different classification schemes based on different criteria. One of the earliest and widely used classification system is based on the CSF dynamic, where it is classified as *obstructive/noncommunicating or non-obstructive/communicating* depending on the presence of blockage of the major CSF circulation pathway. Hydrocephalus can also be classified based on

any association with congenital syndrome or chromosomal anomalies, congenital vs. acquired, pediatric vs. adult hydrocephalus. Hydrocephalus in adults is often subclassified as high or normal pressure hydrocephalus, such as normal pressure hydrocephalus (NPH) and idiopathic intracranial hypertension (IIH). Another form of hydrocephalus in the elderly that is worth mentioning is hydrocephalus ex-vacuo.

Obstructive vs. communicating: Obstructive hydrocephalus, also known as noncommunicating hydrocephalus, refers to abnormal accumulation of CSF due to structural blockage of CSF flow within the ventricular system. This is the most common form of hydrocephalus in children and almost always associated with increased ICP. Communicative hydrocephalus refers to abnormal accumulation of CSF from the subarachnoid space to the venous circulation. Based on this definition, some scholars refer to communicating hydrocephalus as "absorptive" kind.

Acquired vs. congenital: Hydrocephalus can be classified by etiology as either congenital or acquired.

Congenital hydrocephalus is present at birth without any obvious extrinsic cause, while acquired hydrocephalus occurs after birth. Congenital hydrocephalus can be further subdivided into syndromic and non-syndromic forms. Syndromic hydrocephalus is associated with other congenital anomalies and genetic anomalies. There are many syndromes that are associated with hydrocephalus, such as X-linked hydrocephalus, chromosomal defects, Walker–Warburg syndrome, achondroplasia, encephalocele, Chiari type 2 malformation that is associated with myelomeningocele, aqueductal stenosis and Dandy–Walker malformation (DWM). DWM is a complex consisting of hydrocephalus due to atresia of the foramina of luschka and magendie, with hypoplasia or agenesis of the cerebellar vermis and cystic enlargement of the fourth ventricle. Aqueductal stenosis can also be congenital or acquired.

Acquired or secondary hydrocephalus occurs due to other medical conditions, some of which include hemorrhage, IVH due to prematurity, infection, inflammatory processes, and neoplasm causing dynamic obstruction. Inflammation of the meninges or ventricles from the infection or hemorrhage often leads to hydrocephalus due to impairment of CSF circulation and absorption. Infectious diseases causing hydrocephalus include meningitis, encephalitis, congenital syphilis, CMV, and toxoplasmosis. Bacterial meningitis is more commonly associated with hydrocephalus than viral meningitis (Table 11.1).

Normal pressure hydrocephalus (NPH): NPH is a disease of mostly the elderly population with unclear etiology and is characterized by enlarged ventricular size with normal opening pressures on lumbar puncture. NPH is a form of communicating or non-obstructive hydrocephalus without any radiological evidence of obvious obstruction. The etiology can be idiopathic or secondary to previous subarachnoid hemorrhage, meningitis, or head trauma. NPH is commonly seen in the elderly and associated with the classical triad of dementia, gait disturbance, and urinary inconti-

Table 11.1 Common causes of pediatric hydrocephalus

Congenital causes	Acquired causes
Neural tube defect • Spina bifida • Myelomeningocele • Chiari malformation II • Encephalocele	Aqueductal stenosis (can be congenital or acquired)
Dandy–Walker complex • Atresia of foramina of luschka and magendie • Cystic enlargement of the fourth ventricle	Hemorrhage • IVH due to prematurity
X-linked hydrocephalus • Aqueductal stenosis	Infection • Bacterial meningitis • Encephalitis • Congenital syphilis • CMV and toxoplasmosis
Congenital arachnoid cyst	Traumatic brain injury
In utero intraventricular hemorrhage	Brain tumor or cysts
Intracerebral vascular malformation	Idiopathic

nence. Symptoms are potentially reversible by the placement of a VP shunt. It is a diagnosis of exclusion and as such it is important to rule out any other organic causes of dementia.

Idiopathic intracranial hypertension (IIH): IIH also known as pseudotumor cerebri is characterized by elevated ICP with slightly dilated or nondilated ventricles. The term that has been use in the past for this entity is "benign intracranial hypertension." It is common in obese females of child-bearing age. IIH is a clinical entity defined by clinical criteria that include symptoms of elevated ICP—almost all patients have chronic headache, some type of visual disturbances including visual loss, blurred vision and diplopia, pulsatile tinnitus, radicular pain, paresthesia, and facial palsy. The presence of these symptoms as well as papilledema on fundoscopic examination confirms the diagnosis of pseudotumor cerebri, where no other cause of ICP is evident on neuroimaging or other evaluations.

Hydrocephalus ex-vacuo: Patients with neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and Lewy body dementia can present with similar symptoms as seen in NPH, which are progressive dementia, gait disturbance, and urinary incontinence. On radiographic imaging, ventricles can be enlarged due to volume loss or atrophy of brain, hence called hydrocephalus ex-vacuo. Due to overlapping of symptoms, it can be difficult to distinguish between NPH and neurodegenerative disorders and sometimes both diseases can occur at the same time.

Question 4:
What are the clinical presentations of hydrocephalus?

Answer:
Clinical signs and symptoms are related to elevated ICP and depend on age and etiology. Infants and children under 2 years of age who have open fontanelles and nonfused sutures may not show any sign of elevated ICP even in the presence of elevated ICP. A gradual increase in intracranial volume causing increasing head circumference and craniofacial disproportion may be the very first sign. Definitive treatment of hydrocephalus is placement of a ventriculoperitoneal shunt (VPS) to relieve ICP. So acute or chronic shunt failure also presents with similar clinical signs and symptoms of acutely elevated ICP (Figs. 11.1, 11.2 and 11.3 and Tables 11.2 and 11.3).

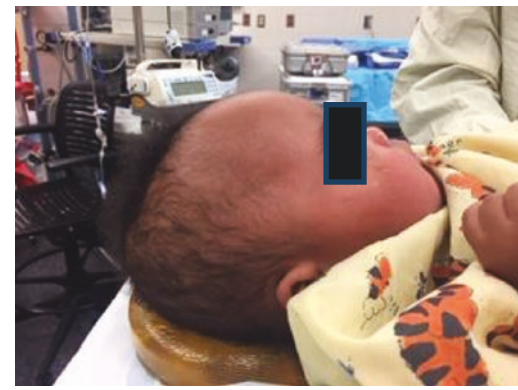


Fig. 11.1 A 11-month-old infant ex-25-week preemie with IVH causing hydrocephalus with large porencephalic cystic dilation of left lateral ventricle required VP shunt placement at early infancy, presented with VP shunt malfunction and worsening hydrocephalus. Visible physical feature of "frontal bossing"

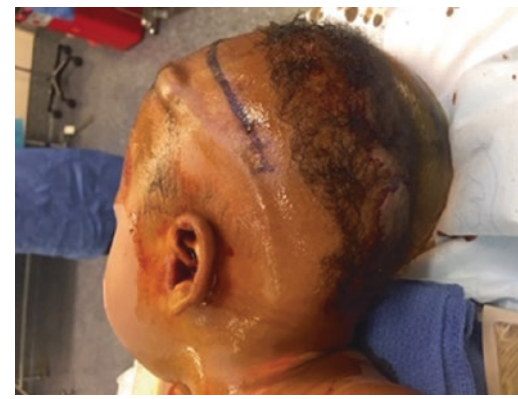


Fig. 11.2 Protruding shunt

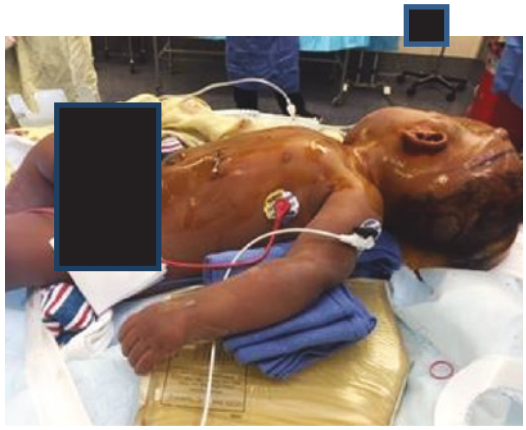


Fig. 11.3 Surgical preparation includes exposure of the entire body and iodine-based preparation of the head and abdomen. Neonate and small children are at increased risk for hypothermia as they lose excessive body heat through body exposure to the cold operating room condition

Table 11.2 Signs of elevated ICP and shunt malfunction in children

Signs of chronic ICP elevation	Late signs of elevated ICP	Signs of shunt malfunction
Increased head circumference and widened cranial sutures (likely early sign in infants)	Lethargy	Bulging fontanelles and increased head circumferences (in infants)
Bulging fontanelles (likely early sign in infants)	Altered mental status or level of consciousness	Irritability
Vomiting (especially in the morning)	HTN/ bradycardia (Cushing's)	Nausea and vomiting
Irritability	Mydriasis	Headache
Headache	Papilledema	Loss of developmental milestones
New onset of seizures	Abnormal response to painful stimuli	Lethargy or any new neurological signs
Poor oral intake/ failure to thrive	"Sun setting sign"—Upper eyelid retraction and up-gaze failure	Poor oral intake

Table 11.3 Clinical presentation of hydrocephalus/ increased ICP in older children, NPH, and IIH

Older children	• Headache (worse in morning) • Vomiting (often will relieve the headache) • Diplopia (sixth cranial nerve palsy) • Sudden onset of seizure • Impaired consciousness and Cushing's
Normal pressure hydrocephalus (NPH)	• Elderly, usually >75 years of age • Triad: Gait impairment, dementia, and incontinence
Idiopathic intracranial hypertension (IIH)/ pseudotumor cerebri	• Female, child-bearing age, obese • Triad: Chronic headache, visual disturbances, and papilledema

Question 5:
How would you evaluate a patient with hydrocephalus or acute shunt failure?

Answer:
Thorough organ-based evaluation is necessary, especially focusing on neurological assessment for signs of acute elevated ICP, while also evaluating for coexisting diseases. Signs of acute increase in ICP and decreased level of consciousness should dictate the urgency of the surgical treatment or the need for temporizing decompression with ventricular tapping and external ventriculostomy. Most neurosurgical patients will have some type of radiologic imaging studies performed preoperatively, either a computed tomography (CT) or magnetic resonance imaging (MRI) of the brain as part of the preoperative neurosurgical evaluation and surgical planning (Figs. 11.4 and 11.5).

Patients with elevated ICP are at increased risk for aspiration of gastric content, thus it is usually best to perform rapid sequence induction and intubation when surgery is indicated. Many patients with chronic or acute intracranial pathology suffer

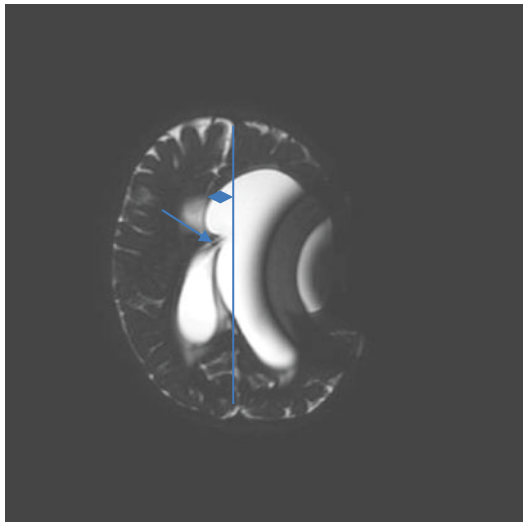


Fig. 11.4 MRI image prior to surgery. Arrow indicating VP shunt entering left ventricle. Marked hydrocephalus, large porencephalic cavity resulting in mass effect on the contralateral right ventricle with left to right midline shift. Line in the middle indicating midline and shift

Table 11.4 System-based evaluation for patient with hydrocephalus prior to surgery

Cardiovascular	Congenital heart disease, arrhythmias, congestive heart failure, electrolyte abnormalities, hypoxia, paradoxical emboli
Respiratory	Bronchopulmonary dysplasia (BPD), chronic lung disease (CLD) due to prematurity, aspiration pneumonia, postoperative apnea, vocal cord paralysis
Gastrointestinal system	GERD, nausea, vomiting
Urinary system	Latex sensitivity, recurrent or chronic UTI
Nervous system	Seizures, mental status changes, neurologic deficits
Airway evaluation	Craniofacial anomaly or syndromes associated with difficult airway anatomy

Source: Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthsia. Boca Raton, FL: Taylor and Francis, CRC;2017. p. 405–21

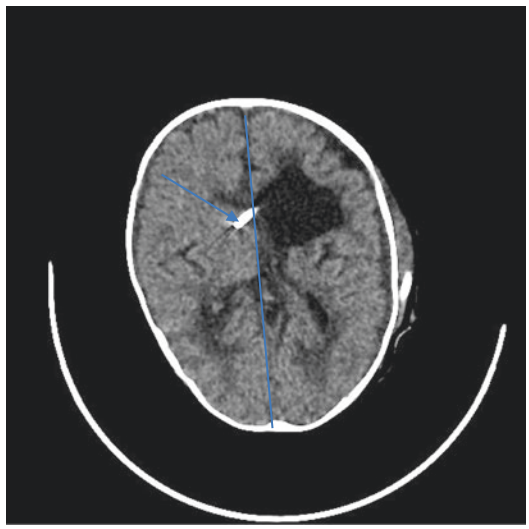


Fig. 11.5 CT image after revision of left VP shunt. Arrow indicating shunt entering to left ventricle. Moderate decrease in size of left porencephalic cyst and decreased mass effect and midline shift

from nausea, vomiting, and general malaise, thus these patients may be intravascularly volume depleted and may have electrolyte imbalances. Premedication with anxiolytics in the preoperative area should be administered cautiously based on the neurological status. Children with developmental delay or neurologic impairment may not need any anxiolytics. The use of premedication or anxiolytics can cause hypoventilation increasing the $PaCO_2$, thus increasing ICP. Older children tend to be more anxious leading to intense crying and fighting, which may cause significant elevation in ICP as well. It is best to avoid premedication with narcotics as they may worsen nausea and cause hypoventilation. If indicated, oral midazolam 0.25–0.5 mg/kg (maximum 20 mg) can be administered 10–20 min before surgery to relieve anxiety. If an indwelling intravenous (IV) catheter is in place, small dosage of IV midazolam can be titrated to effect. Lastly, consider that the use of premedication may delay recovery from anesthesia and obtaining a timely neurologic exam (Table 11.4).

Question 6:
How would you proceed with induction of a patient with elevated ICP?

Answer:
There is no standard way to induce anesthesia for patient with chronic or acute hydrocephalus.

Induction planning should be dictated by the patient's acute neurological status and coexisting medical issues. With patients presenting with symptoms of acutely elevated ICP, precaution should be taken during induction of anesthesia to prevent hypoventilation leading to hypercarbia, hypoxia, and hyper/hypotension to prevent further elevation of ICP. The primary goal should be neuroprotection by maintaining cerebral perfusion. Without any evidence of acute ICP elevation, it is safe to perform inhalational induction in pediatric patients and adults with difficult venous access. In patients with obvious signs of increased ICP, IV access and induction with IV anesthetic is recommended by most scholars, as potent volatile anesthetic's deleterious effects on CBF and ICP are well described in the literature.

11.2 Intraoperative

Question 7:
What is the incidence and causes of VPS failure?

Answer:
The primary management option for patients with hydrocephalus is implantation of a VP shunt allowing drainage of excess CSF from the cerebral ventricles into the peritoneal cavity. Risk of VP shunt failure is the highest during the first year after implanting a VP shunt, especially in premature infants and infants during their first year of life. Proximal or distal obstruction and infection are the most common causes. All types of mechanical problems have been reported, including not just proximal or distal obstruction, but disconnection, disruption, and valve-related problems as well. Depending on the sources, the rate of obstruction ranges from 10 to 52% and the rate of infection was observed as high as 39% in the past, while more recent studies report infectious complications in only 5–10% of shunt insertions. VP shunts were introduced in the 1950s and their design has changed very little since then; small changes introduced in recent years have had only minimal impact on those long-standing problems. Approximately 40% of shunts fail within two years of implantation and 98% fail after a 10-year span (Table 11.5).

Table 11.5 Risk factors for VP shunt infection

Age at shunt placement (higher risk at younger age)
Prematurity
Etiology of hydrocephalus (higher risk after IVH, infection or malignancy)
Postoperative CSF leak
Duration of surgical procedure
Number of manual contacts between surgeon and shunt system
Single glove use
Experience of surgeon
Previous shunt insertion

Question 8:
What types of cerebrospinal shunts are currently available for clinical use?

Answer:
A shunt typically consists of four components:

- Proximal (inflow) catheter with a tip placed within the CSF in one of the lateral cerebral ventricles
- Reservoir
- A one-way valve to regulate CSF flow
- Distal (outflow) catheter that facilitates drainage of CSF into a body cavity, where CSF can be absorbed

Various shunts have been used including **VP**, **ventriculo-atrial (VA)**, **ventriculo-pleural (VPI) shunt** and **ventriculo-gallbladder shunt**. In a case of a communicating hydrocephalus, CSF can be also drained from the lumbar subarachnoid space by **a lumbo-peritoneal (LP) shunt**. The VP shunt is used most commonly but in a case of VP shunt contraindication due to abdominal surgery, adhesion, or peritonitis, other sites for CSF absorption are possible.

Most shunts fall into two categories: a single setting fixed pressure valve (mono valve) or an adjustable variable pressure valve. The valve

functions as a flow-resistant mechanism, allowing control of ICP in a variety of different positions and pressures. Differential pressure (DP) is the pressure gradient between the proximal and the distal catheter tip, preventing a rise of ICP. **Mono valve** contains a ball and spring mechanism which has a static tension. When the CSF reaches a high enough pressure, the ball compresses the spring, and the CSF flows into the distal catheter via one-way flow valve, functioning as a pop-off valve. The valve has also an "antechamber," a reservoir allowing one to sample CSF fluid, measure ICP, and check for obstruction. This type of shunt has fewer parts, is smaller and associated with less complications (preferred for young patients) and MRI compatible. However, it does not allow for any additional adjustments if the CSF drainage rate changes and it would require reoperation.

A variable pressure valve accommodates changing pressure and prevents over- or underdraining. To adjust the valve, a magnetic field is applied by an external magnet to rotate the valve, adjusting the opening and closing pressures without the need for an additional surgical procedure. Although the programmable valves are more expensive, they may be associated with fewer reoperations offsetting the initial price. However, it is important to note that the programmable shunt needs to be checked following an MRI exam. The magnetic field in the MRI scanner can redial the valve to an inappropriate setting and if uncorrected, it can lead to over- or underdrainage of CSF. The Food and Drug Administration (FDA) also recommends that programmable shunts using a magnetic field should be kept at least 2 in. away from devices with magnetic fields including cell phones or headsets. Patients should use the opposite side for cell phone or earbuds use.

Question 9:
What are the specific anesthetic considerations for intraoperative management of shunt insertion?

Answer:
There is no single one anesthesia technique recommended for maintenance of anesthesia. The main goals of anesthetic management are to decrease elevated ICP, prevention of further increase of ICP as well as maintenance of favorable cerebral hemodynamics, immobility and rapid recovery from anesthesia. Reports describe the use of inhalation, total IV and combination technique for maintenance anesthesia. Any anesthesia technique should avoid hypercarbia, hypoxia and hypertension or the use of nitrous oxide to prevent ICP increase.

Small doses of short-acting opioid analgesics with adjunctive non-depolarizing muscle relaxants are useful. Local anesthetics for wound infiltration are encouraged. Administration of preoperative antibiotics is important to decrease the risk of postoperative infection.

Ventricular tap and shifts in CSF during the operation can be associated with hypotension, bradycardia, and cardiac arrhythmias. Subcutaneous tunneling and abdominal incisions are stimulating and may require deepening of anesthesia or additional small doses of opioids.

More recently, some centers are performing laparoscopically assisted placement of the distal portion of shunt catheter. Some studies showed decreased shunt revision rates and decreased length of stay with this approach. This surgical technique does add challenges to the management by introducing pneumoperitoneum, hypercarbia, increased intra-abdominal and intrathoracic pressure. This can lead to decreased cardiac output, hypotension, decreased pulmonary compliance, and hypoxemia. Increased intra-abdominal pressure can further elevate ICP and decrease cerebral perfusion.

Question 10:
Are there any concerns about fluid management for patients undergoing VP shunt placement or revision? Or any patient for VP shunt insertion surgery?

Answer:
Placement or revision of a VP shunt typically does not carry a high risk of excess blood or third space losses. However, patients could be dehydrated coming into surgery secondary to induced diuresis to control ICP or from emesis secondary

to increased ICP. The goal is to maintain normovolemia and avoid hyperglycemia or hypoglycemia. Use of balanced normotonic crystalloid solutions is preferable. Colloids are not usually necessary in routine neurosurgery. Hypotonic crystalloids are dangerous in pediatric neurosurgical patients as these solutions cause water to shift from the intravascular compartment into the cells of the brain, causing brain edema and brain swelling. Therefore solutions such as Ringer's lactate (osmolality 273 mOsm/L) and half normal saline (osmolality 143 mOsm/L) should be avoided during neurosurgical procedures. Normal saline solution (osmolality 290 mOsm/L) is isotonic and will not lead to increased brain water. However, if given rapidly and in large amounts, it can result in hypernatremia, hyperchloremia, and hyperchloremic metabolic acidosis. Plasma-Lyte (osmolality 294 mOsm/L) is isotonic and well suitable for fluid replacement. Glucose-containing solutions should be administered at a lower rate to premature infants, newborns, and diabetic patients to prevent hypoglycemia, while blood glucose levels are carefully monitored. Otherwise glucose containing solutions should be avoided to prevent hyperglycemia which could cause or increase cerebral injury.

Hyperosmolar therapy like mannitol or hypertonic saline and loop diuretics should be given only after consultation with the neurosurgeon.

Question 11:
Are there any special concerns about temperature control in patients undergoing insertion or revision of a VP shunt?

Answer:
During the insertion of the VP shunt, a large portion of the child's body is exposed to the ambient temperature and covered with disinfectant solution leading to enhanced heat loss via conduction and radiation with a quickly developing hypothermia. Since there is no clinical evidence supporting induced hypothermia neuroprotection in pediatric patients, all efforts should be made to maintain normothermia during hydrocephalus surgery.

These measures include increasing the operating room temperature, use of underbody warming blankets, radiant heat lamps, warm prep solutions, and warm IV fluids.

There are many potential side effects from hypothermia, especially in premature and term infants and small children. **Hypothermia** can induce coagulopathy, peripheral vasoconstriction, and poor tissue perfusion, decrease oxygen delivery and cause metabolic acidosis. It can inhibit drug metabolism and prolong recovery from anesthesia. It can also lead to rewarming-induced increases in oxygen consumption with an increased cardiac output. Finally, and perhaps most importantly, hypothermia is also linked to an increased rate of postoperative infection.

Hyperthermia can be also equally harmful, with the central nervous system being especially vulnerable, particularly if prolonged or excessive. The neurological injury may manifest in several ways, including cognitive dysfunction and agitation.

Question 12:
What are the benefits and disadvantages of endoscopic third ventriculostomy (ETV) compared to insertion of a VP shunt? What are the main anesthetic considerations for an ETV procedure?

Answer:
Neuroendoscopic third ventriculostomy (ETV) is the most common intraventricular endoscopic procedure. It aims to treat obstructive hydrocephalus due to a congenital aqueductal stenosis or an obstruction blocking the aqueduct of Sylvius by making a perforation in the floor of the third ventricle.

There are several possible acute intraoperative complications arising from the irrigation fluid, mechanical injury to brain structures, and during the fenestration of the floor of the third ventricle. Cold irrigation fluid can acutely distend the ventricles, causing an increase of ICP and Cushing-type response with bradycardia or tachycardia and hypertension. This is the result of impaired perfusion and/or stimulation of the pre-optic area. Vigorous irrigation can also cause

neurogenic pulmonary edema. Mechanical trauma to the fornix can lead to transient memory loss, personality changes, or injury to cranial nerves III and VI.

Hypothermia is common, giving the large surface area of the infant's head. All efforts should be made to maintain normothermia with the use of warm ambient room temperature, an underbody forced air warming blanket, and warm fluids.

Failure of ETV can be defined as primary (failure to create an opening) or secondary (obstruction of previously patent communication). ETV is attractive as a minimally invasive procedure with ideal results of definitive cure of the obstructing hydrocephalus. Unfortunately, it is not without complications which may include obstruction, infection, CSF leakage, IVH, and damage to the tuber cinereum with diabetes insipidus. Better long-term follow-up is still needed.

Question 13:
What preoperative antibiotic would you recommend? Which bacterial flora are you worried about?

Answer:
The incidence of infection after insertion of a VP shunt is reported to be anywhere from 1 to 39% with more recent studies reporting a lower incidence than in the past, about 4–5%. Most shunt infections present in the first 2 months postoperatively, supporting the theory that the infecting agent is introduced at the time of surgery. The most prevalent species are Gram-positive bacteria, especially Staphylococcus species with Staphylococcus epidermidis accounting for more than half of the cases and Staphylococcus aureus up to another third. If there are any Gram-negative bacteria detected, in most cases they are nosocomial pathogens, such as Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter related to intraperitoneal inflammation or hematogenous spread from a different site. Late shunt infection is considered a different entity. The shunt is acting as a foreign body and attracting bacterial colonization with mostly Gram-negative bacteria or Candida spp., likely retrograde infection from the distal portion of the VPS catheter. The rate of late VPS infection is 1–30% of all infections.

Perioperative antibacterial prophylaxis should have a bactericidal effect as well as the capacity to sufficiently penetrate the blood–brain barrier. The introduction of perioperative antibiotic prophylaxis has helped to decrease the incidence of VPS infections. Second- or third-generation cephalosporins (or clindamycin for patients with penicillin allergy) are common antibiotic choices. Intraoperatively, intraventricular application of gentamycin or vancomycin has been recommended. Colonization of patients with resistant bacterial pathogens may require additional antibiotics. However, single shot prophylaxis with a glycopeptide in MRSA and MRSE colonized patients may not reach minimal inhibitory concentration in the CSF.

Antibiotically impregnated shunt catheters (AIS) reduce VPS infection rate with statistical significance documented in several studies. Catheters were impregnated with rifampicin with or without minocycline or clindamycin. The antimicrobial activity of the shunt catheter in these studies lasted up to 127 days.

Question 14:
What would be the anesthetic considerations for women with a cerebrospinal shunt during labor and delivery?

Answer:
Pregnancy in women with CSF shunts can be complicated by shunt failure and an increase in ICP. The anatomical site of a CSF shunt and its function are important determinants in choosing the mode of delivery and type of anesthesia. The anesthetic management of pregnant patients with CSF shunts requires a team approach between the obstetrician, neurosurgeon, neurologist, and anesthesiologist. The choice of anesthetic technique depends on CSF shunt function, ICP, and the urgency of delivery. Vaginal delivery is preferred in women with normally functioning shunts and no signs of increased ICP. Both vaginal and cesarean delivery can be safely done

under neuraxial anesthesia if increased ICP is not present and being meticulous about sterile placement to avoid subsequent shunt infection.

CSF shunt malfunction is high during pregnancy (up to 30%) and any new neurological symptoms require careful evaluation of shunt function. If any concerns arise, and imaging is needed, MRI is preferred over computer tomography during pregnancy due to risk of radiation exposure. Abdominal ultrasound provides good information about the distal catheter and presence of a pseudo cyst or an abscess. Causes of failure of the CSF shunt during pregnancy can be due to obstruction, fracture, migration, disconnection, misplacement, infection, and peritoneal pseudocyst formation from chronic low-grade infection, just like in the non-pregnant population. Mechanical obstruction by the gravid uterus and the increase of intra-abdominal pressure can cause malfunction of an otherwise normally functioning shunt. Labor and delivery can cause increased ICP with the onset of uterine contractions and pain. VA shunts may have less obstruction during pregnancy but are generally associated with a higher rate of complications including arrhythmias, migration of the catheter tip, scarring of myocardium, and valvular regurgitation.

Cesarean delivery is indicated for patients with shunt failure and increased ICP and in this case general anesthesia is the preferred technique. Induction agents typically include propofol and short-acting medications such as remifentanil, esmolol, and lidocaine for attenuating increased sympathetic responses during intubation. Succinylcholine should be avoided in patients with increased ICP but remains the drug of choice in pregnant women with anticipated difficult airway. Ergot derivatives should be avoided post-delivery as they may further increase ICP. The distal catheter can be damaged or infected during the cesarean delivery and postoperative adhesions around the catheter may predispose the shunt for the future failure. Caution should be taken to prevent both by strictly aseptic technique, antibiotic irrigation, and preoperative ultrasound marking indicating the location of the distal tip of the shunt.

11.3 Postoperative

Question 15:
What possible complications of VP shunt placement are to be watched for?

Answer:
The most common complications are related to either shunt malfunction or infection.

Shunt malfunction: *CSF overdrainage* can result in shrinking or collapse of the cerebral ventricles also known as slit ventricle syndrome, referring to computer tomography (CT) or MRI finding of very small ("slit-like") ventricles. Slit ventricle syndrome can cause severe intermittent headaches in the upright position, typically relieved by lying down. In adult patients, one can even see arterial or venous blood vessel tears with resultant subdural hematoma. This is caused by a "siphoning" effect, where in the upright position gravity siphons fluid out of the shunt causing overdrainage and negative ICP. Most current shunts contain siphon resistive device (SRD).

CSF underdrainage presents as failure to drain the enlarged ventricles and increased ICP with the typical signs and symptoms of hydrocephalus. This typically needs a surgical revision of the shunt or interrogation of the valve if an adjustable shunt is in place.

Shunt obstruction can happen at any part of the system. This is most often caused by CSF protein buildup and can acutely present with signs of increased ICP (headache, nausea, vomiting, lethargy, irritability, confusion).

Intracranial hemorrhage: Intracranial hemorrhage can result from erosion of the catheter into cerebral vasculature or sudden ICP reduction after VPS placement resulting in subdural hematoma, intracerebral hemorrhage, or both.

Shunt infection: Early infection is usually caused by skin flora contamination, most likely Staphylococci. Signs and symptoms of infection include fever, lethargy, irritability, abdominal pain, headache, nuchal rigidity, and elevated

white blood cell count. Shunt infection can quickly lead to meningitis.

Abscesses can be formed as a result of shunt infection. If a patient complains of abdominal pain, one must consider abdominal abscess due to shunt contamination or migration into the bowels.

Abdominal injury: Peritonitis can develop as a response to foreign body and secondary to intestinal perforation.

Bowel perforation and volvulus are less common but possible intra-abdominal complications.

Ascites can be a result of CSF malabsorption from the peritoneal cavity. It presents with abdominal discomfort and distention.

Incisional pain is to be expected and can be treated with acetaminophen and small amounts of opioids.

Pneumothorax is another rare but possible complication. The distal portion of the VP shunt is tunneled subcutaneously in the neck and thorax before entering the peritoneal cavity. In obese patients, the tip of the tunneling catheter may inadvertently enter the chest cavity causing pneumothorax, subcutaneous emphysema, and even acute pneumocephalus. Most of the time, however, pneumocephalus is usually a delayed event, presenting months after VP shunt insertion. In this case, it occurs as a result of skull base defect, visceral perforation, or skin defect. The negative ICP allows intracranial air collection, similarly to CSF fistula. Beware that pneumothorax at the time of surgery can lead to developing a subcutaneous emphysema and that air can track into the subdural space.

Question 16:
What are some possible non-surgical therapies of hydrocephalus?

Answer:
Hydrocephalus is typically a surgical disease. Medical management can aim to decrease the rate of CSF formation such as with acetazolamide which slows the rate of CSF production in patients with a slight mismatch of production and absorption. Most commonly it is used for benign extra-axial CSF collection and transient postoperative inflammatory meningitis with impairment in CSF resorption.

Multiple Choice Questions

1. A 3-month-old baby presents for emergent external ventricular drain placement. Mom states the infant was born full term, poor weight gain but otherwise was doing well, irritable since this morning and noticed abnormal eye movement. CT head reveals large intraventricular mass with obstructive hydrocephalus. In the ED IV placement was attempted but unsuccessful. On exam, you find a malnourished, irritable baby, "sun downing gaze" and anterior fontanel is full—How would you like to induce this baby?
   (a) Mask induction, followed by PIV
   (b) Suction stomach and proceed with mask induction
   (c) Obtain a PIV and IV induction
   (d) IM ketamine, followed by PIV placement and IV induction

   Answer: c

   The safest way to induce this infant would be to obtain an IV access, followed by iv rapid sequence induction with propofol and rocuronium. This baby is presenting with obstructive hydrocephalus with evidence of acutely elevated ICP and is thus at increased risk of aspiration of gastric content. In the setting of a dehydrated patient and difficulty in iv access, another option would be decompressing stomach with soft suction catheter, followed by mask induction with volatile anesthetic and iv placement. An important consideration is that mask induction in a patient who is dehydrated will cause acute hypotension and in the setting of acutely elevated ICP this will compromise cerebral perfusion. The use of ketamine and succinylcholine is controversial in the setting of elevated ICP. Recently there is evidence that ketamine can be safely administered in patient with elevated ICP. Administration of

succinylcholine increases ICP transiently but can be abolished with the administration of non-depolarizing muscle relaxants.

2. After induction the infant is hypotensive, what is your next step?
   (a) IV phenylephrine
   (b) IV ephedrine
   (c) IV glycopyrrolate
   (d) IV fluid bolus of isotonic solution 20 mL/kg
   Answer: d

   This infant is likely dehydrated, and hypotension should be treated with fluid bolus 20 mL/kg with an isotonic fluid like Plasma-Lyte. It is best to avoid hypotonic solutions like lactated Ringers, which may further worsen cerebral edema. If isotonic solution like Plasma-Lyte is not available, mild hypertonic solution like 0.9% normal saline is acceptable, but excessive administration of normal saline contributes to hyperchloremic metabolic acidosis.

3. Mom also reports that the infant has been spitting up more often recently and he was placed on omeprazole, but this did not help. How would you asses his fluid status?
   (a) You cannot assess fluid status
   (b) Poor capillary refill
   (c) Electrolytes values
   (d) Urine output
   Answer: d

   Both capillary refill and urinary output can be used to assess fluid status. In small children, decreased urine output is probably the first sign of dehydration. Poor capillary refill is the late sign of dehydration due to tissue hypoperfusion.

4. You are evaluating a 15-year-old patient for a urological procedure. PMH consists of myelomeningocele which was repaired as an infant. He had neurogenic bladder and has had many surgeries in the past. He is wheelchair bound and has patchy sensation L2 and below and poor muscle tone. During the intraoperative period, he is at increased risk for:
   (a) Rebound hypertension
   (b) Anaphylaxis/anaphylactic shock
   (c) Respiratory complication
   (d) Cardiac complication
   Answer: b

   In patients with neural tube defects, neurogenic bladder is common, which requires self-catheterization and multiple surgeries where they might be exposed to latex. Caregivers of these children should avoid latex products to avoid eventual development of latex sensitivity.

5. This patient is also at risk for what other neurological condition?
   (a) Chiari malformation type II
   (b) Seizure disorder
   (c) Cerebrovascular disease
   (d) Chronic headache
   Answer: a

   Chiari malformation type II is frequently associated with myelomeningocele. Also, 85–95% of myelomeningocele patients develop hydrocephalus and require VP shunt placement.

6. You are taking care of an infant from the neonatal ICU for a VP shunt placement. The case has started, you are warming the infant with an underbody Bair Hugger, which is set at 41°, the OR temperature is at 68°, and the esophageal temp probe is reading 35°. What do you think is the most likely cause?
   (a) False reading and disregard
   (b) Due to excessive heat loss
   (c) Due to cold IV fluid
   (d) Due to room temperature
   Answer: b

   There could be multiple reasons for this infant being cold on this scenario. Neonate and small children are at increased risk for hypothermia as they lose excessive body heat through body exposure to the cold operating room condition, especially for VP shunt placement, where head and abdomen are exposed. Head in neonate is larger than the body and thus has greater surface area. Especial precaution should be undertaken to keep neonate warm, such as keeping the operating room temperature > 70° and using warm irrigation for the surgical wound. Hypothermia is related to increased surgical site infection, delayed

wake-up, arrhythmias, bleeding, poor tissue perfusion due to vasoconstriction and apneas in neonate.

7. You finished a case of emergent VP shunt placement on a 20-year-old, and you dropped the patient off to PACU. He was not completely wake when you dropped him off, it's been 30 min now and the PACU RN is calling you that the patient is still not awake. Vital signs are stable, pupils equal, small but not pin point. He received 150 μg fentanyl and 0.5 mg dilaudid in the OR, what is the next most appropriate step?
   (a) Administer naloxone
   (b) Rush to CT
   (c) Send electrolytes
   (d) Get MRI

   Answer: a

   The most likely immediate postoperative complications after VP shunt placement are bleeding into the ventricle, overdrainage of CSF, and obstruction/malfunction. Like any other neurosurgical procedure, it is extremely important to wake the patient up immediately after surgery for proper neuro assessment. In this case, the first thing to rule out is excessive intraoperative narcotic administration with iv naloxone starting with 0.5–1 μg/kg. If the patient does not respond after naloxone, he needs to be evaluated with a stat CT scan. It is hard to obtain an MRI and time consuming. Minor changes to electrolytes should not cause delayed wakening, unless there were any concern prior to surgery, e.g., hyponatremia and hypoglycemia.

References

Question 1

1. Bir SC, Patra DP, Maiti TK, et al. Epidemiology of adult-onset hydrocephalus: institutional experience with 2001 patients. Neurosurg Focus. 2016;41(3, E5):1–12.
2. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.
3. Kandasamy J, Jenkinson MD, Mallucci CL. Contemporary management and recent advances in paediatric hydrocephalus. BMJ. 2011;343:d4191.
4. Macdonald PR. Hydrocephalus. In: Online case bases pediatric chapter. June 2014. https://www.hawaii.edu/medicine/pediatrics/pedtext/s18c09.html.
5. McClain GD, Soriano SG. The central nervous system: pediatric neruroanesthesia. In: Holzman RS, Mancuso TJ, Polaner DM, editors. A practical approach to pediatric anesthesia. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 177–214.
6. Toma AK. Hydrocephalus. Surgery. 2015;33(8):384–9.

Question 2

7. Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthsia. Boca Raton: Taylor and Francis, CRC Press; 2017. p. 405–21.
8. Bir SC, Patra DP, Maiti TK, et al. Epidemiology of adult-onset hydrocephalus: institutional experience with 2001 patients. Neurosurg Focus. 2016;41(3, E5):1–12.
9. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.
10. Haridas A, Tomita T. Hydrocephalus in children: physiology, pathogenesis, and etiology. In: Patterson MC, editor. UpToDate; 2018
11. Kahle KT, Kulkarni AV, Limbrick DD Jr, et al. Hydrocephalus in children. Lancet. 2016;387(Feb 20):788–99.
12. Macdonald PR. Hydrocephalus. In: Online case bases pediatric chapter. June 2014. https://www.hawaii.edu/medicine/pediatrics/pedtext/s18c09.html.
13. McClain GD, Soriano SG. The central nervous system: pediatric neruroanesthesia. In: Holzman RS, Mancuso TJ, Polaner DM, editors. A practical approach to pediatric anesthesia. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 177–214.
14. Toma AK. Hydrocephalus. Surgery. 2015;33(8):384–9.
15. Yasuda T, Tomita T, McLone D, Donovan M. Measurements of cerebrospinal fluid output through external ventricular drainage in one hundred infants and children: correlation with cerebrospinal fluid production. Pediatr Neurosurg. 2002;36:22–8.

Question 3

16. Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthsia. Boca Raton: Taylor and Francis, CRC Press; 2017. p. 405–21.
17. Avellion AM, Ransom B, Hu S. Normal pressure hydrocephalus http://providerresource.uwmedicine.org/flexpaper/neuroscience-pearls-normal-pressure-hydrocephalus.

18. Bir SC, Patra DP, Maiti TK. Epidemiology of adult-onset hydrocephalus: institutional experience with 2001 patients. Neurosurg Focus. 2016;41(3, E5):1–12.
19. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.
20. Friedman DI. The pseudotumor cerebri syndrome. Neurol Clin. 2014;32(2):363–96.
21. Graff-Radford NR. Normal pressure hydrocephalus. In: DeKosky ST, editor. UpToDate; 2018
22. Kahle KT, Kulkarni AV, Limbrick DD Jr, et al. Hydrocephalus in children. Lancet. 2016;387(Feb 20):788–99.
23. Kandasamy J, Jenkinson MD, Mallucci CL. Contemporary management and recent advances in paediatric hydrocephalus. BMJ. 2011;343:d4191.
24. Lee AF, Wall M. Idiopathic intracranial (pseudotumor cerebri): epidemiology and pathogenesis. In: Brazis PW, editor. UpToDate; 2015
25. Macdonald PR. Hydrocephalus. In: Online case bases pediatric chapter. June 2014. https://www.hawaii.edu/medicine/pediatrics/pedtext/s18c09.html.
26. McClain GD, Soriano SG. The central nervous system: pediatric neruroanesthesia. In: Holzman RS, Mancuso TJ, Polaner DM, editors. A practical approach to pediatric anesthesia. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 177–214.
27. TomaAK. Hydrocephalus. Surgery. 2015;33(8):384–9.

Question 4

28. Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthsia. Boca Raton: Taylor and Francis, CRC Press; 2017. p. 405–21.
29. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.

Question 5

30. Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthsia. Boca Raton: Taylor and Francis, CRC Press; 2017. p. 405–21.
31. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.

Question 6

32. Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthsia. Boca Raton: Taylor and Francis, CRC Press; 2017. p. 405–21.
33. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.

Question 7

34. Hasanin AA, Abdullah A, Alsawy MF, et al. Incidence of causes for ventriculoperitoneal shunt failure in children younger than 2 years: a systematic review. J Neurol Surg A Cent Eur Neurosurg. 2019;80(1):26–33.
35. Soler GJ, Bao M, Jaiswal D, Zaveri HP, DiLuna ML, Grant RA, Hoshino K. A review of cerebral shunts, current technologies and future endeavors. Yale J Biol Med. 2018;91(3):313–21.
36. Lutz BR, Venkataraman P, Browd SR. New and improved ways to treat hydrocephalus: pursuit of a smart shunt. Surg Neurol Int. 2013;4(Suppl 1):S38–50.
37. Prusseit J, Simon M, Von der Brelie C, et al. Epidemiology, prevention and management of ventriculoperitoneal shunt infections in children. Pediatr Neurosurg. 2009;45:325–36.

Question 8

38. Soler GJ, Bao M, Jaiswal D, Zaveri HP, et al. A review of cerebral shunts, current technologies, and future endeavors. Yale J Biol Med. 2018;91:313–21.
39. Garton HJ. Cerebrospinal fluid diversion procedures. J Neuroophthalmol. 2004;24:146–55.
40. Browd SR, Ragel BT, Gottfried ON, Kestle JR. Failure of cerebrospinal fluid shunts part 1: obstruction and mechanical failure. Pediatr Neurol. 2005;34:83–92.
41. Vacca V. Ventriculoperitoneal shunts: what nurses need to know. Nursing. 2018;18(12):20–6.
42. U.S. Food & Drug Administration. Cerebral spinal fluid shunts systems. www.fda.org.

Question 9

43. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.
44. Bani A, Hassler WE. Laparoscopy-guided insertion of peritoneal catheters in ventriculoperitoneal shunt procedures: analysis of 39 children. Pediatr Neurosurg. 2006;42:156–8.

Question 10

45. Lima MF, Neville IS, Cavalheiro S, et al. Balanced crystalloids versus saline for perioperative intravenous fluid administration in children undergoing neurosurgery: a randomized clinical trial. J Neurosurg Anesthesiol. 2019;31(1):30–5.
46. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.

Question 11

47. Pearce B, Christensen R, Voepel-Lewis T. Perioperative hypothermia in the pediatric population: prevalence, risk factors and outcomes. J Anesth Clin Res. 2010;1:102.
48. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med. 1996;334:1209–15.
49. Walter EJ, Carraretto M. The neurological and cognitive consequences of hyperthermia. Crit Care. 2016;20:199.

Question 12

50. Jernigan SC, Berry JG, Graham DA, Goumnerova L. The comparative effectiveness of ventricular shunt placement versus endoscopic third ventriculostomy for initial treatment of hydrocephalus in infants. J Neurosurg Pediatr. 2014;13(03):295–300.
51. Vinchon M, Rekate H, Kulkarni AV. Pediatric hydrocephalus outcomes: a review. Fluids Barriers CNS. 2012;9:18.
52. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.

Question 13

53. Erps A, Roth J, Constantini S, et al. Risk factors and epidemiology of pediatric ventriculoperitoneal shunt infection. Pediatr Int. 2018;60:1056–61.
54. Prusseit J, Simon M, Von der Brelie C, et al. Epidemiology, prevention and management of ventriculoperitoneal shunt infections in children. Pediatr Neurosurg. 2009;45:325–36.
55. Ragel BT, Browd SR, Schmidt RH. Surgical shunt infection: significant reduction when using intraventricular and systemic antibiotic agents. J Neurosurg. 2006;105:242–7.

Question 14

56. Rajagopalan S, Gopinath S, Trinh VT, Chandrasekhar S. Anesthetic consideration for labor and delivery in women with cerebrospinal shunts. Int J Obstet Anesth. 2017;30:23–9.
57. Littleford JA, Brockhurst NJ, Bernstein EP, Georgoussis SE. Obstetrical anesthesia for parturient with a ventriculoperitoneal shunt and third ventriculostomy. Can J Anaesth. 1999;46:1057–63.
58. Freo U, Pitton M, Carron M, Ori C. Anesthesia for urgent sequential ventricculoperitoneal shunt revision and cesarean delivery. Int J Obstet Anesth. 2009;18:622–6.
59. Browd SR, Ragel BT, Gottfried ON, Kestle JR. Failure of cerebrospinal fluid shunts part 1: obstruction and mechanical failure. Pediatr Neurol. 2005;34:83–92.
60. Browd SR, Gottfried ON, Ragel BT, Kestle JR. Failure of cerebrospinal fluid shunts: part II: overdrainage, loculation and abdominal complications. Pediatr Neurol. 2006;36:171–6.

Question 15

61. Hydrocephalus Association Complications of shunt systems. www.hydrosssoc.org/complications-of-shunt-systems.
62. Kim WJ, Kim MM. Slit ventricle syndrome in pediatric patient presenting with only visual symptoms. Korean J Ophthalmol. 2017;31(1):92–3.
63. Rinker EK, Williams TR, Myers DT. CSF shunt complications: what the abdominal imager needs to know. Abdom Imaging. 2015;40(6):2030–40.
64. Wroe WM, Dire DJ, Marco CA. Cerebrospinal fluid shunt emergencies. Pediatr Emerg Med Rep (e-pub 1 Sept 2015).
65. U.S. Food & Drug Administration. Cerebral spinal fluid shunts systems. www.fda.org.
66. Vacca V. Ventriculoperitoneal shunts: what nurses need to know. Nursing. 2018;18(12):20–6.
67. Schul DB, Wof S, Lumenta CB. Iatrogenic tension pneumothorax resulting in pneumocephalus after insertion of a ventriculoperitoneal shunt: an unusual complication. Acta Neurochir. 2010;152:143–4.
68. Honeybul S, Bala A. Delayed pneumocephalus following shunting for hydrocephalus. J Clin Neurosci. 2006;13:939–42.

Question 16

69. Afroze F, Oechsner H, Ehlers M. Pediatrics. In: Prabhakar H, Mahajan C, Kapoor I, editors. Manual of neuroanesthesia. Boca Raton: Taylor and Francis, CRC Press; 2017. p. 405–21.
70. El Beheiry H, Hayes J. Hydrocephalus. In: Prabhakar H, editor. Pediatric neuroanesthesia. New Delhi: Oxford University Press; 2018. p. 213–9.
71. Tully HM, Dobyns WB. Infantile hydrocephalus: a review of epidemiology, classification and causes. Eur J Med Genet. 2014;57:359–68.

Management of Patient with Lumbar PIVD

12

Adam Yu Yuan and Saket Singh

Stem Case Terminology

Sixty-eight years old Caucasians male present in preoperative unit in the morning with chief complain of CBP, lumbar spinal stenosis, and spinal instability. L_2-L_4 laminectomy and T_{12}-L_5 pedicle screws spinal instrumentation and fusion. His past medical history includes OSA on CPAP, mild COPD, HTN, CAD s/p two stent placements in middle LAD and RCA, type 2 diabetes mellitus with peripheral neuropathy, CRI, and GERD. The patient is 6′1″ tall and 340 lbs in weight with body mass index (BMI) 44.9, had 42 pack year smoking history and is still smoking 1 pack a day, 4 cases of beer per week. Had multiple back surgeries in the past, including L_{45} discectomy in 20 years ago, L_{34} discectomy, and $L_{4–5}$ laminectomy 8 years ago. Also had PSHx of ACD and fusion of $C_{4–5}$ and $C_{5–6}$, PTCA, ORIF of left leg. His home medications include metoprolol, lisinopril, ASA, oxycontin, gabapentin, metformin, robaxin, and occasionally albuterol inhaler. Patient took metoprolol and lisinopril the morning of surgery.

PE on admission: BP 189/98 mmHg, HR 58 bpm, RR 28/min, T 36.9. Airway MP 3 with multiple decayed teeth, no limitation of neck movement, CTA bilateral lungs, heart regular with mild systolic murmurs. Mild numbness on all distal extremities due to peripheral neuropathy, unable to lay flat due to back pain. Bilateral LE pain with claudication.

CBC: HB 8.4, Platelet 120, BMP: Na 138, K 3.6, BUN 35, Cr 1.4, Glu 188. EKG: SR with occasional PVC and V_3, V_4, V_5 Q-wave which is unchanged comparing to his old EKG. Recent adenosine stress test with perfusion: LVEF 50% with mild LV diastolic dysfunction. RV normal in function. Small fixed perfusion defect was found in antero-inferior area. MRI lumbar spine revealed L_1-L_5 stenosis, L_{34}, L_{45} spondylolisthesis, osteoarthritis in multiple intervertebral edges with root canals narrowing.

12.1 Preoperative

Question 1:
You got a call from the surgeon's office regarding the preoperative medication management for this patient. What are your recommendations?

Answer:
ACE inhibitors or ARA preoperatively are associated with increased incidence of refractory intraoperative hypotension. It is widely accepted that for patients currently taking ACE inhibitor or ARA that are scheduled for surgery, the medication should be stopped on the morning of surgery or the day before. After surgery, ACEI or ARA should be restarted with oral intake [1, 2]. While

A. Y. Yuan
Allegheny General Hospital, Allegheny Health Network, Pittsburgh, PA, USA

S. Singh (✉)
Piedmont Medical Center, Rock Hill, SC, USA

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_12

for those who are taking beta blockers, it should not be stopped and patient should continue to take it. Gabapentin and acetaminophen should be continued, since multiple studies suggest that preoperative use was able to reduce postoperative pain and total narcotic consumption [3, 4].

Question 2:
During your preoperative evaluation, patient mentioned that someone has recommended donating his own blood for his surgery. Patient asks about the benefit of preoperative autologous donation (PAD), and what you can do to decrease the risks of allogenic transfusion. How would you respond to the patients request and why?

Answer:
PAD was initially popular in the 1980s when concern for transfusion-transmitted HIV was high; however, it has since become less useful given the reduced risk of transfusion-related infections and new realization about the disadvantages of receiving stored blood. Current indications for PAD are mostly limited in patients who are difficult to find compatible blood types, those who refuse to receive allogenic transfusion, and adolescent scoliosis surgery. Preoperative erythropoietin is usually used for PAD since it has been shown to increase the tolerance for repeat donations. Iron supplementation is generally not helpful unless the patient is known to be iron deficient prior to PDA. Other autologous transfusion includes acute normovolemic hemodilution (ANH) and intraoperative blood salvage (IOBS). ANH is the process of extracting multiple units of blood immediately before surgical incision while maintaining euvolemia with crystalloids or colloid supplementation. However, a large meta-analysis documented no significant decrease in the need for allogenic blood products. IOBS involves the collection of noncontaminated shed blood in surgical field, which is filtered and washed prior to reinfusion. Over the past decade, RBC salvage techniques have improved drastically and now offer an efficient, cost-effective, and safe method for perioperative blood conservation [5, 6].

Question 3:
Patient told you that he had trouble swallowing for a while after his neck surgery, and he was asking you why did that happen?

Answer:
Dysphagia is a common complication of anterior cervical spinal surgery. The incidence of postoperative dysphagia may be as high as 71% within the first two weeks after surgery, but gradually decreases during the following months. However, 12–14% of patients may have some persistent dysphagia over one year after the procedure. It has been shown that female gender, advanced age, multilevel surgery, longer operating time, and severe preoperative neck pain may be risk factors. Although the etiology remains unclear and is probably multifactorial, proposed causes include esophageal retraction, prominence of the cervical plate, and prevertebral swelling. Recently, preoperative tracheal traction exercises and the use of retropharyngeal steroids have been proposed as methods of reducing postoperative dysphagia [7].

Question 4:
Surgeon requested electrophysiological monitoring during surgery for patient's safety. What monitors are you expecting the surgeon to use?

Answer:
The modern technical development enabled the more accurate neurophysiological monitoring of nervous system. Neurophysiological monitoring is currently common and standard practice for the intraoperative safety of neurosurgical procedures. For spinal surgery, the most frequently used techniques for intraoperative monitoring include somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), and electromyography (EMG). EMG can either be spontaneous free-running (sEMG) or triggered (tEMG). All these above monitors are featured with the surgical site locating between the trigger point and recording site. While EEG is also used in many neurosurgeries, it basically reflects the cortical neuroelectric change, not usually for

spinal monitoring. SSEPs use peripheral nerve stimulation and central recording on either cortex or subcortical level at upper spine to monitor the sensory pathway from peripheral nerve, nerve root, dorsal columns in spinal cord, all the way to sensory cortex area. Any functional injury on the pathway may cause change in amplitude or latency of the recorded waveform. MEP is recording in the reverse direction from stimulation on motor cortex to anterior corticospinal tract, nerve root and all the way to the muscle. While the specificity of SSEP is relatively high but the sensitivity is relatively low, the MEP is with higher sensitivity. Multimodal monitoring was reported to have higher sensitivity and specificity. sEMG and tEMG are both used for monitoring the function of nerve roots, specifically during the pedicle screw placement [4, 8].

12.2 Intraoperative

Question 5:
The surgeon decided that the MEP was needed for intraoperative monitoring. How would you tailor the anesthetic plan for this patient, compare it to management if other modalities were used?

Answer:
MEP is the most vulnerable monitoring in response to inhalational agents due to the nature of weak stimulating reception to certain motor conduction. While the intravascular agents have less effect, the inhalational agents are usually limited to below 0.3–0.5 MAC. Muscle relaxant is avoided in MEP [4, 9].

All anesthetics affect nervous system, they also affect the neurophysiological monitors in different degree (see the Table below).

Effects of various anesthetic agents on neurophysiological monitoring

Anesthetic agents	SSEPs	MEPs	EMGs
Inhalational agents[a]			
0.5 MAC	+	++/+++	+/−
Over 1 MAC	++/+++	+++/++++	+/−
Propofol	+	+	+/−
Etomidate	+/−	−	−
Ketamine	+/−	−	−
Benzodiazepines	+	+	−
Opioids	+/−	+	−
Muscle relaxants	−	Not use	Not use

[a]Inhalational agents include isoflurane, sevoflurane, and desflurane

The amplitude and latency of SSEP waveform are usually monitored. It is minimally affected by low level inhalational agents up to 1 MAC, as well as intravascular agents, while higher concentration of inhalational agents or big bolus of intravascular agents causes significant SSEP waveform change. The peripheral nerve monitoring and EMG are much less affected by anesthetics, but muscle relaxant is avoided in the motor nerves and EMG.

12.3 Postoperative

Question 6:
What are the risk factors for postoperative visual loss (POVL) according to the American Society of Anesthesiologists Task Force on Perioperative Visual Loss practice advisory?

Answer:
POVL is rare but devastating complication associated with a variety of non-ocular surgeries including cardiac, spine, and major orthopedic procedures. The incidence of POVL in posterior approach spinal surgeries is the next highest following cardiac surgeries. Types of POVL after spine surgery included ischemic optic neuropathy (ION), central retinal artery occlusion (CRAO), and cortical blindness. While the etiology of ION in spine surgery remains unclear, risk factors include male sex, obesity, use of Wilson frame, longer anesthetic duration, greater blood loss, and a lower percentage of intravenous col-

loids in the fluid administration. POVL due to CRAO in spine surgery is associated with periorbital trauma from improper patient positioning or external compression on the eye. Cortical blindness is the least frequent cause on POVL and is usually associated with pediatric cases. Significant recovery of vision after POVL in spine surgery is rare, and there are currently no established treatments [4, 10, 11].

Question 7:
What is the most common reason for POVL for patients who are undergoing spinal surgeries?

Answer:
In spinal surgeries, the most common reason for POVL is ION (mostly posterior ION in spinal surgeries vs. anterior ION in cardiac surgeries).

Question 8:
Peripheral nerve injury is always a concern for neuro or orthopedic surgeries. Which of the peripheral nerve is the most common nerve being affected during surgery?

Answer:
Peripheral nerve injury during the perioperative period can occur when a nerve is subjected to stretch, compression, hypoperfusion, direct trauma, exposure to neurotoxic material, or a combination of these factors. The severity of the nerve injury is related to the degree and duration of the ischemic insult. While the majority of this kind of nerve injury are temporary, it can be severe and permanent. Established peripheral neuropathy, pre-existing (may be subclinical) peripheral neuropathy, profound hypothermia, hypovolemia, hypotension, hypoxemia, electrolyte disorders, malnutrition, small or large body mass index (BMI), tobacco use, and anatomical variants (such as the presence of cervical ribs) may increase the susceptibility of peripheral nerves to perioperative injury. Anesthesia-related peripheral nerve injuries are usually related to improper patient position or padding, or regional nerve block. The ulnar nerve is the most vulnerable one due to its special anatomy. The ulnar nerve is the only nerve locating on the extensive aspect of joint and superficial on prominent bony surface. Male tend to be affected more than female patients. The other nerves that are more likely injured perioperatively include brachial plexus and common peroneal nerve [12].

Question 9:
At the beginning of surgery, you asked the CRNA to give dexamethasone for antiemetic prophylaxis, and surgeon expressed the concerns of wound infection and bone graft healing. What should you tell the surgeon regarding the current concept of intraoperative steroid use?

Answer:
The synthetic glucocorticoid dexamethasone is widely used as a first-line antiemetic in the perioperative period. Due to its nature of immune suppression and hyperglycemic effect, the concerns of increased risk of infection and delayed wound healing always exist. Tremendous studies in this topic have been done, and so far, no evidence indicates that single dose perioperative dexamethasone increase the risk of infection and wound healing as well as bone graft healing. However, it was suggested to be cautious in using dexamethasone in patients who are in higher risk of infection, such as diabetic patients [13, 14].

Question 10:
After surgery, you were called by PACU nurse that the patient felt pain and sensation of foreign body in his left eye, you carefully examined patient and found redness and tearing in his left eye. What will be your diagnosis and your subsequent management?

Answer:
Corneal abrasion is the most common perioperative ocular complication for anesthesia and is more concerned in spinal surgery patients due to the prone position and multiple turning of patient. The etiologies may include mechanical scratching and chemical burning of cornea. It is prudent to well protect the eyes perioperatively. Usually taping eyes lids close or goggle protection are necessary. Careful in manipulating any activities around face is important, such as intubation or moving patients. However, the

management of corneal abrasion postoperatively includes careful examination of the eyes to exclude the foreign body or other pathologies first. Ophthalmic antibiotic ointment/solution can be applied on cornea and patch covering the affected eye if corneal abrasion is confirmed. An ophthalmologist should be notified or consulted if the abrasion is severe or other possible ocular abnormality could not be excluded. Explain and reassure to the patient that corneal abrasion sometime happened perioperatively and is usually resolved with 24–48 h, and consult ophthalmologist if the symptoms persist. Topical application of anesthetic drops and steroids to the cornea is contraindicated because these drugs retard healing [15].

Question 11:
Due to the major back surgery and the patient's history of chronic narcotic use, what approach would be most appropriate to decrease postoperative pain and narcotic need?

Answer:
Perioperative pain managements in patients who are having major spinal fusion remain mostly unchanged for decades. Parenteral narcotics are still playing the major role in this area. The greatest challenge to managing major back surgeries is the need to provide superior analgesia with minimal side effects and early mobilization. To achieve this goal, the multimodal approach to analgesia using various drugs and techniques has been widely studied and become popular in recent years. The multimodal perioperative analgesia management was designed to target different pathway of pain and enhance the early functioning recovery. Preoperative acetaminophen and gabapentin have been shown to reduce pain score and decrease opioid use in spinal surgery [3, 16, 17]. Low dose ketamine or lidocaine infusion may also be effective at improving postoperative pain control after complex spinal cases or in patients with chronic pain and opioid tolerance [16, 18–20]. Wide variety of other adjuvants has been studied and used in perioperative analgesic control of this group of patients, which include: cyclooxygenase-2 (COX-2), steroids, alpha-2 agonists, magnesium, neuroleptics, etc. Use of nonsteroidal anti-inflammatory drugs (NSAIDs) for analgesic control in spinal surgery has been controversial and the concerns about bleeding and bone graft healing still exist. However, narcotics remain the cornerstone for perioperative analgesia control in spinal surgery. Intraoperative and postoperative titration of iv opioid to achieve the level of anticipated pain should be managed carefully [16, 17, 20, 21].

Question 12:
Surgeon discussed with you preoperatively about possible medication that could help to decrease blood loss perioperatively. What should be your recommendation?

Answer:
Massive bleeding is always a concern in major spinal surgery. Every effort should be taken to minimize perioperative bleeding, i.e., avoiding preoperative anticoagulants, careful position to avoid abdominal pressure, avoiding venous return blockage, etc. Antifibrinolytic agents have been always a focus to be used in decreasing perioperative hemorrhage. A meta-analysis of commonly used antifibrinolytics agents aprotinin, tranexamic acid, and Ɛ-aminocaproic acid showed that these agents were able to reduce perioperative blood loss and transfusion requirements in spine surgery. However, tranexamic acid seems superior to the other two in perioperative prophylaxis of hemorrhage. There was no evidence that the antifibrinolytic agents increase the risk of thromboembolism in spine surgery [22]. Protamine is used in reversing the anticoagulating effect of heparin only. Prothrombin complex concentrate is an expensive blood clotting factors concentrate, usually reserved for patients who are having certain clotting factor deficiency or in certain critical massive bleeding patients. It is not indicated for prophylactic use. Aprotinin or Ɛ-aminocaproic acid are preferred antifibrinolytic agents to be used in spinal surgery for the purpose of decreasing perioperative bleeding.

Question 13:
Perioperative glucose management for spine surgeries. What approach do you recommend?

Answer:
A substantial body of literature demonstrates a clear association between perioperative hyperglycemia and adverse clinical outcomes [23]. It was shown that diabetes increases the risks of postoperative mortality, surgical site infection, deep venous thrombosis, and a prolonged hospitalization time after spinal surgery [24]. Insulin administration intra- and postoperatively has been shown to improve clinical outcomes. It was recommended that perioperative blood sugar should be controlled between 180 and 140 mg/dL in non-cardiac surgery [23, 25]. While perioperative hyperglycemia mostly happens in diabetic patients, 12–30% of the hyperglycemia are stress hyperglycemia which could be differentiated from the undiagnosed diabetes by A1c level [23].

Question 14:
Which of the following is not a risk factor for respiratory complications in spinal surgeries?

Answer:
Respiratory complications following surgery are a major cause of increased length of stay and perioperative morbidity and mortality. It was widely accepted that respiratory complications are more common after surgeries with extended surgical time, abdominal surgery, and thoracic surgery [26]. Recent study revealed that the spinal surgeries are also accompanied by increased respiratory complications. Patients who have a history of smoking, COPD, or diabetes mellitus are at a greater risk for respiratory complications following lumbar spine surgery. No evidence that renal insufficiency increases the risk of respiratory complication. Patients undergoing spinal fusion procedures have higher respiratory complication rates than those undergoing discectomies or laminectomies. Furthermore, patients undergoing multilevel fusion have greater respiratory complication rates than those undergoing single level fusion, especially among older patients. The most morbid postoperative respiratory complications include pneumonia, respiratory failure, atelectasis, and exacerbation of underlying chronic lung disease [26, 27].

Question 15:
What are the common risk factors of infections after spinal surgeries?

Answer:
Postoperative spinal wound infection is a potentially devastating complication after spine procedures. Tremendous amount of studies have been conducted to better recognize the risk factors which may help decrease the infection rate in spinal surgeries. Numerous factors were identified by studies as the potential influences on the development of postoperative infection. They could be divided in unchangeable (patient-related) and changeable (procedure-related) factors. The unchangeable risk factors include: patient's age (older than 70 years), ASA score, and medical conditions such as diabetes mellitus, cardiovascular disease, obesity, smoking, malignancy, steroid use, previous lumbar surgery, nutritional status, chronic obstructive pulmonary disease, immunologic competency. The changeable risk factors mainly include: duration of surgery, estimated blood loss, transfusions, use of instrumentation, multiple staged interventions, amount of levels fused, duration of patient stay in the postanesthesia care unit, prolonged preoperative hospital stay, and a large number of people in the operating room during the surgical procedure (specifically the number of nurses). Not all risk factors can be eliminated, but preoperative modification of the changeable risk factors can lead to decrease in infection rate [28–30].

Patient's age (older than 70 years).

Multiple Choice Questions

1. Perioperative medication management should include all those following except:
   (a) Stop taking aspirin 7 days before surgery
   (b) Continue metoprolol until the morning of surgery
   (c) Take his morning lisinopril on the day of surgery
   (d) Take his morning gabapentin on the day of surgery with a sip of water
   (e) Can also take tylenol in the morning of surgery

Answer: c

It is widely accepted with evidences that for patients who are currently taking ACE inhibitor or ARA scheduled for surgery, the medication should be withdrawn on the morning of surgery.

2. The surgeon decided that the MEP was needed for intraoperative monitoring. Which of the following anesthesia plan is not appropriate for this patient?
   (a) 1 MAC of inhalational agent will be used to maintain anesthesia.
   (b) Muscle relaxant is being avoided during surgery.
   (c) Radial arterial line is to be placed after intubation.
   (d) Remifentanil infusion is an option for analgesic management.
   (e) Propofol infusion is used for this patient.

   Answer: a

   MEP is the most vulnerable monitoring in response to inhalational agents due to the nature of weak stimulating reception to certain motor conduction. While the intravascular agents have less effect, the inhalational agents are usually limited to below 0.3–0.5 MAC.
3. According to American Society of Anesthesiologists Task Force on Perioperative Visual Loss practice advisory, all of the following risk factors are reported to be related to postoperative vision abnormality in the spinal surgery patients, except
   (a) Duration of surgery
   (b) Blood loss
   (c) Hypertension
   (d) Use of Wilson spine frame
   (e) Male patient

   Answer: c

   Risk factors include male sex, obesity, use of Wilson frame, longer anesthetic duration, greater blood loss, and a lower percentage of intravenous colloids in the fluid administration.
4. Due to the major back surgery and the patient's history of chronic narcotic use, what approach is not appropriate for the patient in order to decrease postoperative pain and narcotic need?
   (a) Intraoperative continuous lidocaine infusion.
   (b) Routine perioperative NSAID use is recommended.
   (c) Ketamine has been proved to be benefit.
   (d) Magnesium can decrease muscle cramping and thus is helpful in postoperative pain.
   (e) Narcotic is still needed if necessary.

   Answer: b

   Use of NSAIDs for analgesic control in spinal surgery has been controversial and the concerns about bleeding and bone graft healing still exist.
5. Regarding hyperglycemia management in this patient, which statement is not appropriate based on current consensus.
   (a) No evidence that suboptimal control of hyperglycemia leads to increased risk of infection and poor outcomes in spinal surgery.
   (b) Patient with diabetes have a higher risk of infection when undergoing spinal surgery than patients without diabetes.
   (c) Diabetes increases the risks of postoperative mortality, surgical site infection, and deep venous thrombosis.
   (d) Insulin should be used on this patient to control the BS between 180 mg/dL and 140 mg/dL, and perioperative monitoring of BS is important.
   (e) A1c can be used to differentiate the stress hyperglycemia and undiagnosed diabetes.

   Answer: a

   Hyperglycemia increases the risks of postoperative mortality, surgical site infection, deep venous thrombosis, and a prolonged hospitalization time after spinal surgery.

References

1. Comfere T, et al. Angiotensin system inhibitors in a general surgical population. Anesth Analg. 2005;36:644.
2. Castanheira L, et al. Guidelines for the management of chronic medication in the perioperative period:

systematic review and formal consensus. J Clin Pharm Ther. 2011;36(4):446–67.
3. Liu B, et al. A meta-analysis of the preoperative use of gabapentinoids for treatment of acute postoperative pain following spinal surgery. Medicine. 2017;96(37):e8031.
4. Pajewski TN, et al. Anesthesia for anterior/posterior spine surgery. In: Traul DE, Osborn IP, editors. Neuroanesthesia: a problem-based learning approach. Oxford: Oxford University Press; 2019. p. 87–97.
5. Carabini LM, et al. Hemostasis and transfusion medicine. In: Barash PG, et al., editors. Clinical anesthesia. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013. p. 429–31.
6. Cardone D, et al. Perioperative blood conservation. Eur J Anesthesiol. 2009;26(9):722–9.
7. Dysphagia following anterior cervical spinal surgery: a systematic review. Bone Joint J. 2013;95B(7):868–73.
8. Sutter M, et al. The impact and value of uni- and multimodal intraoperative neurophysiological monitoring (IONM) on neurological complications during spine surgery: a prospective study of 2728 patients. Eur Spine J. 2019;28(3):599–610. https://doi.org/10.1007/s00586-018-5861-0.
9. Cofano F, et al. Intraoperative neurophysiological monitoring during spinal surgery: technical review in open and minimally invasive approaches. Neurosurg Rev. 2019;42(2):297–307. https://doi.org/10.1007/s10143-017-0939-4.
10. Postoperative Visual Loss Study Group. Risk factors associated with ischemic optic neuropathy after spinal fusion surgery. Anesthesiology. 2012;116(1):15–24.
11. American Society of Anesthesiologists Task Force on Perioperative Visual loss. Practice advisory for perioperative visual loss associated with spine surgery: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Visual Loss. Anesthesiology. 2012;116(2):274–85.
12. Hewson DW, et al. Peripheral nerve injury arising in anesthesia practice. Anesthesia. 2018;73(Suppl.1):51–60.
13. Corcoran T, et al. Intraoperative dexamethasone does not increase the risk of postoperative wound infection: a propensity score-matched post hoc analysis of the ENIGMA-II trial (EnDEX). Br J Anaesth. 2017;118(2):190–9.
14. Assante J, et al. Infection associated with single-dose dexamethasone for prevention of postoperative nausea and vomiting: a literature review. AANA J. 2015;83(4):281–8.
15. Malafa MM, et al. Perioperative corneal abrasion updated guidelines for prevention and management. Plast Reconst Surg. 2016;137:790–8e.
16. Mathiesen O, et al. A comprehensive multimodal pain treatment reduces opioid consumption after multilevel spine surgery. Eur Spine J. 2013;22:2089–96.
17. Gritsenko K, et al. Multimodal therapy in perioperative analgesia. Clin Anesth. 2014;28:59–79.
18. Himmelseher S, et al. Ketamine for perioperative pain management. Anesthesiology. 2005;102:211–20.
19. Loftus RW, et al. Intraoperative ketamine reduces perioperative opiate consumption in opiate-dependent patients with chronic back pain undergoing back surgery. Anesthesiology. 2010;113:639–46.
20. Ortiz-Cardona J, et al. Perioperative pain management in the neurosurgical patient. Anesthesiol Clin. 2007;25:655–74.
21. Pradhan BB, et al. Ketorolac and spinal fusion. Spine. 2008;33:2079–82.
22. Li G, et al. Efficacy of antifibrinolytic agents on surgical bleeding and transfusion requirements in spine surgery: a meta-analysis. Eur Spine J. 2017;26(1):140–54.
23. Duggan EW, et al. Perioperative hyperglycemia management: an update. Anesthesiology. 2017;126(3):547–60.
24. Lou W, et al. The effect of diabetes on perioperative complications following spinal surgery: a meta-analysis. Ther Clin Risk Manage. 2018;14:2415–23.
25. Guzman JZ, et al. Outcomes and complications of diabetes mellitus on patients undergoing degenerative lumbar spine surgery. Spine. 2014;39(19):1596–604.
26. Qaseem A, et al. Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians. Ann Intern Med. 2006;144(8):575–80.
27. Murgai R, et al. Incidence of respiratory complications following lumbar spine surgery. Int J Spine Surg. 2018;12(6):718–24.
28. Pawar AY, et al. Postoperative spine infections. Asian Spine J. 2016;10(1):176–83.
29. Koutsoumbelis S, et al. Risk factors for postoperative infection following posterior lumbar instrumented arthrodesis. J Bone Joint Surg Am. 2011;93:1627–33.
30. Christodoulou AG, et al. Reduction of postoperative spinal infections based on an etiologic protocol. Clin Orthop Relat Res. 2006;444:107–13.

Suggested Reading

American Society of Anesthesiologists Task Force on Perioperative Visual loss. Practice advisory for perioperative visual loss associated with spine surgery: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Visual Loss. Anesthesiology. 2012;116(2):274–85.

Mathiesen O, et al. A comprehensive multimodal pain treatment reduces opioid consumption after multilevel spine surgery. Eur Spine J. 2013;22:2089–96.

Pajewski TN, et al. Anesthesia for anterior/posterior spine surgery. In: Traul DE, Osborn IP, editors. Neuroanesthesia: a problem-based learning approach. Oxford: Oxford University Press; 2019. p. 87–97.

Sutter M, et al. The impact and value of uni- and multimodal intraoperative neurophysiological monitoring (IONM) on neurological complications during spine surgery: a prospective study of 2728 patients. Eur Spine J. 2019;28(3):599–610. https://doi.org/10.1007/s00586-018-5861-0.

Management of Patient with Moyamoya Disease

13

Elias Nammour and Eman Nada

Stem Case Terminology

A 45-year-old male patient with moyamoya disease (MMD) is scheduled for a superficial temporal to middle cerebral artery (MCA) bypass. He has a past medical history of hypertension and stroke with residual left arm weakness.

13.1 Preoperative

Question 1:
What is moyamoya disease?

Answer:
Moyamoya disease (MMD) is a progressive, occlusive disease of the distal internal carotid arteries (ICA) associated with secondary stenosis of the circle of Willis, which may include the posterior cerebral arteries. The vessel stenosis results from hyperplasia of smooth muscle and luminal thrombosis. Moyamoya is a Japanese word that means a "puff of smoke," which refers to the image seen on angiography. This image is seen due to the formation of reticular anastomosis and collaterals between the internal and external carotid arteries [1–3].

Question 2:
What is the clinical picture of MMD?

Answer:
MMD has an ethnic and familial predisposition. It is highest in Japan, Korea, and other Asian countries compared to the rest of the world. It also has a female predominance [4]. The main presentation is transient ischemic attacks (TIAs), ischemic stroke, and headache. Less common symptoms include seizures, choreiform movements, intracranial hemorrhage, and rarely cognitive decline and visual impairment [2, 5].

MMD is a progressive disease that involves symptomatic progression in approximately two-thirds of patients over a 5-year period [6].

Question 3:
What are the treatment options of MMD?

Answer:
Medical management is used to prevent the occurrence of ischemic events. It includes the use of antiplatelet medications and vasodilators such as calcium channel blockers and pentoxifylline [1, 5, 7–9].

Question 4:
What are the surgical techniques used for revascularization?

E. Nammour
University of Massachusetts Medical School, Worcester, MA, USA

E. Nada (✉)
Department of Anesthesiology and Perioperative Medicine, University of Massachusetts Medical School, Worcester, MA, USA
e-mail: Eman.Nada@umassmemorial.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_13

Answer:
The surgical treatment is indicated in patients with recurrent or progressive cerebral ischemic events and reduced cerebral perfusion. It relies mainly on bypassing the obstructed blood vessels, either directly or indirectly [1, 10–12].

Direct Bypass Procedures: The direct bypass technique is the most commonly done procedure. It entails anastomosing the superficial temporal artery (STA) to MCA (Fig. 13.1). It remains the primary treatment option for adults with MMD and can be used in conjunction with several other surgical procedures if necessary.

An alternative procedure is the combined external carotid artery (ECA) internal carotid artery (ICA) bypass. Direct bypass procedures are usually done in adults as it is technically difficult to conduct in children [13, 14].

Indirect Bypass Procedures:
A variety of procedures exist as the following:

- Encephaloduroarteriosynangiosis (EDAS): A procedure in which the STA is mobilized and then sutured to the edges of the opened dura.

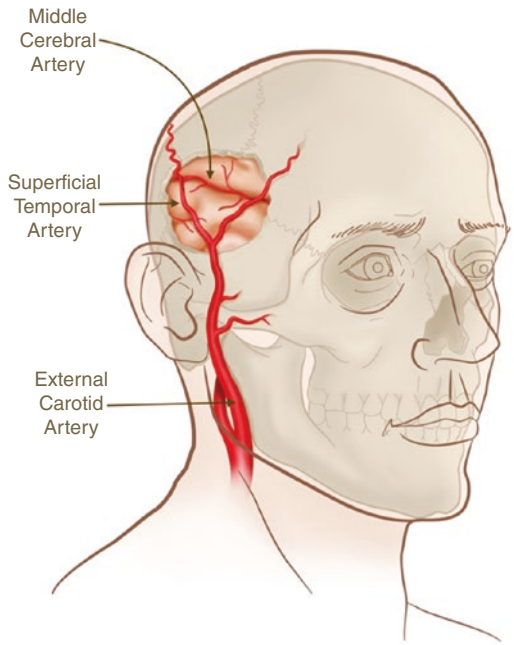


Fig. 13.1 Cerebral artery bypass procedure. Anastomosis of the superficial temporal artery to the middle cerebral artery

- Encephaloduroarteriomyosynangiosis (EDAMS): It is a modification of EDAS that combines the placement of temporalis muscle, a segment of STA or middle meningeal artery and a section of a galeal flap over the involved cerebrum to promote angiogenesis.
- Dural flaps created are folded into the dural/epiarachnoid space with middle meningeal neovascularization formation.
- Pial synangiosis: A branch of the STA is sutured directly into the pial surface.
- Encephalomyosynangiosis (EMS): An indirect revascularization procedure in which temporalis muscle is attached to the surface of the brain to promote collateral vessel formation.
- Drilling of burr holes without vessel synangiosis.

They are used more commonly in children due to the difficulty to anastomose the small arteries [1, 15, 16].

Other Procedures: Cervical sympathectomy, and omental transposition symptomatic hyperperfusion owing to increased cerebral blood flow (CBF) [3, 10, 17]

Question 5:
What are the preoperative anesthetic considerations for MMD?

Answer:
History, exam, and workup should be used to find the relevant information. History of strokes, TIA, and seizures should be reviewed. The presence of motor deficits and cognitive deficits should be documented. Antiseizure medications and calcium channel blockers should be continued until the day of surgery. Low-dose aspirin is continued at some centers until the day of surgery while at others, it is stopped 7–10 days before the surgery and replaced with low molecular weight heparin (LMWH). Aspirin is restarted after the surgery on the first postoperative day [10, 11, 18]. The radiological workup should be thoroughly reviewed. Computed tomography (CT) and magnetic resonance imaging (MRI) will show evidence of infarcts. MRA and cerebral angiography will

show signs of low perfusion or cerebrovascular reactivity [2, 19]. Premedication for anxiolysis is especially beneficial in children. Crying causes hyperventilation, hypocapnia, and cerebral ischemia. TIAs induced by crying or exercise were reported in children [10, 20–22]. Preoperative hydration may be helpful in avoiding the development of the postoperative ischemic complication [10].

13.2 Intraoperative

Question 6:
What are the anesthetic goals in patients with MMD?

Answer:
The main goal of anesthesia for MMD disease is to preserve the balance between O_2 supply and demand of the brain. CBF should be maintained by avoiding hypotension, maintaining normocarbia, and avoiding an increase in cerebral oxygen consumption ($CMRO_2$) [2, 10, 23].

Autoregulatory response to hypotension is substantially diminished in children compared with adults. Reduction of CBF is better tolerated in adults than children who have higher $CMRO_2$. Children with MMD have higher oxygen extraction ratio than adults, explaining the higher frequency of ischemic symptoms [23–25].

Question 7:
What are the anesthetic considerations in a patient with MMD?

Answer:
The general anesthetic considerations in a patient with MMD are:

- Strict control of the cerebral perfusion pressure (CPP)
- Carbon dioxide control
- Temperature control
- Maintenance of hemoglobin level

Question 8:
What are your choices of anesthetic medications?

Answer:
Propofol or etomidate are preferred for induction because they decrease both the cerebral metabolic rate for oxygen ($CMRO_2$) and CBF in a dose-dependent fashion. Also, because they are cerebral vasoconstrictors, there is no risk of steal phenomenon. Propofol produces higher regional cortical flow and lower intracranial pressure than sevoflurane [26]. However, there were no differences in the postoperative complications between the incidence of early postoperative complications under inhaled anesthesia versus total intravenous anesthesia [27–31].

Question 9:
How do you manage the hemodynamics intraoperatively?

Answer:
Besides the use of standard American Society of Anesthesiologists (ASA) monitors, advanced monitoring methods may be needed. Meticulous monitoring of the blood pressure and volume status are best done using an invasive arterial pressure catheter. A fall in mean arterial blood pressure will result in a decrease in CBF and CPP with resultant cerebral ischemia.

The autoregulation of CBF to the ischemic cerebral areas in MMD is impaired and is totally pressure dependent. Thus, during the revascularization techniques, the blood pressure is maintained in the normal to the higher side. Hypotension during the procedure may lead to ischemia and later to thrombosis of the bypass graft. Reduction in CBF is especially poorly tolerated in children who have a higher cerebral metabolic rate and diminished autoregulatory response [2].

Hypertension may lead to bleeding especially at the site of the anastomosis. The optimal or best level of arterial blood pressure is difficult to define. It is recommended to keep the blood pressure within 10–20% of the preoperative established baseline blood pressure for all patients [2, 21, 23, 32–34].

The intravascular volume should be kept in the range of hypervolemia. Ischemic complications were noted to occur in patients who had

lower urine output compared to those with greater urine output. Monitoring the volume status using pulse pressure variations can help differentiate the causes of hypotension and in treating them accurately [10, 35, 36].

Cerebral ischemia can be monitored by electroencephalography (EEG), near-infrared spectroscopy (NIRS), and somatosensory-evoked potentials. Transcranial Doppler (TCD) is used in a few centers. However, there is no evidence that the use of NIRS or TCD monitoring leads to the earlier detection of cerebral ischemia or favorably impacts the outcome [2, 10, 21, 36, 37].

Question 10:
What is the effect of hypo- and hypercarbia on patients with MMD?

Answer:
In MMD, the cerebral vasculature is already maximally dilated at ischemic tissues and in the collateral network of vessels, vasodilation of the normal vessels will result in decreased perfusion to the ischemic areas "intracerebral steal" [25, 29]. During hypercapnia, a decrease in CBF may occur when other normal vessels vasodilate [29, 36, 38]. The cerebrovascular response to hypercapnia is severely decreased over the cerebral cortices in patients with MMD [5, 24, 25, 29, 39]. On the other hand, hyperventilation with a $PaCO_2$ below 29 mmHg resulted in decreased regional CBF in children with MMD. Intraoperative hypocapnia less than 35 mmHg was shown to be associated with delayed recovery of consciousness and postoperative neurological deficits when compared with patients who had general anesthesia with $PaCO_2$ between 40 and 50 mmHg [36, 40]. Intraoperative and postoperative hypercapnia has been associated with an increased incidence of perioperative TIA [36]. Maintenance of normocapnia is generally recommended in revascularization procedures [32, 41, 42].

Question 11:
What is the effect of anemia on patients with MMD?

Answer:
Severe anemia should be corrected. There is no consensus at what hematocrit the patient with MMD should be transfused. A hematocrit of 30–42% has been proposed as adequate. On the other hand, polycythemia increases viscosity is regarded as a risk factor for cerebral infarction [34, 35, 43].

Question 12:
What is the effect of hypothermia on cerebral vessels during the revascularization of MMD?

Answer:
During STA-MCA bypass neuroprotective measures are used including mild hypothermia and burst suppression [41, 42, 44]. However, a marked drop in body temperature can induce cerebral vasospasm and rise may provoke the ischemic attack [45].

Question 13:
Towards the end of the procedure the surgeon asks for indocyanine green injection, what is indocyanine green, and why is it needed?

Answer:
Indocyanine (ICG) videoangiography is used as a noninvasive technique to assess the patency of the bypass graft. A microscope with an integrated ICG camera emits near-infrared light directly on the operative field, and the ICG fluorescences when excited by near-infrared light [46, 47].

ICG comes in 25 mg of preservative-free powder, and it is used after dilution in 10 ccs of aqueous solvent; the usual dose range is 5–25 mg.

ICG can cause erroneous desaturation readings on the pulse oximeter, and both anaphylactic and anaphylactoid reactions have been reported with its use [48, 49].

Question 14:
Can regional anesthesia be used in patients with MMD?

Answer:
Recent reports have reported that STA-MCA bypass can be done under local anesthesia [50].

There are case reports of the use of spinal and epidural in labor and cesarean section in patients with MMD [51–54].

The use of scalp block during EDAMS surgery in children age 3–13 years with MMD has been shown to provide calm awakening, better pain relief, and possibly reduced postoperative morbidity [55].

13.3 Postoperative

Question 15:
What are the postoperative considerations for patients after revascularization for MMD?

Answer:
After revascularization procedures, it is important to avoid both hypertension which may cause bleeding and hypotension which may result in graft thrombosis. Postoperative intravenous fluids at one and one-half times the normal maintenance rate and starting aspirin on the first postoperative day is recommended [10]. Inadequate pain control may result in cerebral infarcts and can increase stress that may affect the bypass [34, 56].

Question 16:
What are the possible postoperative complications?

Answer:
Postoperative complications include new postoperative ischemia, hyperperfusion, impaired wound healing, and subdural effusion, vascular bypass occlusion, bypass anastomotic aneurysm and scalp necrosis [57].

Question 17:
What are the risk factors for cerebral ischemia?

Answer:
Postoperative cerebral ischemia has been reported to happen in 3.5% in adults and 16.9% of pediatric patients. The mechanisms of stroke are usually related to hypoperfusion and/or the occurrence of artery-to-artery emboli [3, 36].

Previous history and the frequency of TIAs are the most important risk factor for the development of ischemic complications. Low-density areas seen on preoperative CT scan are another risk factor. Intraoperative risk factors include hypercapnia, hypotension, decreased intraoperative urinary output, and decrease in the hematocrit [31, 35, 36].

Surgically sparing the vital collateral vessels and minimum brain retraction are important to avoid perioperative complications [58].

Question 18:
How effective is the revascularization surgery in MMD?

Answer:
Revascularization surgery in patients with MMD has been found to be effective at preventing future ischemic events and improving the quality of life [59]. The risk for stroke after revascularization surgery in the first month is 4%. The cumulative 5-year risk of perioperative or subsequent stroke or death is 5.5% from mostly direct bypass procedures compared with 65% in symptomatic patients without surgery [12]. Comparing the revascularization to no revascularization, there was a significant drop in the incidence of the strokes over 5 years [9]. There was no significant difference between the indirect and direct/combined groups [12, 59, 60].

Indirect bypass procedures promote angiogenesis and reduce recurrent ischemic episodes, but it takes months to develop adequate collateral circulation and symptomatic relief. Also, the direct STA-MCA procedure cannot be carried out once the STA has been used in EDAS [3, 6, 10, 36, 59].

Question 19:
What are the possible complications following surgery?

Answer:
The exact incidence of MMD complications occurring after the direct bypass is still unknown. The surgical morbidity rate was 3.5%–9.2% and the mortality rate was 0.7%–4.61% per treated hemisphere [12, 61–64].

Question 20:
What is cerebral hyperperfusion syndrome (CHS)?

Answer:
CHS happens due to increased blood flow after the bypass procedure. The blood flow increases due to increasing amounts of released oxygen free radicals together with impaired autoregulation. Patients with MMD have a significantly higher risk for CHS after bypass surgery than patients with other atherosclerotic occlusive cerebrovascular diseases [65]. It is also more common after direct bypass procedures, although direct STA-MCA surgery is considered a low-flow anastomosis; the incidence of CHS is not low; it is around 18% [66–68].

Question 21:
How can CHS be diagnosed?

Answer:
The clinical symptoms of CHS can be in the focal symptoms with transient neurological deficits or intracranial hemorrhage. The focal symptoms can be in the form of unilateral headache, face pain, seizures, and transient neurological deficits. Patients in the indirect bypass group could have partial or complex seizures. CHS generally happens during the first postoperative week, and it usually improves by the second postoperative week [16, 57, 69].

Besides the clinical picture, CT and MRI imaging are used to identify indirect evidence of HS, such as hemorrhage and edema. TCD and Single Photon Emission Computed Tomography (SPECT) scan are dynamic studies to measure the blood flow. SPECT is considered the gold standard method for detecting intracranial vascular blood flow [70].

Question 22:
What is the treatment of CHS?

Answer:
The treatment of CHS starts with the control of blood pressure. The upper limit of the systolic blood pressure recommended is controversial. Fujimura et al. [71] found that prophylactic maintenance of SBP less than 130 mmHg in every patient resulted in a better outcome than lowering it only in patients who develop CHS [72]. More specifically a systolic blood pressure < 120 mmHg in normotensive patients and < 140 mmHg in hypertensive patients for a week postoperatively is recommended, especially if pial hyperemia is observed intraoperatively [73]. However, it should be noted that with the lowering of blood pressure, the risk of cerebral ischemia might increase because hyperperfusion is a local phenomenon associated with global hypoperfusion. In patients with advanced MMD and involvement of the posterior cerebral artery, intentional hypotension resulted in ischemic stroke in the hemisphere contralateral to the one operated on. Maintaining the patient's postoperative blood pressure near their preoperative level is recommended [74].

Routine postoperative monitoring of CBF using TCD and/or dynamic studies should be used for follow-up [73].

Edaravone—a free radical scavenger—proved to be helpful for prevention of transient neurological deficits [75]. Dehydrating agents are used to reducing edema after the CHS happens. Minocycline is a neuroprotective antibiotic that plays a role in blocking matrix metalloproteinase, which is correlated to the formation of cerebral edema, that has been found effective in preventing focal neurological deterioration [76].

Multiple Choice Questions

1. A 45-year patient with a history of MMD develops a TIA. What is the underlying pathology?
   (a) Cerebral atherosclerosis
   (b) Rupture of the small cerebral blood vessels
   (c) Progressive stenosis of the ICA
   (d) Hypercoagulable state
   Answer: c
   The vessel stenosis results from hyperplasia of smooth muscle and luminal thrombosis.
2. A 9-month-old patient with MMD is scheduled for an EDAS. In the preoperative area, the child begins to cry even in the presence of

her mother. Why is crying specifically a concern in MMD?

(a) It increases the anxiety of the mother.
(b) It increases the risk of cerebral infarction.
(c) It increases the blood pressure and can result in cerebral hemorrhage.
(d) It is disruptive to the hospital staff.

Answer: b

A study of 169 patients coming in for this procedure showed hyperventilation (in the form of crying) in pediatric patients increased the risk of cerebral infarction. Six patients (3.6%) developed cerebral infarction as a result of hyperventilation associated with crying. Therefore, it is important to prevent this in the perioperative setting with proper premedication, smooth inhalational or intravenous induction, and proper post-op pain control. Typically, parents presence and post-op morphine are sufficient for patient comfort [77].

3. A 44-year-old female with MMD is undergoing STA to MCA revascularization. During maintenance of anesthesia for a patient with MMD, your hemodynamic goals are:

(a) Use hypotensive anesthesia so you can help produce a bloodless field.
(b) Increase the blood pressure 50% above baseline so you can perfuse the ischemic area.
(c) Be conservative on fluid administration to avoid hemodilution.
(d) Maintain the blood pressure within 10–20% of the baseline.

Answer: d

The autoregulation of CBF to the ischemic cerebral areas in MMD is impaired and is totally pressure dependent. Hypotension during the procedure may lead to ischemia and later to thrombosis of the bypass graft. Reduction in CBF is especially poorly tolerated in children who have a higher cerebral metabolic rate and diminished autoregulatory response [2].

Hypertension may lead to bleeding especially at the site of the anastomosis. The optimal or best level of arterial blood pressure is difficult to define. It is recommended to keep the blood pressure within 10% to 20% of the preoperative established baseline blood pressure for all patients [2, 21, 23, 32–34].

4. A 37-year-old male with a history of MMD presents for a revascularization procedure. Which of the following increases his chances of developing an ischemic stroke postoperatively?

(a) History of hypertension
(b) The frequency of the ischemic attacks
(c) History of deep venous thrombosis
(d) History of coronary heart disease

Answer: b

A study of 124 children who underwent surgery for MMD, it found that 21 patients experienced infarctions, and 10 experienced reversible ischemic neurological deficits without new lesions. They found that frequent preoperative TIAs are a significant risk factor for perioperative ischemic complications. The frequent occurrence of TIAs may be an indicator of the instability of cerebral hemodynamics [36].

5. Indocyanine green is a medication that is used to assess the patency of the graft, and it can cause one of the following:

(a) Increases the incidence of postoperative nausea and vomiting.
(b) It can cause anaphylaxis.
(c) It causes hypertension.
(d) It interacts with the muscle relaxants.

Answer b

Indocyanine green can cause erroneous desaturation readings on the pulse oximeter, and both anaphylactic and anaphylactoid reactions have been reported with its use [48, 49].

6. A 37-year-old male patient with past medical history of several ischemic attacks and hypertension. The patient undergoes right-sided STA to MCA, his blood pressure was difficult to control intraoperatively. He wakes up well; however, a few hours later he complains of right-sided headache and facial pain then he starts to have an altered mental status. Which of the following conditions the patient most likely is having?

(a) TIA
(b) Stroke

(c) CHS
(d) Hypertensive encephalopathy
Answer: c

The clinical symptoms of CHS can be in the form of two categories, focal symptoms with transient neurological deficits or intracranial hemorrhage. The focal symptoms can be in the form of unilateral headache, face pain, seizures, and transient neurological deficits. Patients in the indirect bypass group could have partial or complex seizures. CHS generally happens during the first postoperative week, and it usually improves by the second postoperative week [57, 69].

References

1. Scott RM, Smith ER. Moyamoya disease and moyamoya syndrome. N Engl J Med. 2009;360(12):1226–37.
2. Parray T, Martin TW, Siddiqui S. Moyamoya disease: a review of the disease and anesthetic management. J Neurosurg Anesthesiol. 2011;23(2):100–9.
3. Baaj AA, et al. Surgical management of moyamoya disease: a review. Neurosurg Focus. 2009;26(4):E7.
4. Kuriyama S, et al. Prevalence and clinicoepidemiological features of moyamoya disease in Japan: findings from a nationwide epidemiological survey. Stroke. 2008;39(1):42–7.
5. Chiu D, et al. Clinical features of moyamoya disease in the United States. Stroke. 1998;29(7):1347–51.
6. Choi JU, et al. Natural history of moyamoya disease: comparison of activity of daily living in surgery and non surgery groups. Clin Neurol Neurosurg. 1997;99(Suppl 2):S11–8.
7. Yilmaz EY, et al. Moyamoya: Indiana University Medical Center experience. Arch Neurol. 2001;58(8):1274–8.
8. Hosain SA, et al. Use of a calcium channel blocker (nicardipine HCl) in the treatment of childhood moyamoya disease. J Child Neurol. 1994;9(4):378–80.
9. Hallemeier CL, et al. Clinical features and outcome in north American adults with moyamoya phenomenon. Stroke. 2006;37(6):1490–6.
10. Smith ER, Scott RM. Surgical management of moyamoya syndrome. Skull Base. 2005;15(1):15–26.
11. Kuroda S, Houkin K. Moyamoya disease: current concepts and future perspectives. Lancet Neurol. 2008;7(11):1056–66.
12. Guzman R, et al. Clinical outcome after 450 revascularization procedures for moyamoya disease. Clinical article. J Neurosurg. 2009;111(5):927–35.
13. Mesiwala AH, et al. Long-term outcome of superficial temporal artery-middle cerebral artery bypass for patients with moyamoya disease in the US. Neurosurg Focus. 2008;24(2):E15.
14. Andrews BT, Chater NL, Weinstein PR. Extracranial-intracranial arterial bypass for middle cerebral artery stenosis and occlusion. Operative results in 65 cases. J Neurosurg. 1985;62(6):831–8.
15. Sakurai K, et al. A novel susceptibility locus for moyamoya disease on chromosome 8q23. J Hum Genet. 2004;49(5):278–81.
16. Trigeminal neuralgia. Surg Neurol. 1996;45(5):406–8.
17. Fujimura M, et al. Incidence and risk factors for symptomatic cerebral hyperperfusion after superficial temporal artery-middle cerebral artery anastomosis in patients with moyamoya disease. Surg Neurol. 2009;71(4):442–7.
18. Manceau E, Giroud M, Dumas R. Moyamoya disease in children. A review of the clinical and radiological features and current treatment. Childs Nerv Syst. 1997;13(11–12):595–600.
19. Suzuki J, Takaku A. Cerebrovascular "moyamoya" disease. Disease showing abnormal net-like vessels in base of brain. Arch Neurol. 1969;20(3):288–99.
20. Fukuyama Y, Umezu R. Clinical and cerebral angiographic evolutions of idiopathic progressive occlusive disease of the circle of Willis ("moyamoya" disease) in children. Brain Dev. 1985;7(1):21–37.
21. Baykan N, et al. Moyamoya disease and anesthesia. Paediatr Anaesth. 2005;15(12):1111–5.
22. Nomura S, et al. Perioperative management protocols for children with moyamoya disease. Childs Nerv Syst. 2001;17(4–5):270–4.
23. Soriano SG, Sethna NF, Scott RM. Anesthetic management of children with moyamoya syndrome. Anesth Analg. 1993;77(5):1066–70.
24. Ogawa A, et al. Cerebral blood flow in moyamoya disease. Part 2: autoregulation and CO2 response. Acta Neurochir. 1990;105(3–4):107–11.
25. Kuwabara Y, et al. Response to hypercapnia in moyamoya disease. Cerebrovascular response to hypercapnia in pediatric and adult patients with moyamoya disease. Stroke. 1997;28(4):701–7.
26. Kikuta K, et al. Effects of intravenous anesthesia with propofol on regional cortical blood flow and intracranial pressure in surgery for moyamoya disease. Surg Neurol. 2007;68(4):421–4.
27. Astrup J, et al. Minimum cerebral blood flow and metabolism during craniotomy. Effect of thiopental loading. Acta Anaesthesiol Scand. 1984;28(5):478–81.
28. Cold GE, et al. CBF and CMRO2 during continuous etomidate infusion supplemented with N2O and fentanyl in patients with supratentorial cerebral tumour. A dose-response study. Acta Anaesthesiol Scand. 1985;29(5):490–4.
29. Kurehara K, et al. Cortical blood flow response to hypercapnia during anaesthesia in Moyamoya disease. Can J Anaesth. 1993;40(8):709–13.
30. Adachi K, et al. Early postoperative complications in patients with Moyamoya disease—a comparison of

inhaled anesthesia with total intravenous anesthesia (TIVA). Masui. 2005;54(6):653–7.
31. Sakamoto T, et al. Risk factors for neurologic deterioration after revascularization surgery in patients with moyamoya disease. Anesth Analg. 1997;85(5):1060–5.
32. Michenfelder JD. Anesthesia for cerebral surgery. In: Stanley TH, Petty WC, editors. New anesthetic agents, devices and monitoring. 1st ed; 1983. p. 45–9.
33. Brown SC, Lam AM. Moyamoya disease—a review of clinical experience and anaesthetic management. Can J Anaesth. 1987;34(1):71–5.
34. Kansha M, et al. Anesthetic management of children with moyamoya disease. Clin Neurol Neurosurg. 1997;99(Suppl 2):S110–3.
35. Sato K, Shirane R, Yoshimoto T. Perioperative factors related to the development of ischemic complications in patients with moyamoya disease. Childs Nerv Syst. 1997;13(2):68–72.
36. Iwama T, Hashimoto N, Yonekawa Y. The relevance of hemodynamic factors to perioperative ischemic complications in childhood moyamoya disease. Neurosurgery. 1996;38(6):1120–5. discussion 1125-6
37. Orihashi K, et al. Near-infrared spectroscopy for monitoring cerebral ischemia during selective cerebral perfusion. Eur J Cardiothorac Surg. 2004;26(5): 907–11.
38. Yusa T, Yamashiro K. Local cortical cerebral blood flow and response to carbon dioxide during anesthesia in patients with moyamoya disease. J Anesth. 1999;13(3):131–5.
39. Tagawa T, et al. Regional cerebral blood flow, clinical manifestations, and age in children with moyamoya disease. Stroke. 1987;18(5):906–10.
40. Sumikawa K, Nagai H. Moyamoya disease and anesthesia. Anesthesiology. 1983;58(2):204–5.
41. Zipfel GJ, Fox DJ Jr, Rivet DJ. Moyamoya disease in adults: the role of cerebral revascularization. Skull Base. 2005;15(1):27–41.
42. Kim SH, et al. Risk factors for postoperative ischemic complications in patients with moyamoya disease. J Neurosurg. 2005;103(5 Suppl):433–8.
43. Lee SH, et al. Optimum degree of hemodilution for brain protection in a canine model of focal cerebral ischemia. J Neurosurg. 1994;80(3):469–75.
44. Veeravagu A, et al. Moyamoya disease in pediatric patients: outcomes of neurosurgical interventions. Neurosurg Focus. 2008;24(2):E16.
45. Malley RA, Frost EA. Moyamoya disease: pathophysiology and anesthetic management. J Neurosurg Anesthesiol. 1989;1(2):110–4.
46. Januszewski J, et al. Flow-based evaluation of cerebral revascularization using near-infrared indocyanine green videoangiography. Neurosurg Focus. 2014;36(2):E14.
47. Pandey P, Steinberg GK. Neurosurgical advances in the treatment of moyamoya disease. Stroke. 2011;42(11):3304–10.
48. Chu W, et al. Anaphylactic shock after intravenous administration of indocyanine green during robotic partial nephrectomy. Urol Case Rep. 2017;12:37–8.
49. Olsen TW, et al. Anaphylactic shock following indocyanine green angiography. Arch Ophthalmol. 1996;114(1):97.
50. Kaku Y, et al. STA-MCA bypass under local anesthesia. Acta Neurochir Suppl. 2018;129:79–84.
51. Ngan Kee WD, Gomersall CD. Extradural anaesthesia for caesarean section in a patient with moyamoya disease. Br J Anaesth. 1996;77(4):550–2.
52. Sharma SK, et al. Epidural anesthesia for a patient with moyamoya disease presenting for cesarean section. Anesth Analg. 1994;79(1):183–5.
53. Venkatesh B, Taggart PC. Anaesthetic management of a patient with Moyamoya disease for caesarean section. Can J Anaesth. 1994;41(1):79–80.
54. Abouleish E, Wiggins M, Ali V. Combined spinal and epidural anesthesia for cesarean section in a parturient with moyamoya disease. Acta Anaesthesiol Scand. 1998;42(9):1120–3.
55. Ahn HJ, et al. Effect of preoperative skull block on pediatric moyamoya disease. J Neurosurg Pediatr. 2008;2(1):37–41.
56. Chui J, et al. Anesthetic management of patients undergoing intracranial bypass procedures. Anesth Analg. 2015;120(1):193–203.
57. Yu J, et al. Progress on complications of direct bypass for moyamoya disease. Int J Med Sci. 2016;13(8):578–87.
58. Iwama T, et al. Peri-operative complications in adult moyamoya disease. Acta Neurochir. 1995;132(1–3):26–31.
59. Fung LW, Thompson D, Ganesan V. Revascularisation surgery for paediatric moyamoya: a review of the literature. Childs Nerv Syst. 2005;21(5):358–64.
60. Scott RM, et al. Long-term outcome in children with moyamoya syndrome after cranial revascularization by pial synangiosis. J Neurosurg. 2004;100(2 Suppl Pediatrics):142–9.
61. Aoki N. Cerebrovascular bypass surgery for the treatment of Moyamoya disease: unsatisfactory outcome in the patients presenting with intracranial hemorrhage. Surg Neurol. 1993;40(5):372–7.
62. Huang Z, et al. Clinical features and outcomes in 154 patients with haemorrhagic moyamoya disease: comparison of conservative treatment and surgical revascularization. Neurol Res. 2015;37(10):886–92.
63. Park W, et al. Intracranial hemorrhage after superficial temporal artery-middle cerebral artery direct anastomosis for adults with moyamoya disease. World Neurosurg. 2018;119:e774–82.
64. Yoshida Y, et al. Clinical course, surgical management, and long-term outcome of moyamoya patients with rebleeding after an episode of intracerebral hemorrhage: an extensive follow-up study. Stroke. 1999;30(11):2272–6.

65. Fujimura M, et al. Significance of focal cerebral hyperperfusion as a cause of transient neurologic deterioration after extracranial-intracranial bypass for moyamoya disease: comparative study with non-moyamoya patients using N-isopropyl-p-[(123)I] iodoamphetamine single-photon emission computed tomography. Neurosurgery. 2011;68(4):957–64; discussion 964-5.
66. Fujimura M, Tominaga T. Lessons learned from moyamoya disease: outcome of direct/indirect revascularization surgery for 150 affected hemispheres. Neurol Med Chir (Tokyo). 2012;52(5):327–32.
67. Zhao WG, et al. Cerebral hyperperfusion syndrome after revascularization surgery in patients with moyamoya disease. Br J Neurosurg. 2013;27(3):321–5.
68. Abd-El-Barr MM, et al. Recombinant human bone morphogenetic protein-2 as an adjunct for spine fusion in a pediatric population. Pediatr Neurosurg. 2011;47(4):266–71.
69. Zhao M, et al. Risk factors for and outcomes of postoperative complications in adult patients with moyamoya disease. J Neurosurg. 2018;1:1–12.
70. Bacigaluppi S, et al. The contribution of imaging in diagnosis, preoperative assessment, and follow-up of moyamoya disease: a review. Neurosurg Focus. 2009;26(4):E3.
71. Fujimura M, et al. Efficacy of prophylactic blood pressure lowering according to a standardized postoperative management protocol to prevent symptomatic cerebral hyperperfusion after direct revascularization surgery for moyamoya disease. Cerebrovasc Dis. 2012;33(5):436–45.
72. Inoue T, et al. Annual rupture risk of growing unruptured cerebral aneurysms detected by magnetic resonance angiography. J Neurosurg. 2012;117(1):20–5.
73. Sekhar LN, et al. Cerebral revascularization for ischemia, aneurysms, and cranial base tumors. Neurosurgery. 2008;62(6 Suppl 3):1373–408; discussion 1408-10.
74. Jung YJ, et al. Ischemic complications occurring in the contralateral hemisphere after surgical treatment of adults with moyamoya disease. J Korean Neurosurg Soc. 2011;50(6):492–6.
75. Uchino H, et al. Edaravone reduces hyperperfusion-related neurological deficits in adult moyamoya disease: historical control study. Stroke. 2016;47(7):1930–2.
76. Fujimura M, et al. Minocycline prevents focal neurological deterioration due to cerebral hyperperfusion after extracranial-intracranial bypass for moyamoya disease. Neurosurgery. 2014;74(2):163–70; discussion 170.
77. Matsushima Y, et al. Perioperative complications of encephalo-duro-arterio-synangiosis: prevention and treatment. Surg Neurol. 1991;36(5):343–53.

Management of a Patient with Meningomyelocele

14

Summit D. Bloria, Rajeev Chauhan, Ankur Luthra, and Charu Mahajan

Stem Case Terminology

A 2-day-old 3.2 kg male child who is born through caesarean section (in view of large swelling at the back) is posted for surgery of a lower back swelling which his mother says was diagnosed before his birth. The mother did not give any history of any folic acid intake during her antenatal period and also gives history of a similar swelling in his elder sibling 3 years back.

The swelling is of the size of a tennis ball and there is clear fluid oozing out from it. The child is not moving his lower limbs. On examination, he is afebrile. His mother says that he has not passed urine since birth. This child appears to have a slightly enlarged head with an OFC of 36 cm and the swelling measures 4.8 × 4.6 cm which has ruptured recently. He is started on antibiotic prophylaxis (for meningitis) and is advised to be nursed in prone position. He is catheterised and 60 mL of urine is drained. He is started on intravenous (IV) dextrose-saline after measurement of his blood sugar and routine lab investigations sent. One unit of fresh blood has also been arranged.

After adequate OT preparation, he is taken for the surgery. He is administered fentanyl 6 μg, thiopentone 15 mg and atracurium 1.5 mg and intubated in lateral position with a 3.5 mm micro-cuffed ETT. After checking bilateral air entry, he is made prone and put on PCV mode of ventilation with O_2/air/sevoflurane. 25 mL of RL is infused IV and 30 mL of fresh blood is administered. Rest of the surgery is uneventful after an initial blood loss of 30–35 mL. The child is reversed and extubated on OT table and shifted to the recovery in prone position.

14.1 Preoperative

Question 1:
What is your diagnosis on the basis of history and examination? Explain the embryologic basis of this defect.

Answer:
The child is suffering from meningomyelocele, a type of neural tube defect. To understand the classification of various neural tube defects, we need to understand the development of neural tube first.

Central nervous system arises from ectoderm. Around the third week of gestation, ectodermal cells organise on the dorsal aspect of developing embryo around midline to form **neural plate**.

S. D. Bloria · R. Chauhan · A. Luthra (✉)
Department of Anaesthesia and Intensive Care, Post Graduate Institute of Medical Education and Research, Chandigarh, India

C. Mahajan
All India Institute of Medical Sciences, New Delhi, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_14

The plate is wider at its cephalic end than at its caudal end. In next few days, the lateral edges of the neural plate elevate to form the **neural folds**. The **neural groove** then develops as a result of invagination of the neural plate along its central axis, between the neural folds. The neural folds move together, fuse by the end of week 3, and convert the plate into a tube, known as **neural tube.**

The neural tube extending cranially to caudally eventually divides into 4 subdivisions which give rise to different parts of CNS as follows:

1. Prosencephalon—cerebrum and diencephalon
2. Mesencephalon—midbrain
3. Rhombencephalon—pons, cerebellum and medulla oblongata
4. Spinal cord

The clinical spectrum of neural defects thus consists of:

1. Anencephaly—When the rostral end of the neural tube fails to close.
2. Craniorachischisis—Anencephaly accompanied by a contiguous bony defect of the spine and exposure of neural tissue.
3. Encephalocele—It is a sac-like structure formed by protrusion of intracranial contents through a defect in skull.
4. Iniencephaly—Characterised by a defect to the occipital bone, spina bifida of the cervical vertebrae and retroflexion (backward bending) of the head on the cervical spine. Stillbirth occurs in most of cases.
5. Spina bifida (can be spina bifida occulta, meningocele or meningomyelocele).

Spina bifida can be classified as:

(a) Spina bifida occulta—Characterised by absence of spinous process and variable amounts of vertebral laminae. There is failure of fusion of neural arches; however, there is no herniation of meninges or spinal elements. The defect may be palpable, and there may be overlying cutaneous manifestations like hypertrichosis, lipomas, haemangiomas, dermal sinus, etc. These cases may present with **tethered cord syndrome** (explained later).

(b) Meningocele—Along with failed fusion of neural arches, there is cystic distension of meninges.

(c) Meningomyelocele—Along with cystic dilatation of meninges and defect in vertebral arches, there is presence of structural or functional abnormality of spinal cord or cauda equina.

Question 2:

What is tethered cord syndrome/tethered spinal cord/tethering induced symptomatology?

Answer:

It is defined as a stretch-induced functional disorder associated with the fixation (tethering) effect of inelastic tissue on the caudal spinal cord, limiting its movement [1]. As the child ages, this abnormal attachment of spinal cord causes progressive stretching of spinal cord leading to symptoms like pain, ankle deformity, muscle atrophy, sensory deficits, bladder dysfunction, etc. Tethered cord syndrome is classified as primary (isolated tethered cord syndrome) or secondary (associated with lesions like meningomyelocele, split cord malformation, lipoma, etc.).

If not treated in time, tethered cord can cause neurological and urological symptoms. Children mostly present with pain, followed by loss of functions of the feet, legs, bowel, or bladder and urinary/anal incontinence. The classic radiological features of tethered cord syndrome include a low-lying conus medullaris (below L2) and thick filum terminale (>2 mm) [2, 3].

Treatment is surgical and includes untethering of the spinal cord. Clinical signs or symptoms of deterioration become an indication for detethering of cord.

Preoperative neurological and urological functions determine the post-operative neurological and urological recovery. The complication rate of the untethering surgery is usually between 1 and 2% and complications include CSF collection and leakage, infection, haematoma, and neural damage to the spinal cord or rootlets.

Originally described in children, it is being reported in adults more and more [4–6]. The presenting features in adults include pain, motor weakness, stool and urinary incontinence. Tethered cord syndrome may be misdiagnosed as a case of degenerative spine disease (disc disease, spondylolisthesis), spine diseases, spinal cord disorders (such as tumours, syringomyelia) and peripheral nerve disease.

Question 3:
What other anomalies are associated with neural tube defects?

Answer:
The following associations have been found in addition to neural tube defects:

1. Club feet.
2. Hydrocephalus.
3. Hip dislocation.
4. Neurogenic bladder.
5. Facial clefts.
6. Musculoskeletal defects.
7. Arnold–Chiari malformation.
8. Umbilical hernia.
9. VACTERL anomalies have been found to be associated with neural tube defects. VACTERL implies:
   - V—Vertebral defects, hypoplastic or hemivertebrae; vascular anomalies
   - A—Anorectal anomalies
   - C—Cardiac anomalies, most common being atrial septal defects, ventricular septal defects and tetralogy of Fallot
   - TE—Tracheo-esophageal fistula
   - R—Renal defects
   - L—Limb defects like polydactyly, displaced thumbs, syndactyly and forearm defects

VACTERL/VATER association is typically defined by the presence of at least three of the above congenital malformations. It is important to remember that VACTERL remains an association (these malformations occur together more often than would be expected by chance) and not a syndrome.

Question 4:
What is Chiari malformation?

Answer:
Chiari malformations are a group of defects associated with congenital caudal "displacement" of the cerebellum and brainstem. They are subdivided into types 1 to 5.

- Type 1—Most common type, characterised by downward displacement of cerebellar tonsils into the upper cervical canal through the foramen magnum.
- Type 2—Also known as **Arnold–Chiari malformation**. Usually associated with a lumbosacral spinal myelomeningocele. It is characterised by displacement of the medulla, fourth ventricle and cerebellar vermis through the foramen magnum. Although the aetiology of CM-II is not well understood, it has been suggested that both open neural tube defect and incomplete spinal occlusion lead to CSF leakage from the foetal spinal canal and ventricular system. The resulting lack of ventricular CSF distention precludes the full development of the normal-size posterior fossa, which in turn leads to the caudal displacement of the rapidly developing cerebellum into the spinal canal along with the brainstem.
- Type 3—An occipital and/or high cervical encephalocoele associated with type 2 Chiari malformation.
- Type 4—Severe hypoplasia of cerebellum without displacement of the cerebellum through the foramen magnum.
- Type 5—Characterised by an absent cerebellum and herniation of cerebellum through the foramen magnum.

Question 5:
What is the prevalence of various neural tube defects? What factors predispose to development of neural tube defects?

Answer:
The prevalence of NTDs varies widely in different regions of the world. For example, the prevalence

of NTDs in the USA and many European countries is estimated at 0.5–0.8/1000 births, whereas prevalence in some regions of China has been reported to be more than 20 times higher [7, 8].

Neural tube defects are the most common birth defects in India [9]. The birth prevalence of NTDs reported ranged from 0.5 per 1000 total births to 18.2 per 1000 total births [10, 11].

The following have been proposed as the risk factors for development of neural tube defects:

- Genetic factors (Trisomy 13, 21 and 18)
- Lack of folate supplementation at any time of pregnancy[6]
- Passive smoking [12]
- Alcohol consumption [13]
- Mother's education level [14]
- Previous history of a child born with neural tube defects
- Diabetes mellitus
- Obesity [15]
- Drugs like carbamazepine, valproate, thalidomide [16, 17]

For a particular woman, her empirical recurrence risk after an affected pregnancy is approximately 3%, rising to around 10% after two NTD pregnancies.

Question 6:
How can neural tube defects be diagnosed prior to birth?

Answer:
Two approaches have been used for NTD screening: biochemical testing of maternal blood for alpha-fetoprotein (AFP) or the use of traditional 2D ultrasound

1. **Biochemical screening:**
   (a) **Maternal serum level of AFP:** Named due to its electrophoretic properties and its foetal origin, AFP is structurally and functionally related to albumin. This is a screening test for neural tube defect screening, a positive MSAFP result does not mean that the patient has an affected foetus but warrants further studies as a positive MSAFP test can be found in a multitude of other conditions. The maternal serum values are calculated and then expressed as a MoM by dividing the AFP concentration by the median value for the appropriate week of gestation. The median MSAFP value for each week of gestation is designated as 1.0 MoM. Most commonly, MSAFP in open spina bifida has a median MoM of 3.3 to 3.8; anencephaly, 7.7 MoM; gastroschisis, 7.8 MoM; and omphalocele, 4.5 MoM [18]. Using 2.5 multiples of mean as screen positive in singleton pregnancies, the detection rate for anencephaly is expected to be >95% and for open NTD between 65 and 80%.
   (b) **Amniotic fluid levels of AFP and acetylcholinesterase (AChE):** Estimation of AChE levels in amniotic fluid is a sensitive test for confirming an open NTD. Amniocentesis is often used to differentiate the disorders responsible for a maternal serum AFP elevation. If there is an amniotic fluid AFP elevation, a secondary test for the presence or absence of the AChE enzyme by gel electrophoresis is performed on the fluid. AChE is normally not present in amniotic fluid. Tissues containing AChE include red blood cells, neural tissue and muscle. Concentrations of AChE are much higher in foetal cerebrospinal fluid than in foetal serum. If the foetus has an open NTD, amniotic fluid AFP and AChE are usually both elevated and the high concentration of AChE in cerebrospinal fluid transudates across the defect into the amniotic fluid.

   At the time of amniocentesis for elevated MSAFP, karyotype analysis should also be performed to rule out chromosome aneuploidy.
2. **Ultrasound**: The following cranial ultrasound markers are used:
   (a) Banana sign: It is a consequence of the Arnold–Chiari malformation. It is attributed to a downward displacement of the cerebellum that is caused by protrusion of

the neural contents through the foramen magnum, which results from the NTD.
(b) Lemon sign: It is caused by a scalloping of the frontal bones secondary to decreased intracranial pressure from extrusion of the NTD.
(c) Foetuses with open spina bifida have smaller BPDs by approximately 2 weeks' gestation than expected for their gestational age.

Question 7:
Discuss the preoperative management of a case of meningomyelocele.

Answer:
The preoperative management can be discussed in the following 3 headings:

1. Assessment and management of lesion:
   (a) Measure the size of lesion.
   (b) Start antibiotics if the lesion has ruptured.
   (c) Prevent desiccation by covering the lesion with normal saline (NS) or RL soaked swabs. Once the dressing is in place and if repair is planned within 24–48 h, do not change dressing unless it is soiled. If closure is delayed greater than 48 h, change the dressing bid and keep it moist.
   (d) Nurse the patient in prone position/lateral/Trendelenburg position.
   (e) Avoid contamination of site and dressing from stool and urine.
   (f) Keep the neonate warm.
   (g) Monitor for signs of meningitis.
2. Neurological assessment and management:
   (a) Assess the neonate for neurodeficit, and determine the upper level of neurodeficit.
   (b) Meningomyelocele is usually associated with Chiari type 2 malformation; so measure head circumference periodically, get a head USG done and watch out for sudden onset of respiratory distress. Many of these patients have to undergo VP shunting due to presence of hydrocephalus.
3. Ancillary management:
   (a) Rule out other associated anomalies (VACTERL). Get urologic, orthopaedic, etc. evaluation done whenever warranted.

   Maintain strict asepsis always while caring for these patients and prevent exposure to latex, as latex allergy is seen in up to 70% of these patients [19].

Question 8:
Discuss the role of folate administration in prevention of neural tube defects.

Answer:
The role of folate in prevention of neural tube defects has been proved since 1991, when it was demonstrated that women who had prior pregnancies with isolated NTDs had a 72% reduction of a recurrence of the NTD when supplemented with 4 mg of folate per day at least 4 weeks before conception through the 12th week of gestation [20]. Now it is recommended that all females of child bearing age should be supplemented with 400 μg of folate and women previously diagnosed with a foetus affected with an NTD be supplemented with 4 mg of folic acid per day. Supplementation should begin at least 1 month before conception and should be continued for the first 3 months of pregnancy.

The exact mechanism by which folic acid prevents spina bifida and other NTDs remains unclear. Exogenous folic acid may enhance embryonic cell proliferation through stimulation of pyrimidine and purine synthesis, and the finding of disordered embryonic cell proliferation in several mouse NTD models supports such a role [21]. In addition, folic acid may enhance the methylation of key macromolecules including DNA, which can affect embryonic gene expression, thereby contributing to the epigenetic regulation of early nervous system development [22, 23]. A further possibility is that folic acid could in some cases be detrimental for neural tube closure, worsening foetal outcome and leading to miscarriage [24].

Question 9:
What surgical procedures do these patients undergo?

Answer:
The following surgical procedures are usually taken up in these patients:

1. Primary closure of defect: Since the defect is visible on ultrasound prenatally, many centres perform elective prenatal repair before birth. If performed postnatally, the surgery should be performed as early as possible (24–48 h) to decrease the chances of infection. It must be emphasised that early surgery does not improve the neurological deficit.
2. VP shunt: Done in view of hydrocephalus. In patients without hydrocephalus, most surgeons wait at least 3 days after MM repair before shunting. VP shunting and repair of lesion may be done in same sitting in patients with overt hydrocephalus.
3. Surgical management for associated anomalies.
4. Posterior spine fusion, later on in life.

14.2 Intraoperative

Question 10:
What are the salient features in history and clinical examination in the patients with meningomyelocele?

Answer:
Salient features in history are:
1. History of folate supplementation before and during pregnancy. Any history of any drug intake predisposing to folate deficiency like eptoin, oral contraceptive pills, methotrexate, etc.
2. History of previous child birth with similar anomalies.
3. History of antenatal diagnosis with ultrasound.
4. History of antenatal surgery for correction of lesion.
5. Any history of associated anomalies. Non-neurologic findings in patients with meningomyelocele are as follows: hip dislocation, clubfeet, kyphoscoliosis, chest wall malformation, hydronephrosis, hydroureter, horseshoe kidney, undescended testes, hydrocele, malrotation, omphalocele, Meckel's diverticulum and inguinal hernia [25].

Clinical examination:
1. Level of lesion: The lesion can be at the level of cervical, thoracic, lumbar or sacral level. There is a strong correlation between the axial level of lesion and the degree of disability experienced by individuals with MMC.
2. Assessment of neurological deficit: Look for spontaneous movements in lower extremities. Check movement of lower extremities in response to painful stimuli.
3. Examine for presence of hydrocephalus: Look for increased head circumference and bulging fontanelles.
4. Any presence of pressure sores in patients with neurodeficit.

Question 11:
What investigations are needed prior to surgery for meningomyelocele? What are fasting guidelines for paediatric patients?

Answer:
Baseline investigations include blood glucose, haemoglobin, total leukocyte count, blood grouping and urine routine and microscopy. Blood should be matched and readily available when managing larger lesions.

Additional investigations include cardiac echo, renal USG and urodynamic studies.

The preoperative fasting guidelines for paediatric patients is as follows:

- Clear liquids up to 2 h prior to surgery. Clear liquids would include fluids without pulp; clear tea or coffee without milk products.
- Breast milk for 4 h.
- Infant formula feed for 6 h

  This is sometimes described as the 6-4-2 regimen.
- Finally, solid food for 8 h.

These guidelines have been criticised of late. It has been demonstrated that even a 2 h fasting interval for fluids does not guarantee an empty stomach and there seems to be a considerable inter-individual variation as well [26, 27].

Prolonged fasting must be discouraged in paediatric patients as it can result in hypoglycaemia, metabolic acidosis, dehydration, cardiovascular instability, discomfort, hunger and thirst.

Question 12:
What concerns will you take into consideration while managing a case of meningomyelocele? Discuss the role of regional anaesthesia in meningomyelocele.

Answer:
The special concerns will be regarding:
- Age-related pathophysiology—preterm/term/neonate
- Airway
- Associated congenital anomalies (discussed above)
- Concerns related to meningomyelocele—location of lesion, ruptured or not
- Concerns related to surgery—positioning, blood loss, hypothermia, latex allergy

Role of regional anaesthesia in meningomyelocele:

Regional anaesthesia in neonates for meningomyelocele surgery has been suggested as it has several advantages over general anaesthesia. There is no airway manipulation with regional anaesthesia along with reduced stress response of surgery. Also, the incidence of postoperative apnoea is minimized with the use of regional anaesthesia. The patient is placed prone and dural puncture is performed in the most caudad region of the meningomyelocele sac, in an area devoid of neural elements using a tuberculin syringe.

Question 13:
How will you premedicate this child?

Answer:
Neonates usually do not need anxiolysis. Older children, especially those undergoing repeated surgical procedures must be premedicated to allay anxiety. Oral midazolam in a dose of 0.5–1.0 mg/kg is the most commonly used drug. After administration of premedication, the child should be kept under observation to detect any respiratory depression the earliest.

Question 14:
What all monitoring is employed intraoperatively for meningomyelocele?

Answer:
The following monitors are routinely used intraoperatively:

1. ECG
2. Saturation probes
3. Non-invasive Blood pressure
4. Temperature
5. Urinary output
6. End tidal CO_2

The additional monitors can be employed:
1. Invasive blood pressure: It provides beat-to-beat monitoring of blood pressure and helps early diagnosis of haemodynamic instability. Patients with large lesions should have invasive BP monitored. VAE has been described in cases of tethered cord syndrome due to entrainment of air via a bony spur [29].
2. Intraoperative neuromonitoring.

Question 15:
Discuss the role of intraoperative neuromonitoring in a case of meningomyelocele?

Answer:
Intraoperative neuromonitoring is now an important modality in neuroanaesthesia to prevent iatrogenic injury to nervous tissue. The modalities employed for the purpose of intraoperative neuromonitoring are:

Sensory evoked potentials (SSEP): It is the most commonly monitored sensory evoked potential. The SSEP is produced by stimulation of a peripheral sensory nerve with the response measured along the sensory pathway.

Motor evoked potentials (MEP): It is produced by transcranial multipulse electrical stimulation of the motor cortex using scalp electrodes. If MEPs are to be utilised perioperatively, use of neuromuscular blockers is not possible.

It has been suggested that intraoperative neuromonitoring minimises neurological morbidity in tethered cord surgery [30]. In addition to SSEP and MEP, bulbocavernosus reflex has also been monitored intraoperatively.

Question 16:
What precautions will you take while inducing this patient?

Answer:
Before shifting patient to operation theatre, all paediatric airway equipment and monitors should be available. The operation theatre temperature must be warm.

If the child has an IV cannula, IV induction will be done. For a patient without IV cannula, inhalational induction with sevoflurane can be done. In short, the patient is handed over a face mask and encouraged to apply it over his/her nose. He/she is then told to take deep breaths while sevoflurane is started and incrementally increased. Once the child gets sedated, an IV access is taken.

Propofol is the most commonly used IV induction agent, with use of opioids and a non-depolarizing muscle relaxant. While administration of propofol, watch out for development of hypotension. Muscle relaxant should be administered only after ensuring adequate mask ventilation. Cis-atracurium is the most commonly used muscle relaxant in this age group because of its spontaneous degradation at room temperature (Hoffmann elimination).The current use of succinylcholine has decreased owing to its production of hyperkalemia in patients with neurological deficits. Also, succinylcholine causes a transient increase in intracranial pressure.

Intubation should be attempted only after ensuring an adequate depth of anaesthesia lest increase in ICP may result. If the duration of surgery is small, one can use uncuffed endotracheal tube. Use of uncuffed tubes lowers the resistance to breathing, allows easy suctioning and prevents trauma to subglottic region. For procedures of long duration, use of paediatric cuffed tubes is advisable. Their use allows employment of lower fresh gas flows, reduces air pollution, avoids multiple intubation attempts and provides better end tidal CO_2 monitoring.

For determination of appropriate size and length of the endotracheal tube, various formulas have been suggested. Some of the most commonly used among them are:

The internal diameter (ID) of an endotracheal tube: (Age in years/4) + 4

The ID of endotracheal tube = Diameter of the fifth finger

The following formulas have been used to suggest the depth of endotracheal tube insertion from teeth:

$$\text{Depth of tube : Height } (\text{in cm})/10+5$$

or

$$\text{Weight } (\text{in kg})/5+12$$

or

3 times the ID from the alveolar ridge

or

$$(\text{Age in years}/2)+12$$

or

Advance the endotracheal tube into a bronchus, then withdraw it, 2 cm

Question 17:
What precautions will you take while intubating this patient?

Answer:
The important considerations while intubating patients with meningomyelocele are:

1. Taking care of the lesion. There may be difficulty in positioning the child for intubation because placing the defect in the middle of a "doughnut" not only causes pressure on the open defect but also necessitates additional padding beneath the shoulders and head [31]. Some patients may need to be intubated in lateral position.
2. In syndromic patients, incidence of difficult airway is increased. Airway management may be more challenging in the infant with MMC because of associated neck pathology (Chiari

malformation, Klippel–Feil syndrome), positioning, and increased association with short trachea. Attention must be paid to identifying the carina and properly positioning the endotracheal tube to prevent endobronchial intubation.
3. Prevent development of hypotension during induction.
4. All usual considerations taking in view the age of the patient like temperature management, fluid management, etc.

Question 18:
What is steal induction?

Answer:
As described by Meyers et al. in 1977, it is a special type of inhalational induction where the child is brought to the operating room already asleep and undergoes induction without being awakened [32]. Droperidol, ketamine, melatonin and clonidine have been employed for steal induction [33–35]. While avoiding moving or awakening the child, 70% nitrous oxide at high flows via an anaesthesia mask is held closely over the child's face. At first the mask should not touch the skin, but as sedation deepens it is placed gently on the face and the concentration of sevoflurane is increased incrementally. Monitoring devices should be attached as soon as possible. Once adequately anaesthetised, the child can be transferred to a stretcher or operating room.

Question 19:
How will you position this patient for surgery?

Answer:
The child will be positioned prone during the surgery. During turning the patient, at least one monitor should be connected to the patient and the period of turning should not be an unmonitored period. The weight of the child is supported on bolsters under the chest and pelvis, and the abdomen hangs free between bolsters. Excessive pressure on the abdomen due to an abnormal position should be prevented as it impedes ventilation, compresses vena cava, and increases epidural venous pressure and bleeding. Other important considerations are:

1. Ensure proper positioning of endotracheal tube after attaining the prone position.
2. Maintain adequate padding of pressure points.
3. Care of the lesion during turning the patient.
4. Covering the patient adequately to prevent occurrence of hypothermia intraoperatively.

Question 20:
How will you maintain anaesthesia in this case?

Answer:
Anaesthesia is maintained with inhalational agents and opioids for pain relief. Isoflurane, sevoflurane or desflurane are the inhalation agents used for maintenance of anaesthesia. Sevoflurane provides better recovery profile as compared to isoflurane in children [36]. Neuromuscular blockade with nondepolarizing muscle relaxants is achieved to prevent patient movement and to minimise the amount of anaesthetics required. Cis-atracurium and atracurium are the preferred agents in view of them undergoing spontaneous Hoffmann elimination. Fentanyl is the most commonly used opioid, but its half-life increases with repeated dosing. It undergoes hepatic metabolism, which is immature in premature infants. Hence, the sedative and respiratory depressive effects of fentanyl may be prolonged in these children. Remifentanil is a newer narcotic agent, cleared rapidly by the plasma esterases and an attractive choice wherever available.

Question 21:
Discuss intraoperative fluid management in this case.

Answer:
The aim of intraoperative fluid administration is to maintain normovolemia and haemodynamic stability.

Intraoperative fluid administration has to provide maintenance fluid, correct preoperative deficit (caused by preoperative fasting) and replace third-space and blood losses.

The 4-2-1 rule given by Holliday and Segar has been used to calculate hourly fluid requirement in paediatric patients.

Fluid deficit is calculated as: Hourly maintenance requirements × hours of fluid restriction. Of the total deficit, 50% is to be administered first hour and 25% each in next 2 h.

Blood losses are replaced with either 1:1 ratio of blood or colloid, or 3:1 ratio for crystalloid. Third-space losses should be replaced with crystalloid. Third-space losses can be 2–5 mL/kg depending upon the size of lesion.

Blood administration is usually not required in meningomyelocele unless the lesion is very large. The maximum allowable blood loss (MABL) is calculated as follows:

$$\text{MABL} = \text{EBV}\left(\text{estimated blood volume}\right) \times \left(\text{Initial haematocrit} - \text{Minimum acceptable haematocrit}\right) / \text{Initial haematocrit}$$

The estimated blood volume varies with the age of the patient:

- Preterm infant: 90–100 mL/kg
- Term neonate: 80–90 mL/kg
- Infants between 3 months and 1 year old: 70–80 mL/kg
- Older child: 70 mL/kg

Accurate estimation of blood loss may be difficult in paediatric patients.

NS is the most commonly used fluid. In neonates and premature infants, the danger of hypoglycaemia should be borne in mind. Blood glucose should be closely monitored in these children along with continuous infusion of glucose at 5–6 mg/kg/min.

14.3 Postoperative

Question 22:
Describe awakening and extubation in this case.

Answer:
After the surgery is complete, the child should be turned supine, and inhalational agents stopped. Infants with meningomyelocele may be at increased risk of post-operative apnoea. Extubation after primary repair of the defect may take place in haemodynamically stable infants who are awake and can maintain their airway. Infants should recover in a monitored setting with respiratory and cardiac monitors.

Question 23:
What is an encephalocele and what are the associated anaesthetic challenges?

Answer:
Encephalocele is a form of cranial dysraphism wherein the intracranial contents protrude through a bony defect in the cranium. These can be anterior or posterior based on the location of the defect. In India, Europe and USA, posterior encephaloceles are more common while in other parts of south-east Asia, frontoethmoidal encephaloceles are generally seen.

Multiple congenital anomalies like hydrocephalous, Arnold–Chiari malformation, agenesis of corpus callosum, microcephaly, developmental delay, etc. may be associated with it. Other extracranial anomalies are also commonly present like micrognathia, cardiac defects, cleft lip/palate, renal and pulmonary anomalies. Small children with congenital anomalies involving various systems including airway make anaesthetic management quite challenging. In addition, the site of encephalocele may pose a challenge during mask ventilation, intubation and positioning. Children having large frontal encephalocele with a big sac may be difficult to mask ventilate while those having occipital encephalocele may be difficult to posi-

tion and intubate. The incidence of difficult mask ventilation and intubation is around 5.9% and 19.5%, respectively [37]. Larger the size of sac, more is the difficulty in positioning and laryngoscopy.

Question 24:
How will you manage a case of giant occipital encephalocele?

Answer:
In the preanaesthetic evaluation, assess for the difficulty in venous access, ventilation and intubation and positioning. Look for other coexisting congenital anomalies. Investigations required are same as for other neural tube defect cases and blood has to be arranged preoperatively. Sedative premedication is usually not given. Operation room has to be prepared according to the requirement of a paediatric patient and difficult intubation.

A giant occipital encephalocele makes positioning difficult as compression over the sac has to be avoided. For this, the child is placed either lateral or supine with sac placed inside a doughnut to avoid any compression on it. The routine monitors like electrocardiography, non-invasive blood pressure monitoring, and pulse oximetry are attached.

The inhalational induction is preferred over IV induction in view of difficult intubation. A sac in occipital area not only makes head placement difficult but also limits extension of neck [38]. The child can be placed in various positions like lateral, supine with sac resting inside the doughnut or head held beyond the edge of table with an assistant holding it [39]. Various modifications of such techniques have been used by various authors but the main focus remains the same that is to avoid any compression of sac [39]. Slow needle aspiration of fluid from the very large sac under sterile condition makes it slack and easier to position the head for laryngoscopy [40]. We prefer to place the patient in left lateral position for intubation when a right handed anaesthesiologist is performing laryngoscopy [41]. Anaesthesia is maintained with short acting volatile agents in air or nitrous oxide with oxygen. Invasive arterial monitoring helps in beat-to-beat monitoring of BP and frequent blood gas sampling. Urine output and temperature monitoring are also routinely done.

The various intraoperative complications are bradycardia, tachycardia, hypotension, hypothermia, electrolyte disturbances and blood loss [39]. Rapid drainage of CSF from the sac can cause bradycardia, hypotension or cardiac arrest, so it should be done slowly in small aliquots. Often blood transfusion is required in these patients because of loss that occurs during dissection of sac, craniectomy, from blood vessels and venous sinuses. These patients are extubated only when they are completely awake with regular breathing, normothermic, haemodynamic stable and normal metabolic profile.

These patients need to be closely monitored in intensive care unit post-operatively. The various post-operative complications are CSF leak, meningitis and development of hydrocephalous. A major prognostic factor for their neurologic outcome is contents of the sac. More is the herniated and damaged brain tissue inside the sac, poor is the long-term outcome.

Question 25:
Define laryngospasm? What are the risk factors for development of laryngospasm? How will you manage a case of laryngospasm?

Answer:
Laryngospasm is the sustained closure of the vocal cords. Children are more predisposed to develop laryngospasm as compared to adults, its incidence doubles in children and trebles in the very young. Laryngospasm in awake patients is a protective reflex that guards against pulmonary aspiration. However, laryngospasm under lighter planes of anaesthesia can cause hypoxia and bradycardia.

Partial laryngospasm is characterised by presence of stridorous noise from patient and while there is a silent chest in cases of total laryngospasm.

The following risk factors have been described for development of laryngospasm:

1. Patient risk factors:
   (a) Age
   (b) Airway hyper-reactivity (URTI, Asthma)
   (c) Obstructive sleep apnoea
   (d) History of smoking
   (e) Presence of airway anomalies
2. Surgical risk factors:
   (a) Thyroid surgery
   (b) Shared airway
   (c) Application of noxious stimuli during light plane of anaesthesia
3. Anaesthesia-related risk factors:
   (a) Insufficient depth of anaesthesia
   (b) Volatile anaesthetic agents (desflurane>isoflurane>enflurane>halothane>sevoflurane).
   (c) Experience of anaesthetist

Management of laryngospasm includes:

(a) Jaw thrust to lift the tongue off the pharyngeal wall.
(b) Larson's manoeuvre is bilateral firm digital pressure on the styloid process behind the posterior ramus of the mandible.
(c) CPAP with 100% oxygen via a tight-fitting facemask. Positive pressure application, however, may be harmful in cases of complete laryngospasm as it may force the false cords against the tightly closed true cords.
(d) Deepen the plane of anaesthesia with I.V. propofol (0.5 mg/kg increments).
(e) Succinylcholine is the drug of choice if propofol fails to relieve laryngospasm. An IV dose of 0.1–0.2 mg/kg of succinylcholine is used.

In case laryngospasm occurs before securing an IV line and does not break with jaw thrust and CPAP, intra-muscular (IM). succinylcholine in doses of 4 mg/kg is an option. Other modes of succinylcholine that have been utilised are intralingual (2–3 mg/kg) and intraosseous (1 mg/kg).

Once laryngospasm is successfully treated, ventilation should be supported initially with 100% oxygen.

Question 26:
What is latex and where is it used in health care? Write a short note on latex allergy.

Answer:
Natural latex is obtained from the sap of a rubber tree. A number of substances we routinely use contain latex. Some of the latex-containing substances that we use inside hospitals include blood pressure cuffs and tubing; stethoscope tubing; IV tubing injection ports; tourniquets; syringe plungers; face masks; airways; laryngoscope bulb gaskets; skin temperature monitors; rubber suction catheters; arm boards; bite blocks; teeth protectors; ventilator hoses and bellows; resuscitation bags (black or blue, reusable); rubber-shod clamps; breathing tubes; oxygen tubing; reservoir bags, IV bags and tubing ports; medication vial needle ports; tape and other adhesives (e.g. Esmarch bandages, adhesive bandages); dental dams; elastic bandages (Ace wraps); dressings (e.g. Coban, Moleskin, Micropore); rubber pads; protective sheets; drains; electrode pads; rubber aprons; circulating fluid warming blankets; some cast material; goggles; pulmonary artery catheter balloons; epidural catheter adapters; IV medication pump cassettes; electrocardiogram (ECG) electrodes and pads; intestinal and stomach tubes; rubber bands; chest tube drainage system tubing; condom urinals; urinary and nephrostomy catheters; gastrostomy tubes; bulb syringes; adhesive drapes; nipples; instrument mats; specimen traps; catheter bag straps; dilating catheters; etc.

Many chemicals are added to the latex during the manufacturing process. These additional substances may also be responsible for latex allergy. Repeated exposure to products containing natural rubber latex predisposes to development of latex allergy.

Latex allergy can be a:

1. Irritant contact dermatitis: The most common type. Consists of itching, redness, scaling, drying and skin cracking. Latex-glove induced dermatitis increases the chance of hospital-acquired infections, including blood-borne infections, being transmitted.
2. Type IV allergic reaction: Characterised by a delayed skin rash. Unlike irritant contact dermatitis, allergic contact dermatitis often spreads beyond the area of contact with the allergen. Sometimes flushing, rhinitis, dizziness, itching, sinus symptoms, conjunctivitis and eyelid edema may also be present.
3. Type I allergic reaction: Most severe type. May cause severe morbidity and mortality. Such reactions account for a significant proportion of perioperative anaphylactic reaction, especially in children with myelomeningocele [42]. Anaphylactic shock can be provoked in allergic persons by the previous use of latex.
4. Latex-fruit syndrome: People who have latex allergy also may have or develop an allergic response to some plants and/or plant products such as fruits. Fruits (and seeds) involved in this syndrome include, avocado, chestnut, kiwi fruit, mango, banana, pineapple, passion-fruit, fig, strawberry and soy.

Considering the high incidence of latex allergy in patients with meningomyelocele, all latex precautions should be taken. These patients should be provided "latex safe cart" consisting of all latex free substances that the patient may need.

Treatment of latex reactions:

- In cases with irritant contact dermatitis, simply removing the latex product from the patient will do.
- Steroids can be used for allergic reactions. Topical nasal steroids may be used for rhinitis. Topical corticosteroids can be used for a rash. Antihistamines and systemic steroids can be used to treat other mild reactions.
- If the symptoms are more severe, more aggressive treatment is indicated, including antihistamines, systemic steroids, H_2 blockers, oxygen, IV fluids, bronchodilators and epinephrine. The crash cart must not contain latex-containing items.
- If anaphylaxis occurs, early detection is necessary. Artificial airway support may be needed as well as intravascular volume expansion, administration of vasoactive medications and other life-support techniques.

Once latex allergy has manifested, latex precautions should continue throughout the post-operative period of the patient.

Question 27:
What is the importance of post-operative apnoea in former preterm infant?

Answer:
The development of post-operative apnoea is a major concern with surgery in neonates. Up to the age of 60 weeks post conceptional age, infants are predisposed to suffer from post-operative apnoea [43]. A weak central respiratory drive is said to be responsible for this situation. Anaemia (haematocrit <30%) is an independent risk factor associated with apnoea in former preterm infants. Although it is more common in patients undergoing general anaesthesia, it is seen also in preterm infants undergoing regional anaesthesia, especially when sedation is also used [44, 45]. It is imperative that these patients monitored post-operatively for developing apnoea for at least 12–24 h. There is some evidence of caffeine as a respiratory stimulant being helpful as a therapy (10 mg/kg) [46]. Regional anaesthesia without sedation may be a better choice in neonates predisposed to develop post-operative apnoea.

Question 28:
What is the role of foetal surgery in neural tube defects?

Answer:
The neural damage in NTDs is explained by "Two hit hypothesis". It is said that due to a

primary congenital abnormality in anatomic development (first hit), a relatively normal spinal cord is secondarily damaged by a combination of amniotic fluid exposure, direct trauma and hydrodynamic pressure (second hit).This suggested that in utero intervention could prevent further spinal cord damage and the consequent neurologic deficits. Subsequently animal studies were planned to observe the effectiveness of in-utero studies and were found to be successful. The procedure is mostly performed between 19 and 25 weeks of age. Briefly, a maternal laparotomy is performed followed by hysterotomy and MMC is exposed. The cystic membrane of the MMC is excised and the attachments of the meninges to the skin and soft tissues are detached. The foetus is subsequently followed up throughout the pregnancy. Management of meningomyelocele study (MOMS trial) documented prenatal surgery for myelomeningocele reduced the need for shunting and improved motor outcomes at 30 months, although the procedure was associated with maternal and foetal risks [47]. Recently, fetoscopic open neural tube defect repair with a two-port, carbon dioxide insufflation of uterus has been described [48].

Multiple Choice Questions

1. Which of the following anomalies are associated with neural tube defects?
   (a) Ventricular septal defect
   (b) Arnold–Chiari malformation
   (c) Neurogenic bladder
   (d) Cleft lip
   Answer: All except the option (d) have been found to be associated with neural tube defects.
2. Which among the following is not correct regarding preoperative care of meningomyelocele?
   (a) Prevent desiccation by covering the lesion with NS or RL soaked swabs
   (b) Avoid contamination of site and dressing from stool and urine
   (c) Nurse the patient in supine position
   (d) Start antibiotics if the lesion has ruptured
   Answer: c

   These patients should be nursed in prone/lateral position to prevent pressure and hence rupturing of the lesion.
3. Which among the following is not true for tethered cord syndrome?
   (a) Pain is the most common presenting feature
   (b) Predominantly found in adults
   (c) Classic radiological features include a low-lying conus medullaris and thick filum terminale
   (d) Surgical detethering is the treatment
   Answer: b

   Tethered cord syndrome is mostly described in children.
4. Regarding management of laryngospasm, all are true except
   (a) Larson's manoeuvre
   (b) Jaw thrust
   (c) Propofol bolus
   (d) Atracurium
   Answer: d
5. Which of the following is correct in reference to post-operative apnoea?
   (a) Anaemia is a risk factor
   (b) Term infants are more predisposed to suffer from post-operative apnoea
   (c) Regional anaesthesia with sedation will decrease the chances of post-operative apnoea
   (d) The predisposed patients should be monitored for 4 h post-operatively only
   Answer: c

References

Question 2

1. Yamada S, Won DJ, Siddiqi J, Yamada SM. Tethered cord syndrome: overview of diagnosis and treatment. Neurol Res. 2004;26(7):719–21.
2. Kural C, Guresci S, Simsek GG, Arslan E, Tehli O, Solmaz I, et al. Histological structure of filum terminale in human fetuses. J Neurosurg Pediatr. 2014;13(4):362–7.
3. Tehli O, Hodaj I, Kural C, Solmaz I, Onguru O, Izci Y. A comparative study of histopathological analysis of filum terminale in patients with tethered cord syndrome and in normal human fetuses. Pediatr Neurosurg. 2011;47(6):412–6.

4. Akay KM, Ersahin Y, Cakir Y. Tethered cord syndrome in adults. Acta Neurochir. 2000;142(10):1111–5.
5. Lee GY, Paradiso G, Tator CH, Gentili F, Massicotte EM, Fehlings MG. Surgical management of tethered cord syndrome in adults: indications, techniques, and long-term outcomes in 60 patients. J Neurosurg Spine. 2006;4(2):123–31.
6. Romagna A, Suchorska B, Schwartz C, Tonn JC, Zausinger S. Detethering of a congenital tethered cord in adult patients: an outcome analysis. Acta Neurochir. 2013;155(5):793–800.

Question 5

7. International Center on Birth Defects. International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS), Annual Report 2011 with Data for 2009. International Center on Birth Defects; 2011.
8. Li Z, Ren A, Zhang L, Ye R, Li S, Zheng J, et al. Extremely high prevalence of neural tube defects in a 4 county area in Shanxi Province. China Birth Defects Res A Clin Mol Teratol. 2006;76(4):237–40.
9. Prevention and Control of Birth Defects in South-East Asia Region. Strategic Framework. World Health Organization; 2013–2017.
10. Mahadevan B, Bhat BV. Neural tube defects in Pondicherry. Indian J Pediatr. 2005;72:557–9.
11. Sharma JB, Gulati N. Potential relationship between dengue fever and neural tube defects in a Northern District of India. Int J Gynecol Obstet. 1992;39:291–5.
12. De Marco P, Merello E, Calevo MG, Mascelli S, Pastorino D, Crocetti L, et al. Maternal periconceptional factors affect the risk of spina bifda-affected pregnancies: an Italian case-control study. Childs Nerv Syst. 2011;27(7):1073–81.
13. Yin Z, Xu W, Xu C, Zhang S, Zheng Y, Wang W, et al. A population based case-control study of risk factors for neural tube defects in Shenyang, China. Childs Nerv Syst. 2011;27(1):149–54.
14. Onrat ST, Seyman H, Konuk M. Incidence of neural tube defects in Afyonkarahisar, Western Turkey. Genet Mol Res. 2009;8(1):154–61.
15. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and metaanalysis. JAMA. 2009;301:636–50.
16. Robert E, Guibaud P. Maternal valproic acid and congenital neural tube defects. Lancet. 1982;2:937.
17. Rosa FW. Spina bifida in infants of women treated with carbamazepine during pregnancy. N Engl J Med. 1991;324:675–7.

Question 6

18. Haddow JE, Palomaki G, Knight GJ. Prenatal screening for major fetal disorders. In: Haddow JE, editor. Fetal disorders associated with elevated MSAFP levels, vol. 1. Scarborough, ME: Foundation for Blood Research; 1990. p. 4.

Question 7

19. Bernardini R, Novembre E, Lombardi E, Mezzetti P, Cianferoni A, Danti AD, et al. Prevalence of and risk factors for latex sensitization in patients with spina bifida. J Urol. 1998;160:1775–8.

Question 8

20. MRC Vitamin Study Research group. Prevention of neural tube defects: Results of the medical research council vitamin study. Lancet. 1991;338:131–7.
21. Burren KA, Savery D, Massa V, Kok RM, Scott JM, Blom HJ, et al. Gene–environment interactions in the causation of neural tube defects: folate deficiency increases susceptibility conferred by loss of Pax3 function. Hum Mol Genet. 2008;17(23):3675–85.
22. Copp AJ, Greene NDE, Murdoch JN. The genetic basis of mammalian neurulation. Nat Rev B Genet. 2003;4:784–93.
23. Hook EB, Czeizel AE. Can terathanasia explain the protective effect of folic-acid supplementation on birth defects? Lancet. 1997;350:513–5.
24. Molloy AM, Kirke PN, Troendle JF, Burke H, Sutton M, Brody LC, et al. Maternal vitamin B12 status and risk of neural tube defects in a population with high neural tube defect prevalence and no folic acid fortification. Pediatrics. 2009;123:917–23.

Question 10

25. Holzman RS, Mancuso TJ, Polaner DM. Practical approach to paediatric anaesthesia. Philadelphia: Lippincott Williams & Wilkins; 2008.

Question 11

26. Van de Putte P, Vernieuwe L, Jerjir A, Verschueren L, Tacken M, Perlas A. When fasted is not empty: a retrospective cohort study of gastric content in fasted surgicalpatients. Br J Anaesth. 2017;118:363e71.
27. Schmitz A, Kellenberger CJ, Liamlahi R, Studhalter M, Weiss M. Gastric emptying after overnight fasting and clear fluid intake: a prospective investigation using serial magnetic resonance imaging in healthy children. Br J Anaesth. 2011;107:425e9.

Question 12

28. Viscomi CM, Abajian JC, Wald SL, Rathmell JP, Wilson JT. Spinal anesthesia for repair of meningomyelocele in neonates. Anesth Analg. 1995;81(3):492–5.

Question 14

29. Kaloria N, Bhagat H, Singla N. Venous air embolism during removal of bony spur in a child of split cord malformation. J Neurosci Rural Pract. 2017;8(3):483–4.

Question 15

30. Sala F, Squintani G, Tramontano V, Arcaro C, Faccioli F, Mazza C. Intraoperative neurophysiology in tethered cord surgery: techniques and results. Childs Nerv Syst. 2013;29:1611–24.

Question 17

31. Lerman J, Cote C, Steward DJ. Manual of pediatric anesthesia. 6th ed. Philadelphia: Elsevier; 2010.

Question 18

32. Meyers EF, Muravchick S. Anesthesia induction technics in pediatric patients: a controlled study of behavioural consequences. Anesth Analg. 1977;56:538–42.
33. Scherzer W, Fitzal S, Ilias W, et al. Vergleich der Aufwachphasen bei 4 verschiedenen Narkosemethoden. Anasth Intensivther Notfallmed. 1980;15:242–6.
34. Tazeroualti N, De Groote F, De Hert S, De Ville A, Dierick A, Van der Linden P. Oral clonidine vs midazolam in the prevention of sevoflurane-induced agitation in children. A prospective, randomized, controlled trial. Br J Anaesth. 2007;98:667–71.
35. Seabra ML, Bignotto M, Pinto LR Jr, Tufik S. Randomized, double-blind clinical trial, controlled with placebo, of the toxicology of chronic melatonin treatment. J Pineal Res. 2000;29:193–200.

Question 20

36. Singh D, Rath GP, Dash HH, Bithal PK. Sevoflurane provides better recovery as compared to isoflurane in children undergoing spinal surgery. J Neurosurg Anesthesiol. 2009;21:202–6.

Question 23

37. Mahajan C, Rath GP, Dash HH, Bithal PK. Perioperative management of children with encephalocele: an institutional experience. J Neurosurg Anesthesiol. 2011;23:352–6.

Question 24

38. Mahajan C, Rath GP, Bithal PK, Mahapatra AK. Perioperative management of children with giant encephalocele: a clinical report of 29 cases. J Neurosurg Anesthesiol. 2017;29:322–9.
39. Yıldırım ZB, Avci E, Torun F, Cengiz M, Çigdem A, Karabağ H, Karaman H. Airway management for occipital encephalocele in neonatal patients: a review of 17 cases. J Neurosci Rural Pract. 2011;2:159–61.
40. Walia P, Bhargawa P, Sandhu K. Giant occipital encephalocele. Armed Forces Med J India. 2005;61:293–4.
41. Mahajan C, Rath GP. Intubating children with giant occipital encephalocele in lateral position: right or left side? J Anaesthesiol Clin Pharmacol. 2011;27(4):575.

Question 26

42. Banta JV, Bonanni C, Prebluda J. Latex anaphylaxis during spinal surgery in children with myelomeningocele. Dev Med Child Neurol. 1993;35(6):543–8.
43. Kurth CD, Spitzer AR, Broennle AM, Downes JJ. Postoperative apnoea in preterm infants. Anesthesiology. 1987;66:483–8.
44. Welborn LG, Rice LJ, Hannallah RS, Broadman LM, Ruttimann UE, Fink R. Postoperative apnoea in former preterm infants: prospective comparison of spinal andgeneral anesthesia. Anesthesiology. 1990;72:838–42.
45. Krane EJ, Haberkern CM, Jacobson LE. Postoperative apnoea, bradycardia, and oxygen desaturation in formerly premature infants: prospective comparison of spinal and general anesthesia. Anesth Analg. 1995;80:7–13.
46. Welborn LG, Hannallah RS, Fink R, Ruttimann UE, Hicks JM. High-dose caffeine suppresses postoperative apnoea in former preterm infants. Anesthesiology. 1989;71:347–9.

Question 28

47. Adzick NS, Thom EA, Spong CY, Brock JW, Burrows PK, Johnson MP, et al. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med. 2011;364:993–1004.
48. Belfort MA, Whitehead WE, Shamshirsaz AA, Bateni ZH, Olutoye OO, Olutoye OA, Mann DG. Fetoscopic open neural tube defect repair: development and refinement of a two-port, carbon dioxide insufflation technique. Obstet Gynecol. 2017;129(4):734–43.

15 Management of Patient with Pituitary Tumor (Cushing's Disease)

Hui Yang

Stem Case Terminology

A 51-year-old female presents for transsphenoidal resection of a pituitary tumor. Her past medical history is significant for diabetes mellitus (DM), hypertension (HTN), and hyperlipidemia. Over the past 5 months, her DM was poorly controlled despite strict diabetes diet and multiple adjustments of her medications. Her primary care physician noticed that she had unexplained weight gain (18 lbs), worsening HTN, abdominal striae, hirsutism, generalized weakness and fatigue. She was referred to an endocrinologist and then diagnosed with a pituitary tumor. The patient has a surgical history of cholecystectomy and cesarean section previously. Her current medications include metformin, glipizide, metoprolol, lisinopril, aspirin, and simvastatin. Her HbA1c is 7.8, basic metabolic panel shows blood glucose 226 mg/dL and creatinine 1.52. Serum adrenocorticotropic hormone (ACTH) and cortisol levels are abnormally high, and other pituitary hormones are nearly normal. Complete blood count, electrolytes, PT/INR, and APTT are within acceptable ranges. Electrocardiogram (EKG) shows sinus rhythm with moderate left ventricular hypertrophy. There is no other cardiac workup available. She is able to climb a flight of stairs without chest pain or shortness of breath, although she becomes less active due to her fatigue. Magnetic resonance imaging (MRI) of the brain shows a $1.1 \times 1.0 \times 1.3$ cm sellar mass. She denies any medication allergy or previous adverse anesthetic events. She denies visual field defects, headache, or any significant motor or sensory changes. In the preoperative area, her vital signs are BP 168/89 mmHg, HR 62 bpm, RR 16/min, SaO_2 95% in room air, and temperature 36.2 °C. Your physical exam reveals "moon face," "buffalo hump," fragile skin, and hirsutism. Her airway examination is otherwise unremarkable. Her neurological examination reveals no significant abnormality.

Question 1:

What are the surgical approaches for pituitary tumor resection? During transsphenoidal pituitary surgery, what are those important nerves and vasculatures that may be encountered?

Answer:

The two principal approaches for resection of a pituitary tumor are transsphenoidal surgery (TSS) and transcranial surgery (TCS).TSS is performed for excision of tumors that lie within the sella turcica or that have extended to or originated in the immediate suprasellar area.

H. Yang (✉)
General Anesthesiology, Cleveland Clinic, Cleveland, OH, USA
e-mail: yangh@ccf.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_15

Technically, TSS includes microscopic TSS (transnasal or translabial transseptal approach) and endoscopic TSS (endoscopic endonasal approach) [1–3]. TSS is a less invasive procedure in which a surgeon uses either an operating microscope or a flexible endoscope through the nostril, along with neuronavigation, to gain access to the sphenoid sinus and sella turcica, and eventually remove the pituitary tumor. TSS is used in over 90–95% of pituitary tumor surgeries and has significantly lower rates of morbidity and mortality than TCS, since the latter necessitates direct dissection of the brain, vascular structures, and visual pathways [4, 5]. In the cases of a large pituitary tumor with no or only a minor intrasellar component present, TCS may be needed [3]. In rare cases, both TSS and TCS are used in order to completely remove a large tumor that has spread into nearby tissues [6].

The pituitary gland is located within the sella turcica, a boney alcove of the sphenoid (Fig. 15.1). Critical structures surrounding the pituitary gland and sella turcica include [7]:

A. Optic nerve and chiasm, which lie superior to the diaphragma sellae.
B. Cavernous sinus, which surrounds the sella turcica laterally on both sides, is part of the brain's dural venous sinuses and contains multiple nerves and vasculatures:

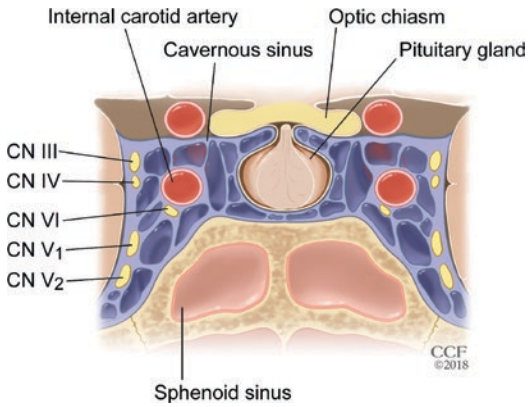


Fig. 15.1 Anatomy of pituitary gland, cavernous sinus, and sphenoid sinus. *CN* cranial nerve. (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2019. All Rights Reserved)

1. Internal carotid artery (ICA)
2. Oculomotor nerve (CN III)
3. Trochlear nerve (CN IV)
4. Ophthalmic division of the trigeminal nerve (CN V1)
5. Maxillary division of the trigeminal nerve (CN V2)
6. Abducens nerve (CN VI)

Question 2:
Discuss the classifications of pituitary tumors and the unique clinical features for each type.

Answer:
Pituitary tumors are classified by their size and hormone-secreting function. Pituitary tumors with size greater than 1 cm in diameter are considered macroadenomas. Macroadenomas often extend beyond the normal boundaries of the sella turcica and cause symptoms secondary to tumor compression on surrounding structures or normal pituitary gland tissues (mass effect). Macroadenomas are usually not hormone-secreting tumors. Patients often present with headache, visual field defects, cranial nerve palsy (e.g., double vision, facial numbness), panhypopituitarism, and diabetes insipidus (DI). Rarely, pituitary tumors cause elevated intracranial pressure (ICP) because of their size or obstruction of the third ventricle. Patients may present with headache, nausea, vomiting, and papilledema. Hemorrhage, infarction, or necrosis within the pituitary tumor may lead to pituitary apoplexy, and the clinical manifestations of pituitary apoplexy include abrupt onset of headache, visual disturbance, ophthalmoplegia, altered mental status, endocrinologic dysfunction, and hemodynamic instability.

Pituitary tumors with size less than 1 cm in diameter are considered microadenomas. Microadenomas generally remain within the confines of the sella turcica. Microadenomas are usually hormone-secreting tumors, often resulting from the neoplastic growth of a single cell type. Excessive production of certain type of pituitary hormone accounts for the unique clinical presentations and the abnormalities on endocrinologic tests.

The most common pituitary tumors are prolactin-secreting microadenomas and nonsecreting macroadenomas. Patients with the former are usually women who present with secondary amenorrhea. There are three other less common hormone-secreting pituitary tumors: growth hormone (GH)-secreting tumor (acromegaly), ACTH-secreting tumor (Cushing's disease), and a very rare thyroid stimulating hormone (TSH)-secreting tumor (hyperthyroidism).

The clinical manifestations of Cushing's disease include centripetal fat distribution ("moon face," "buffalo hump," central obesity), HTN, glucose intolerance, DM, cardiac disease, osteoporosis, adrenal hyperplasia, abdominal striae, easy bruisability with thin skin, immunosuppression, poor wound healing, menstrual irregularity, decreased libido, impotence, emotional disturbance, generalized weakness and fatigue, acne, and hirsutism (Fig. 15.2).

The clinical manifestations of acromegaly include soft tissues overgrowth of upper airway (tongue, soft palate, epiglottis, vocal cords, subglottic tissue), recurrent laryngeal nerve palsy, hoarseness, upper airway obstruction, obstructive sleep apnea (OSA), skeletal overgrowth (mandi-

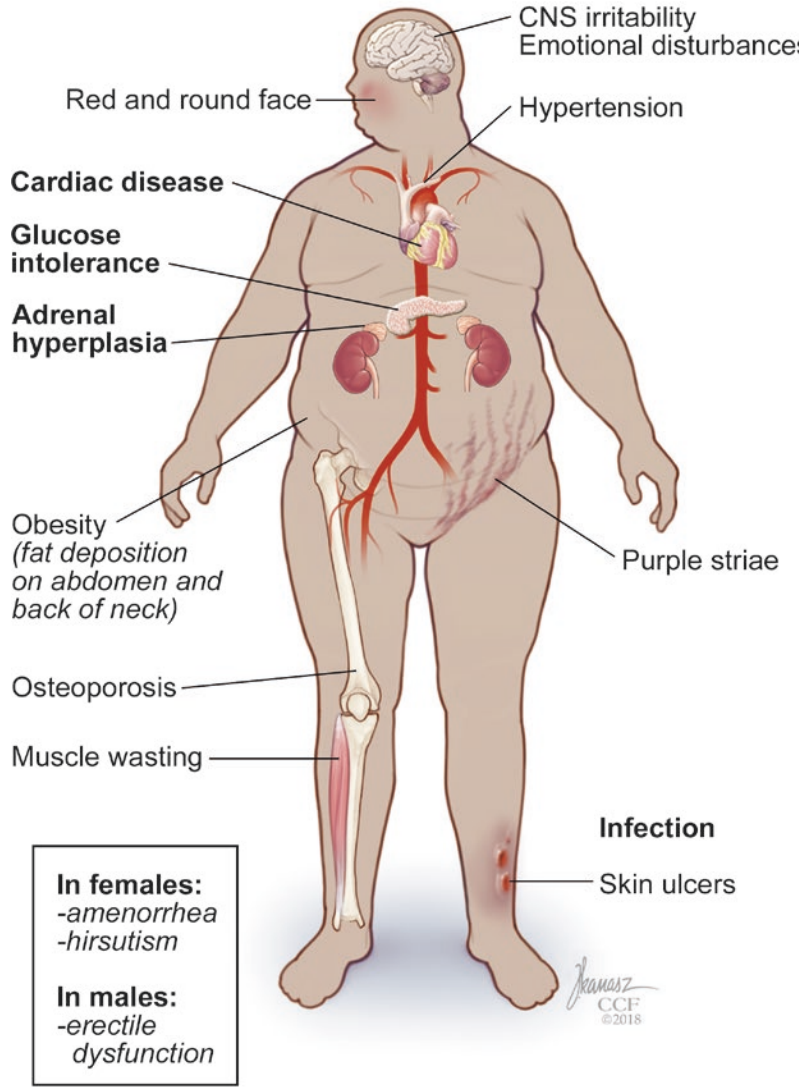


Fig. 15.2 Clinical manifestations of Cushing's disease. *CNS* central nervous system. (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2019. All Rights Reserved)

ble, hand, feet), cervical and lumbar spinal stenosis, increased incidence of cardiovascular disease (CAD, HTN, congestive heart failure (CHF), cardiomyopathy), glucose intolerance, peripheral neuropathy secondary to trapping of nerves by skeletal or soft-tissue overgrowth, carpal tunnel syndrome, compromised ulnar artery blood flow, osteoarthritis, osteoporosis, thickened skin, and visceromegaly.

15.1 Preoperative

Question 3:
What are the preoperative anesthetic considerations for a patient undergoing transsphenoidal resection of a pituitary tumor for Cushing's disease?

Answer:
Patients with Cushing's disease are at risk of cardiovascular disease, such as HTN, ischemic heart disease, CHF, left ventricular hypertrophy, and peripheral vascular disease [8, 9]. Careful assessments of signs of myocardial ischemia or cardiac dysfunction, a patient's functional capacity, and co-existing clinical risk factors are paramount. EKG is usually ordered preoperatively. Other cardiac workup, such as echocardiogram, stress test, or cardiac catheterization, may be considered in selective patients according to AHA/ASA guideline. HTN needs to be controlled before elective surgery.

Glucose intolerance is common [10] due to hypersecretion of cortisol in adrenal gland secondary to excess ACTH released from pituitary tumor. In patients with co-existing DM, close monitoring and treatment of hyperglycemia are critical.

Patients may present with central obesity with fat deposition at neck, face and abdomen, and OSA, which may make airway management difficult. Patients with Cushing's disease have increased incidence of peptic ulcer and GERD, thus at higher risk of aspiration during endotracheal intubation. Myopathy, commonly seen in Cushing's disease, may lead to inadequate ventilation postoperatively.

Immunosuppression, fragile skin, and easy bruisability may lead to poor wound healing, infection, bleeding, and difficult intravenous cannulation. Osteoporosis may increase the risk of fractures during patient positioning.

Patients with Cushing's disease tend to have hypernatremia, hypokalemia, and metabolic alkalosis resulting from higher mineralocorticoids activity.

Before induction of anesthesia, management plans for intraoperative antibiotics, steroid, lumbar subarachnoid drain, and blood pressure control were discussed with surgeon during the surgical huddle.

15.2 Intraoperative

Question 4:
What is your plan for intraoperative monitoring and intravenous (IV) access?

Answer:
In addition to standard ASA monitors, an arterial line is usually placed in our institution. With an arterial line, especially for patients with limited cardiovascular reserve, an anesthesia provider is able to continuously monitor blood pressure during the scenarios that wide swings in blood pressure may occur, such as epinephrine-containing local anesthetics infiltration of nasal mucosa, substantial bleeding from inadvertent injury to ICA, occurrence of venous air embolism (VAE) from inadvertent injury to cavernous sinus. An arterial line may also allow intraoperative monitoring of blood glucose, electrolyte, and $PaCO_2$ during TSS. Other invasive monitoring modalities, including central venous pressure (CVP), pulmonary artery (PA) catheterization, and transesophageal echocardiogram (TEE), are not routinely used and may be considered in selective patients with significant cardiopulmonary disorders.

TSS is not usually associated with significant blood loss or fluid shifts; however, two large-bore peripheral IVs are usually placed in our institution in preparation of substantial bleeding from inadvertent injury to ICA.

Question 5:
Discuss the perioperative steroid management for a patient with Cushing's disease.

Answer:
Cushing's disease is caused by a pituitary corticotroph adenoma that secretes excessive ACTH, which subsequently leads to supraphysiological secretion of glucocorticoids from the adrenal glands. The excessive circulating cortisol disrupts the physiological diurnal variation in cortisol levels and exerts negative feedback inhibition on corticotropin-releasing hormone (CRH) secretion from the hypothalamus. However, a pituitary adenoma is resistant to the inhibition by endogenous circulating cortisol. As a result, Cushing's disease is associated with suppressed secretion of CRH, hypersecretion of ACTH, and hypercortisolism [9].

For a patient with Cushing's disease, usually glucocorticoid is not administered before or during surgery due to the pre-existing hypercortisolism and the probability of interfering with postoperative endocrinology tests. After successful transsphenoidal resection of an ACTH-secreting pituitary adenoma, hypocortisolism may occur and reflect the suppression of hypothalamic–pituitary–adrenal (HPA) axis by long-standing hypercortisolism. Consequently, a patient may require postoperative glucocorticoids replacement. During postoperative glucocorticoid replacement, restoration of HPA axis function is assessed by returning of normal morning cortisol level and/or a normal cortisol response to ACTH stimulation. Glucocorticoids replacement may be then discontinued if those test results are normal [9]. In some centers, 8 AM plasma cortisol value plasma cortisol test and short ACTH 1-24 (Synacthen) test are performed postoperatively to detect and confirm ACTH deficiency. Postoperative glucocorticoid is replaced only if those test results are abnormal. This approach may help avoid unnecessary exposure to glucocorticoids [11].

Question 6:
What are your goals for intraoperative anesthetic management?

Answer:
The main goals for intraoperative anesthetic management include:
1. Maintain hemodynamic stability.
2. Maintain adequate cerebral perfusion.
3. Facilitate surgical exposure (ensure complete immobility of a patient, avoid HTN which may cause nasal bleeding, avoid fluid overloading, and help surgeon access a pituitary tumor by manipulating lumbar subarachnoid drain, performing Valsalva maneuver upon request as well as maintaining $PaCO_2$).
4. Ensure a prompt emergence for postoperative neurological examination.
5. Ensure a smooth emergence (avoid coughing, bucking, straining, or active vomiting) to minimize the risk of postoperative cerebrospinal fluid (CSF) leak and subsequent meningitis.

Question 7:
What is your plan for intraoperative anesthetic maintenance?

Answer:
The principles and anesthetic options for anesthetic maintenance during TSS are basically similar to the other intracranial procedures. Careful titration of anesthetics during surgery to achieve the above-mentioned goals is essential. Short-acting anesthetics are commonly used to facilitate a prompt emergence for postoperative neurological examination. A variety of anesthetics, including volatile agent (e.g., sevoflurane, isoflurane), IV sedatives (e.g., propofol, dexmedetomidine), and narcotics (e.g., fentanyl, remifentanil), have been used successfully. Nitrous oxide should be avoided due to the potential risk of VAE and pneumocephalus (discussed later). Intravenous anesthetics, such as propofol or dexmedetomidine, can help decrease the required anesthetic level of volatile agent, especially if elevated ICP is a concern during surgery. Propofol infusion is very helpful to reduce the risk of postoperative nausea and vomiting (PONV). Dexmedetomidine is a highly selective α2-adrenergic receptor agonist, which is notable for its ability to provide sedation, analgesia, and antihypertensive effects without causing respiratory depression [12]. There are evidences showing that dexmedetomidine infusion helps improve surgical condition, optimize a patient's hemodynamics and improve clinical outcomes in patients undergoing craniotomy and transsphenoidal resection of a pituitary

tumor [12]. Remifentanil infusion has been commonly used during TSS in our clinical practice. Its ultra short-acting feature, easy titratability, and potent analgesic effect help tremendously in ensuring a patient's immobility during surgery, preventing intraoperative HTN, and achieving a smooth emergence. In my clinical practice, titrating remifentanil bolus (usually 25–50 μg) is found to be very helpful to control temporary HTN or tachycardia (resulting from intermittent stimulating surgical manipulations) without undesired prolonged hemodynamic effects. Nondepolarizing neuromuscular blocking agent (NMBA) is also helpful to prevent a patient's coughing or movement during surgery.

Induction of anesthesia was smooth and uneventful. The patient was intubated with the endotracheal tube taped at the left lower lip per surgeon's request. After positioning the patient, you were notified that the surgical resident was going to prepare the patient's nasal mucosa.

Question 8:
How does the surgeon prepare a patient's nasal mucosa during TSS? What are the relevant anesthetic implications?

Answer:
During transsphenoidal pituitary surgery, in order to reduce nasal bleeding and the intensity of surgical stimulation, surgeon usually prepares a patient's nasal mucosa by infiltrating the nasal mucosa with vasoconstrictor (such as epinephrine, cocaine, or oxymetazoline) and local anesthetics (such as lidocaine). The systemic absorption of vasoconstrictor may cause significant HTN, dysrhythmia, or myocardial ischemia, which warrants prompt treatment in patients with limited cardiovascular reserve. Short-acting vasoactive medications, such as nitroglycerin or esmolol, should be readily available. Deepening anesthesia or titrating short-acting opioids (such as remifentanil) may also be considered.

Question 9:
How would you manage intraoperative HTN secondary to surgical stimulations? Why is it particularly important to avoid HTN during TSS?

Answer:
TSS can be intensely stimulating and thus associated with the risk of HTN intraoperatively [13]. Significant HTN may worsen intraoperative nasal bleeding, which will interfere with surgical exposure under microscope or endoscope during TSS. Adequate anesthesia and analgesia should be ensured during TSS, as discussed above, infusion of remifentanil or dexmedetomidine has been found effective in controlling intraoperative HTN [14]. In my clinical practice, titrating remifentanil bolus (25–50 μg) seems very helpful in treating temporary HTN and tachycardia resulting from intermittent surgical stimulations, without undesired prolonged hemodynamic effects. Alternatively, deepening anesthesia may be considered. Short-acting vasoactive medications, such as nitroglycerin or esmolol, should be readily available.

Question 10:
For a pituitary tumor with suprasellar extension, how would you manage $PaCO_2$ if the difficulty of accessing the tumor is encountered during TSS?

Answer:
Controlled hypercapnia has been described as an effective method of temporarily raising ICP to displace the suprasellar portion of a pituitary tumor down into the sella for excision [15]. A target $PaCO_2$ of 40–45 mmHg is generally used [11, 13].

Question 11:
What are the potential benefits of placing a lumbar subarachnoid drain for a patient undergoing TSS?

Answer:
In order to facilitate accessing a pituitary tumor during TSS, especially a large tumor with suprasellar extension, some surgeons may place a lumbar subarachnoid drain which allows the injection of saline or air into subarachnoid space to increase CSF pressure to deliver the tumor back into the sella for excision [16]. If air

is used, nitrous oxide must be discontinued to avoid the development of expanding pneumocephalus [17].

Resection of a large pituitary tumor is associated with risk of CSF leak, which may lead to postoperative meningitis and increased length of hospital stay [18]. Lumbar subarachnoid drain placement is a measure to help decrease the incidence of postoperative CSF leak or promote the resolution of the CSF leak postoperatively [19, 20] by maintaining CSF decompression in the early postoperative period.

Question 12:
What might happen if your patient had copious urine output at the end of surgery? What are the differential diagnoses?

Answer:
The differential diagnoses include central diabetes insipidus (DI, discussed later), polyuria from hyperglycemia or overhydration, and diuresis from mannitol or lasix administered perioperatively.

Question 13:
What are the potential intraoperative complications during the transsphenoidal resection of a pituitary tumor for Cushing's disease?

Answer:
1. Hypotension may occur due to semi-sitting position, infusion of remifentanil or dexmedetomidine, or copious urine output from above-mentioned causes.
2. HTN and dysrhythmia may result from infiltration of nasal mucosa with epinephrine-containing local anesthetics or cocaine.
3. Inadvertent injury to ICA or cavernous sinus may lead to substantial bleeding.
4. VAE and pneumocephalus may occur as a result of inadvertent entry into cavernous sinus in semi-sitting position. Nitrous oxide should be discontinued immediately upon occurrence of VAE.
5. Cranial nerve (CN) III, CN IV, CN V, and CN VI are at risk of injury due to the close proximity to the sphenoid bone.
6. DI (discussed later).
7. Electrolyte abnormalities and hypovolemia may occur as a result of copious urine output.
8. Uncontrolled hyperglycemia.

Five hours later, surgery was finished without issues. Before emergence, surgical resident placed an orogastric tube (OGT), some blood tinged fluid was suctioned out and the OGT was then removed.

Question 14:
Why is it important to decompress a patient's stomach before emergence?

Answer:
During TSS, surgical dissection may lead to accumulation of blood and tissue debris around the pharyngeal area. Therefore, a pharyngeal pack is sometimes placed after endotracheal intubation to limit the filling of stomach with blood and tissue debris, and reduce the likelihood of subsequent aspiration, nausea, or vomiting postoperatively.

In our practice, surgeon usually asks for an OGT from anesthesia provider and places it to decompress a patient's stomach before emergence. Nasogastric tube (NGT) placement, which may cause inadvertent trauma to surgical anastomosis and consequent CSF leak, is contraindicated.

Question 15:
Why is it critically important to ensure a smooth emergence? How would you prepare for the emergence?

Answer:
Vigorous coughing, bucking, straining, or vomiting upon emergence may precipitate hemorrhage, dislodgement of nasal tamponade, high ICP, and CSF leak (especially if there has been an intraoperative CSF leak, that is usually resealed with fibrin glue or by packing the sphenoid sinus with fat or muscle). HTN warrants prompt treatment for the risk of raising ICP and bleeding.

Intraoperative remifentanil or dexmedetomidine infusion [12] has been used successfully to achieve a smooth emergence. Non-narcotic analgesic such as intravenous acetaminophen may be administered before emergence. Intravenous or

topical lidocaine may be considered to reduce the airway reflex upon emergence, although intravenous lidocaine may potentially delay emergence and topical airway spray of lidocaine may potentially trigger coughing if a patient is "light." Any stimulating manipulations such as suctioning oropharyngeal airway, or removal of an OGT should be done promptly after surgical closure and before emergence from general anesthesia. Eye shield should be removed and a patient needs to be re-positioned to a sitting position to facilitate venous drainage, reduce ICP, and reduce the risk of CSF leak. Muscle relaxation should be fully reversed before emergence. In my practice, I usually move the surgical light away from a patient's face, and avoid those stimulating maneuvers (such as shaking a patient's shoulder) upon checking a patient's response during emergence. Short-acting vasoactive medications (e.g., nitroglycerin, esmolol) should be readily available to treat HTN upon emergence.

Your patient woke up and was extubated without issues. You transferred your patient to PACU along with the surgical team.

Question 16:
If a patient needs positive airway pressure ventilation support after extubation, is it a good idea to perform bag-mask ventilation in PACU? If your patient has a history of OSA, would it be safe to order CPAP or BiPAP in PACU?

Answer:
In order to reduce the risk of CSF leak (especially if there has been an intraoperative CSF leak, which is usually resealed with fibrin glue or by packing the sphenoid sinus with fat or muscle), it is essential to avoid any maneuvers that may apply positive pressure to the nasopharyngeal airway (such as bag-mask ventilation, CPAP or BiPAP, incentive spirometry) or any maneuvers that may traumatize the surgical anastomosis (such as placement of nasal trumpet or NGT). A face tent may be used if supplemental oxygen is necessary postoperatively. If a patient is extubated in operating room, he or she should be awake or at preoperative baseline mental status and able to maintain adequate ventilation and oxygenation before he or she is transferred to PACU. This is particularly important for a patient with history of OSA or difficult airway. In case a patient needs positive airway pressure ventilation after extubation, a laryngeal mask airway (LMA) may be placed to ventilate the patient.

15.3 Postoperative

Question 17:
What are the potential postoperative complications after transsphenoidal resection of a pituitary tumor for Cushing's disease?

Answer:
1. Hypopituitarism and pituitary apoplexy
2. DI
3. Electrolyte abnormalities and hypovolemia (as a result of copious urine output)
4. Cranial nerve injury
5. Ophthalmoplegia, visual change, loss of vision
6. CSF leak
7. Meningitis
8. Ischemic stroke
9. Airway: laryngospasm secondary to presence of blood in the oropharyngeal area, increased incidence of OSA due to Cushing's disease
10. Sinusitis, sinus congestion and sinus headache, nasal septum perforation

Question 18:
How would you diagnose and manage DI in PACU?

Answer:
DI is a relative common complication of pituitary surgery [21] due to decreased or loss of antidiuretic hormone (ADH) release. ADH is synthesized in the supraoptic nuclei of the hypothalamus and is transported down the supraoptic-hypophyseal tract to the posterior lobe of the pituitary gland. The mechanisms of DI include

diminished or absent ADH release from the supraoptic nuclei of the hypothalamus secondary to tumor mass effect or neoplastic infiltration [7], or secondary to dissection in and around the hypothalamus during TSS for a pituitary tumor with suprasellar extension.

DI rarely arises intraoperatively, usually occurs 4–12 h postoperatively, and is typically transient [22]. Clinical manifestations of DI are excessive thirst (polydipsia) despite copious fluid intake, hypotonic polyuria, increasing serum osmolality, and hypernatremia. The diagnosis is made based on increased plasma osmolality (>295 mOsmol/kg), hypotonic urine (<300 mOsmol/kg), and high urine output (>2 mL/kg/h) [23]. Urine specific gravity is usually <1.005. It is important to rule out other causes of polyuria, such as perioperative overhydration, osmotic diuresis secondary to mannitol administration or hyperglycemia.

The treatment of DI includes fluid replacement and desmopressin (DDAVP) or vasopressin administration. Free water deficit should be calculated and replaced in addition to maintenance need and other losses [24]. When a patient can tolerate oral intake, liberal oral intake of water should be allowed and encouraged. If a patient cannot tolerate oral intake, IV fluid replacement is necessary. The choice of fluid is dictated by a patient's electrolyte picture. Generally, a patient is losing fluid that is hypoosmolar and relatively low in sodium. Half-normal saline and 5% dextrose in water are commonly used as replacement fluids [22], although hyperglycemia is a risk when large volumes of 5% dextrose in water are employed. If the hourly fluid requirement exceeds 350–400 mL, DDAVP is usually administered [22]. DDAVP can be administered intranasally or intravenously. Aqueous vasopressin can be administered intravenously or intramuscularly. Serum and urine osmolality, urine specific gravity, urine output, and serum sodium level need to be closely monitored during the treatment of DI. Overdose of the medications may lead to an iatrogenic SIADH.

Multiple Choice Questions

1. During transsphenoid pituitary surgery, what are the important nerves and vasculatures that may be encountered?
   (a) ICA
   (b) Trigeminal nerve
   (c) Abducens nerve
   (d) Cavernous sinus
   (e) All of the above

   Answer: e

   The pituitary gland is located within the sella turcica, a boney alcove of the sphenoid. Critical structures surrounding the pituitary gland and sella turcica include [7]:

   A. Optic nerve and chiasm, which lie superior to the diaphragma sellae.
   B. Cavernous sinus, which surrounds the sella turcica laterally on both sides, is part of the brain's dural venous sinuses and contains multiple nerves and vasculatures:
      1. ICA
      2. Oculomotor nerve (CN III)
      3. Trochlear nerve (CN IV)
      4. Ophthalmic division of the trigeminal nerve (CN V1)
      5. Maxillary division of the trigeminal nerve (CN V2)
      6. Abducens nerve (CN VI)
2. The clinical manifestations of Cushing's disease include:
   (a) Central obesity
   (b) Glucose intolerance
   (c) Osteoporosis
   (d) Emotional disturbances
   (e) All of the above

   Answer: e

   Cushing's disease is caused by a pituitary corticotroph adenoma that secretes excessive ACTH, which subsequently leads to supraphysiological secretion of glucocorticoids from the adrenal glands. The clinical manifestations of Cushing's disease include centripetal fat distribution ("moon face," "buffalo hump," central obesity), HTN, glucose intolerance, DM, cardiac disease, osteoporosis, adrenal hyperplasia, abdominal striae, easy

bruisability with thin skin, immunosuppression, poor wound healing, menstrual irregularity, decreased libido, impotence, emotional disturbance, generalized weakness and fatigue, acne, and hirsutism.

3. What is the rationale for controlled hypercapnia if any difficulty of accessing a pituitary tumor with suprasellar extension is encountered during TSS?
   (a) Temporary increase in ICP.
   (b) Displacement of the suprasellar portion of a pituitary tumor down into the sella.
   (c) A target $PaCO_2$ of 40–45 mmHg is generally used.
   (d) All of the above.

   Answer: d

   Controlled hypercapnia has been described as an effective method of temporarily raising ICP to displace the suprasellar portion of a pituitary tumor down into the sella for excision [15]. A target $PaCO_2$ of 40–45 mmHg is generally used [11, 13].
4. What are the potential intraoperative complications during the transsphenoidal resection of a pituitary tumor for Cushing's disease?
   (a) Vascular injury and bleeding
   (b) VAE
   (c) Cranial nerve injury
   (d) Temporary HTN or dysrhythmia during infiltration of nasal mucosa with local anesthetics
   (e) All of the above

   Answer: e

   The potential intraoperative complications during the transsphenoidal resection of a pituitary tumor for Cushing's disease include:
   1. Hypotension may occur due to semi-sitting position, infusion of remifentanil or dexmedetomidine, or copious urine output from above-mentioned causes.
   2. HTN and dysrhythmia may result from infiltration of nasal mucosa with epinephrine-containing local anesthetics or cocaine.
   3. Inadvertent injury to ICA or cavernous sinus may lead to substantial bleeding.
   4. VAE and pneumocephalus may occur as a result of inadvertent entry into cavernous sinus in semi-sitting position. Nitrous oxide should be discontinued immediately upon occurrence of VAE.
   5. Cranial nerve (CN) III, CN IV, CN V, and CN VI are at risk of injury due to the close proximity to the sphenoid bone.
   6. DI.
   7. Electrolyte abnormalities and hypovolemia may occur as a result of copious urine output.
   8. Uncontrolled hyperglycemia.
5. If your patient needs positive airway pressure ventilation support after extubation, which of the following is an appropriate choice for a patient who just had TSS?
   (a) Bag-mask ventilation
   (b) CPAP
   (c) BiPAP
   (d) LMA

   Answer: d

   In order to reduce the risk of CSF leak (especially if there has been an intraoperative CSF leak, which is usually resealed with fibrin glue or by packing the sphenoid sinus with fat or muscle), it is essential to avoid any maneuvers that may apply positive pressure to the nasopharyngeal airway (such as bag-mask ventilation, CPAP or BiPAP, incentive spirometry) or any maneuvers that may traumatize the surgical anastomosis (such as placement of nasal trumpet or NGT). A face tent may be used if supplemental oxygen is necessary postoperatively. If a patient is extubated in operating room, he or she should be awake or at preoperative baseline mental status and able to maintain adequate ventilation and oxygenation before he or she is transferred to PACU. This is particularly important for a patient with history of OSA or difficult airway. In case a patient needs positive airway pressure ventilation after extubation, a LMA may be placed to ventilate the patient.
6. If a patient has copious urine output in PACU, what are the differential diagnoses?
   (a) DI
   (b) Polyuria secondary to hyperglycemia
   (c) Overhydration

(d) Polyuria secondary to mannitol administration
(e) All of the above

Answer: e

DI is a relative common complication of pituitary surgery [21] due to decreased or loss of ADH release. ADH is synthesized in the supraoptic nuclei of the hypothalamus and is transported down the supraoptic-hypophyseal tract to the posterior lobe of the pituitary gland. The mechanisms of DI include diminished or absent ADH release from the supraoptic nuclei of the hypothalamus secondary to tumor mass effect or neoplastic infiltration [7], or secondary to dissection in and around the hypothalamus during TSS for a pituitary tumor with suprasellar extension.

DI rarely arises intraoperatively, usually occurs 4 to 12 h postoperatively, and is typically transient [22]. Clinical manifestations of DI are excessive thirst (polydipsia) despite copious fluid intake, hypotonic polyuria, increasing serum osmolality, and hypernatremia. The diagnosis is made based on increased plasma osmolality (>295 mOsmol/kg), hypotonic urine (<300 mOsmol/kg), and high urine output (>2 mL/kg/h) [23]. Urine specific gravity is usually <1.005. It is important to rule out other causes of polyuria, such as perioperative overhydration, osmotic diuresis secondary to mannitol administration or hyperglycemia.

The treatment of DI includes fluid replacement and desmopressin (DDAVP) or vasopressin administration. Free water deficit should be calculated and replaced in addition to maintenance need and other losses [24]. When a patient can tolerate oral intake, liberal oral intake of water should be allowed and encouraged. If a patient cannot tolerate oral intake, IV fluid replacement is necessary. The choice of fluid is dictated by a patient's electrolyte picture. Generally, a patient is losing fluid that is hypo-osmolar and relatively low in sodium. Half-normal saline and 5% dextrose in water are commonly used as replacement fluids [22], although hyperglycemia is a risk when large volumes of 5% dextrose in water are employed. If the hourly fluid requirement exceeds 350–400 mL, DDAVP is usually administered [22]. DDAVP can be administered intranasally or intravenously. Aqueous vasopressin can be administered intravenously or intramuscularly. Serum and urine osmolality, urine specific gravity, urine output, and serum sodium level need to be closely monitored during the treatment of DI. Overdose of the medications may lead to an iatrogenic SIADH.

References

1. Jane JA Jr, Thapar K, Kaptain GJ, Maartens N, Laws ER Jr. Pituitary surgery: transsphenoidal approach. Neurosurgery. 2002;51(2):435–42.
2. Rudnik A, Kos-Kudła B, Larysz D, Zawadzki T, Bazowski P. Endoscopic transsphenoidal treatment of hormonally active pituitary adenomas. Neuro Endocrinol Lett. 2007;28(4):438–44.
3. Buchfelder M, Schlaffer S. Surgical treatment of pituitary tumours. Best Pract Res Clin Endocrinol Metab. 2009;23(5):677–92.
4. Buchfelder M. Treatment of pituitary tumors: surgery. Endocrine. 2005;28(1):67–75.
5. Barker FG 2nd, Klibanski A, Swearingen B. Transsphenoidal surgery for pituitary tumors in the United States, 1996-2000: mortality, morbidity, and the effects of hospital and surgeon volume. J Clin Endocrinol Metab. 2003;88(10):4709–19.
6. Kuga D, Toda M, Ozawa H, Ogawa K, Yoshida K. Endoscopic endonasal approach combined with a simultaneous transcranial approach for giant pituitary tumors. World Neurosurg. 2019;121:173–9. https://doi.org/10.1016/j.wneu.2018.10.047.
7. Newfield P, Cottrell JE. Chapter 12. Neuroendocrine procedures. In: Handbook of neuroanesthesia; 2012. p. 193–7.
8. Muiesan ML, Lupia M, Salvetti M, Grigoletto C, Sonino N, Boscaro M, Rosei EA, Mantero F, Fallo F. Left ventricular structural and functional characteristics in Cushing's syndrome. J Am Coll Cardiol. 2003;41(12):2275–9.
9. Lonser RR, Nieman L, Oldfield EH. Cushing's disease: pathobiology, diagnosis, and management. J Neurosurg. 2017;126(2):404–17.
10. Nemergut EC, Dumont AS, Barry UT, Laws ER. Perioperative management of patients undergoing transsphenoidal pituitary surgery. Anesth Analg. 2005;101(4):1170–81.
11. Lim M, Williams D, Maartens N. Anaesthesia for pituitary surgery. J Clin Neurosci. 2006;13(4):413–8.

12. Salimi A, Sharifi G, Bahrani H, Mohajerani SA, Jafari A, Safari F, Jalessi M, Mirkheshti A, Mottaghi K. Dexmedetomidine could enhance surgical satisfaction in trans-sphenoidal resection of pituitary adenoma. J Neurosurg Sci. 2014;61(1):46–52.
13. Dunn LK, Nemergut EC. Anesthesia for transsphenoidal pituitary surgery. Curr Opin Anaesthesiol. 2013;26(5):549–54.
14. Thawani JP, Ramayya AG, Pisapia JM, Abdullah KG, Lee JYK, Grady MS. Operative strategies to minimize complications following resection of pituitary macroadenomas. J Neurol Surg B Skull Base. 2017;78(2):184–90.
15. Korula G, George SP, Rajshekhar V, Haran RP, Jeyaseelan L. Effect of controlled hypercapnia on cerebrospinal fluid pressure and operating conditions during transsphenoidal operations for pituitary macroadenoma. J Neurosurg Anesthesiol. 2001;13(3):255–9.
16. Nath G, Korula G, Chandy MJ. Effect of intrathecal saline injection and Valsalva maneuver on cerebral perfusion pressure during transsphenoidal surgery for pituitary macroadenoma. J Neurosurg Anesthesiol. 1995;7(1):1–6.
17. Horvat A, Kolak J, Gopcević A, Ilej M, Zivko G. Anesthetic management of patients undergoing pituitary surgery. Acta Clin Croat. 2011;50(2): 209–16.
18. Bien AG, Bowdino B, Moore G, Leibrock L. Utilization of preoperative cerebrospinal fluid drain in skull base surgery. Skull Base. 2007;17(2):133–9.
19. Smith M, Hirsch NP. Pituitary disease and anaesthesia. Br J Anaesth. 2000;85(1):3–14.
20. Razis PA. Anesthesia for surgery of pituitary tumors. Int Anesthesiol Clin. 1997;35(4):23–34.
21. Nemergut EC, Zuo Z, Jane JA Jr, Laws ER Jr. Predictors of diabetes insipidus after transsphenoidal surgery: a review of 881 patients. J Neurosurg. 2005;103(3):448–54.
22. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. Chapter 63. Neurosurgical anesthesia. In: Miller's anesthesia; 2010. p. 2074.
23. Cusick JF, Hagen TC, Findling JW. Inappropriate secretion of antidiuretic hormone after transsphenoidal surgery for pituitary tumors. N Engl J Med. 1984;311(1):36–8.
24. Newfield P, Cottrell JE. Chapter 12. Neuroendocrine procedures. In: Handbook of neuroanesthesia; 2012. p. 203–4.

Suggested Reading

Dunn LK, Nemergut EC. Anesthesia for transsphenoidal pituitary surgery. Curr Opin Anaesthesiol. 2013;26(5):549–54.

Lonser RR, Nieman L, Oldfield EH. Cushing's disease: pathobiology, diagnosis, and management. J Neurosurg. 2017;126(2):404–17.

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. Chapter 63. Neurosurgical anesthesia. In: Miller's anesthesia; 2010. p. 2074.

Nemergut EC, Dumont AS, Barry UT, Laws ER. Perioperative management of patients undergoing transsphenoidal pituitary surgery. Anesth Analg. 2005;101(4):1170–81.

Newfield P, Cottrell JE. Chapter 12. Neuroendocrine procedures. In: Handbook of neuroanesthesia; 2012. p. 197.

Management of Patient with Posterior Fossa Tumor

16

Nidhi Gupta

Stem Case Terminology

A 58-year-old man, weighing 86 kg, presented to the neurosurgical outpatient department of a tertiary care hospital with a history of "on and off" headache, mild to moderate in intensity, lasting for few hours, since past 3 months. The headaches were associated with occasional episodes of vomiting initially, which increased in frequency in last 1 month. The patient also complained of transient blurring of vision in left eye since last 1 month. There was no associated history of any limb weakness, difficulty in swallowing or speech and gait disturbance. There were no associated comorbidities.

On clinical evaluation, the patient was conscious and oriented. Bilateral pupils were equal in shape (2 mm in diameter) and reacting to light. Visual field testing done by confrontation method was normal in both eyes. Cranial nerve (CN), motor and sensory examination were normal.

Magnetic resonance imaging (MRI) brain scanning was done which revealed a heterogeneous lobulated solid cystic mass lesion, measuring approximately 5.9 × 5.5 × 3.6 cm in the region of posterior third ventricle and pineal gland, the quadrigeminal plate cistern with extension into the superior cerebellar cistern and into the interhemispheric region at the level of body of lateral ventricle. Multiple small gradient recalled echo susceptible foci were noted within the mass suggestive of either hemorrhagic foci or calcification. The mass was found encasing the internal cerebral veins and the great cerebral vein. There was an associated mild obstructive dilatation of both lateral ventricles with mild periventricular ooze. Findings were overall suggestive of a pineal gland neoplasm or a tectal plate neoplasm.

Next day, the patient was posted for craniotomy and tumor decompression via a supracerebellar infratentorial approach in sitting position.

16.1 Preoperative

Question 1:
What preoperative preparation would you consider for this patient and why?

Answer:
In addition to the routine pre-anesthetic check (PAC) as per institutional protocols, the preoperative evaluation of a patient posted for posterior fossa craniotomy entails special considerations regarding the proposed surgical approach and patient positioning [1–4].

Patients are primarily evaluated for electrolyte imbalance and signs of dehydration in view of frequent vomiting episodes, followed by their optimization. Preoperative blood group and cross matching is mandatory and adequate blood

N. Gupta (✉)
Indraprastha Apollo Hospitals, New Delhi, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_16

should be arranged considering the size, vascularity, and close approximation of the tumor with cerebral veins. A detailed neurological examination is performed, specifically documenting the lower CN function including cough and gag reflex.

Since this patient is planned for surgery in the sitting position, care should be taken to assess his suitability for undergoing surgery in this very demanding position. The normal physiological range of head and neck flexion and rotation should be checked and any restriction of neck mobility and symptoms of dizziness and/or paresthesias of limbs on neck flexion are noted. In case any restriction in range of motion is detected, further evaluation of cervical spine is to be done through neck sagittal MRI to rule out severe cervical degenerative disease. If patient complains of dizziness on neck flexion, Doppler study of neck vessels should be done to rule out carotid insufficiency. The head MRI scans are also reviewed for the exact anatomical location of the tumor, its vascularity and relationship with surrounding big vessels and dural venous sinuses, in order to determine the intraoperative risk for blood loss and venous air embolism (VAE).

The patient should be evaluated by a cardiologist to rule out a right-to-left shunt [most commonly through a patent foramen ovale (PFO)] either by contrast-enhanced transcranial Doppler examination or by transesophageal echocardiography (TEE) during the Valsalva maneuver with an intravenous echo-contrast medium, to identify patients at high risk of paradoxical air embolism (PAE) [5–7]. If perioperative use of TEE is contemplated for hemodynamic and VAE monitoring, then the patient should also be assessed for contraindications to transesophageal access, including any esophageal pathology such as stricture, mass, or a previous esophageal surgery.

In presence of any known contraindication to sitting position (Table 16.1), the surgical team should be notified and discussed for a suitable alternative. Furthermore, irrespective of the surgical approach and extent of surgical resection, a detailed informed anesthesia consent should be taken explaining the probable need for postoperative ventilation and extended neurointensive care unit (NICU) stay in view of the close proximity of the lesion to the brainstem.

Table 16.1 Contraindications to the sitting position

Absolute
1. Patent ventriculoatrial shunt
2. Signs of cerebral ischemia when upright and awake
Relative
1. Patent foramen ovale
2. Right to left pulmonary-systemic shunt
3. Cervical spine instability
4. Severe cervical canal stenosis
5. Extremes of age
6. Hemodynamically unstable
7. Severe cardiac disease
8. Severe hypovolemia
9. Severe autonomic neuropathy
10. Anesthesia or surgical team not familiar with the position

Question 2:
Would you advise any preoperative medication to this patient?

Answer:
Cerebrospinal fluid (CSF) pathway within the posterior cranial fossa is very narrow (through the cerebral aqueduct), with high risk of compression or obstruction caused by the surrounding edema or tumor mass itself. Hence, even a minor preoperative fluctuation within the volume of intracerebral contents has the potential to cause sudden life-threatening increase in intracranial pressure (ICP). Consequently, sedative premedication is generally avoided in patients with posterior fossa lesions with their inherent risk of hypoventilation and hypercarbia, thus increasing cerebral blood volume.

However, since this patient is neurologically intact with no signs and symptoms of an acute rise in ICP, a short-acting benzodiazepine (intravenous midazolam, maximum dose 0.02 mg/kg) may be given in the preoperative room while being monitored by pulse oximetry, in case he is anxious [4].

Question 3:
What are the surgical complexities involved in this patient?

Answer:
The posterior fossa craniotomy poses specific challenges to the neurosurgeon in view of the limited maneuverability provided by the narrow confines of posterior cranial fossa and the presence of high density of critical neural structures such as CN nuclei; oculomotor, swallowing and coughing reflex pathways, sensory and motor pathways, cardiovascular and respiratory centers, and the reticular activating system, along with their challenging blood supply [8, 9].

Consequently, surgical manipulation close to brainstem (viz. brain retraction, tumor resection, coagulation, etc.) may result in iatrogenic injury to the brainstem's blood supply or direct CN damage with grave neurological and cardiovascular sequelae. The presence of multiple large veins within the tumor mass (as evident in MRI scan) and venous sinuses contained within the dural folds of the tentorium further adds to the risk of profuse bleeding and air entrainment during surgery, leading to hemodynamic instability and VAE. In addition, operating on a patient placed in the sitting position, though beneficial from surgical standpoint for large and vascularized tumors in posterior cranial fossa, is tiresome for the surgeons and demands expertise.

Question 4:
What are the surgical advantages of a sitting position for posterior fossa lesions?

Answer:
Performing posterior fossa surgery with the patient in the sitting/semisitting position offers several technical advantages to the neurosurgeons and the neuroanesthesia teams over the other proposed positions for posterior fossa craniotomy, viz. lateral, park-bench, and prone position (Table 16.2). Most importantly, it allows an easy surgical orientation and favors the gravity-assisted fall of the cerebellum away from the surgical field, thus avoiding prolonged cerebellar retraction that can be source of cerebellar sequelae [1, 2, 4].

Nonetheless, the sitting position fell out of favor in the last three decades in view of the rising medico-legal concerns from an increased fear of rare but possible serious complications, including VAE, PAE, intraoperative hypotension, and tension pneumocephalus (Table 16.3) [1, 10]. In addition, some surgeons avoid this position citing certain disadvantages such as time-consuming positioning, tiring standing procedure, and an inadequate positioning of the operating microscope. On comparing the outcomes following complex posterior fossa surgery performed in the sitting versus lateral position, Spektor et al. found no advantage in surgical or neurological outcomes for use of the sitting surgical position over the lateral position in technically difficult posterior fossa procedures [11]. Authors thus suggested that the choice of operative position

Table 16.2 Advantages of the sitting position

For the Neurosurgeon:
1. Easier anatomical orientation
2. Improved visualization of midline and deeper structure such as the pineal region and the petroclival junction, with less need for cerebellar retraction
3. Cleaner surgical field due to gravity-aided cerebellar retraction and drainage of the cerebrospinal fluid, blood, or irrigation fluid from the operative field
4. Reduced need for bipolar coagulation and suction allows surgeon for bimanual dissection with an overall reduced surgical time
5. Reduced need for electrocautery also helps to preserve the defined interface between the tumor and the surrounding brain structures
6. Better preserved CN function as the tumor falls away from the CN instead of onto them
7. Reduced intraoperative blood loss and reduced blood transfusion requirements
For the Neuro-anesthesiologist:
1. Immediate access to the airway and chest wall in case of respiratory or cardiac complications
2. Improved ventilation with lower airway pressure and free diaphragmatic movements
3. Decreased intracranial pressure
4. Provides an unobstructed view of the patient's face, enabling observation of motor responses to CN stimulation
5. Easy access to the extremities for monitoring, fluid or blood administration, and blood sampling

Table 16.3 Potential complications of the sitting position

1. Increased incidence of venous air embolism with possible paradoxical air embolism
2. Intraoperative hemodynamic instability
3. Symptomatic tension pneumocephalus
4. Acute subdural hematoma
5. Laryngeal or lingual edema (including trauma from a TEE probe)
6. Quadriplegia due to excessive neck flexion
7. Pressure points sores
8. Compressive peripheral neuropathy
9. Coagulopathy
10. Myocardial ischemia (New ST-T wave changes in ECG)
11. Significant impairment of pulmonary gas exchange
12. Neurogenic pulmonary edema
13. Arrhythmias
14. Pulmonary hypertension
15. Acute right ventricular failure
16. Cardiac arrest

should be based on lesion characteristics and the patient's preoperative medical status as well as the experience and preferences of the surgeons performing the procedure.

From the perspective of lesion characteristics, the supra-cerebellar infratentorial approach in the sitting position remains the most frequently used approach for pineal region tumors as it provides an extra cerebral corridor to approach the pineal region and is not associated with any morbidity that is related to the retraction of the parietal or the occipital lobes [8]. Furthermore, recent literature from several large prospective case series of patients undergoing neurosurgery in semisitting position confirms its safety when used by experienced teams and with modern monitoring techniques [5, 6, 12–14]. Recently, Choque-Velasquez J et al. described the "praying (steeper sitting) position" as a safer and more ergonomic variant of sitting position for pineal region surgery, which may reduce some of the risks associated with sitting position [14].

Question 5:
Is presence of a PFO an absolute contraindication for posterior fossa craniotomy in a semisitting position?

Answer:
Traditionally, PFO has been considered a contraindication for surgery in the semisitting position, because any episode of VAE can potentially result in PAE through the right-to-left shunt causing end-organ damage, including cerebral infarction [15]. However, recent literature have shown that in experienced medical centers, PAE can be avoided via a detailed preoperative workup by a cardiologist, preoperative closure of PFO (if indicated), and close intraoperative monitoring of the patient for prompt detection and management of any episode of VAE [5–7].

In a recent systematic review evaluating the incidence and severity of PAE in 82 patients with a PFO who underwent neurosurgical procedures in the semisitting position, no single episode of PAE was identified despite an occurrence of VAE in 33 of these 82 patients (40.2% incidence of VAE) [7]. Faithi et al. have suggested screening and endovascular PFO closure before surgery in the semisitting position to prevent thromboembolic stroke, with the procedural mean success rate of 99% and less than 1% risk of severe procedure-related complications [6]. However, following PFO closure, posterior fossa surgery has to be electively postponed for 4–6 weeks as the patients are started on antiplatelet therapy (aspirin 75 mg and clopidogrel 75 mg once daily for 1 month, followed by aspirin alone for 6 months) [16].

It is also important to acknowledge that PAE across a PFO may occur during neurosurgical procedures in non-sitting positions as well [5, 6]. Valsalva maneuver, coughing, breath-holding or straining on endotracheal tube (ETT) during induction or emergence from anesthesia are known to transiently increase right atrial (RA) pressure, exceeding left atrial pressures, thereby predisposing to an increased risk of PAE. Hence, considering the low incidence of PAE in patients with PFO who undergo surgery in the semisitting position along with the small but definite risk of PFO closure, performing neurosurgery without previous endovascular PFO closure appears to be reasonably safe option provided that the operating teams are well experienced in preventive and management strategies for VAE. Nonetheless, as recommended by Klein J

et al. preoperative PFO closure should be considered in patients with significantly higher risk of PAE viz. a large-diameter PFO (>4 mm) [13]; permanent right-to-left shunt, and past history of paradoxical embolism, such as a cryptogenic stroke [7]. Alternatively, if the risk of PAE is considered too high, one should preferably opt for an optional horizontal position [3].

Overall, in the wake of current literature, presence of a PFO does not disqualify a patient from undergoing neurosurgery in the semisitting position, albeit with appropriate monitoring [17].

16.2 Intraoperative

Question 6:
What are your anesthetic goals for this patient?

Answer:
The anesthetic goals for this patient include the basic neuro-anesthetic principles, which are inherent to any intracranial neurosurgical procedure along with intraoperative goals pertinent for a posterior fossa craniotomy in sitting position [2, 4]. These include:

(a) Attaining an optimal patient positioning with minimum possibility of positioning-related hazards to the patient.
(b) Maintaining intraoperative arterial pressure close to pre-induction values to preserve cerebral perfusion in upright position and reduce any risk of cerebral ischemic injury.
(c) Titrating intraoperative anesthetics to maintain an adequate depth of anesthesia while avoiding hemodynamic instability.
(d) Providing optimal operating conditions to the surgeon with lax brain.
(e) Providing optimum conditions for intraoperative neurophysiological monitoring (IONM).
(f) Prevention, early identification, and effective management of VAE and intraoperative hypotension.
(g) To allow smooth emergence with early awakening so as to facilitate neurological assessment.

Question 7:
What will be your anesthetic induction plan for this patient?

Answer:
During anesthetic induction in a patient undergoing posterior fossa craniotomy, particular care should be taken to avoid hypotension, hypoxia, and hypercapnia, to prevent cerebral ischemia and brain stem herniation in view of low compliance of the posterior fossa [2].

Anesthetic induction is achieved with the usual intravenous induction doses of an opioid-based analgesic (1–2 μg/kg fentanyl), hypnotic agent (4–6 mg/kg thiopental or 1.0–1.5 mg/kg propofol), and a muscle relaxant (1 mg/kg rocuronium) to facilitate endotracheal intubation. A reinforced ETT is preferred to prevent its kinking during neck flexion in sitting position.

Routine anesthetic monitoring during induction includes 5-lead electrocardiography (ECG), noninvasive blood pressure measurements, pulse oximetry, and the bi-spectral index monitoring. After intubation, a TEE probe or a PCD probe is placed for intraoperative VAE monitoring. If a TEE probe is used, then either a mouth guard or a small oral airway should also be inserted, to prevent the injury to tongue and lips. In particular, care should be taken to avoid large oral airways or bite blocks to prevent obstruction of venous drainage from the face and tongue after neck flexion in sitting position.

In patients with poor preoperative gag and cough reflex and those with possible postoperative lower CN dysfunction, a nasogastric tube should be inserted after intubation to prevent postoperative aspiration pneumonia.

Question 8:
What all invasive monitoring modalities would be required intraoperatively for the safe conduct of the surgery?

Answer:
During posterior fossa surgeries, patients are susceptible to intraoperative hemodynamic instability secondary to blood loss, cardiac

arrhythmias, and VAE. Invasive arterial monitoring is thus, mandatory in these patients so as to allow continuous assessment of arterial blood pressure and repeated blood gas analysis in the event of massive bleeding. In addition, insertion of a triple lumen central venous catheter (CVC) is quintessential as it is helpful for aspirating air from circulation during an event of VAE. However, precautions should be taken to ensure that the tip of the multi-orifice catheter is located 2 cm below the junction of the superior venae cava and RA at an inclination of 80° for maximal efficacy while aspirating air [18]. Appropriate placement of the tip of catheter may be confirmed either by plain chest X-ray, real-time X-ray imaging, intravascular ECG (point of large negative P complex), with TEE guided placement or by withdrawing the catheter after eliciting right ventricular waveform on pressure transducer.

Semi-invasive cardiac output monitoring via a PiCCO system (Pulsion Medical Systems, Munich, Germany and Philips Medical Systems) or the Vigileo FloTrac (Edwards LifeSciences, Irvine, CA) is specifically recommended in high-risk surgical cases with poor cardiac reserves for continuous cardiac output monitoring. In addition, it has also been found useful in sitting position craniotomies for goal-directed hemodynamic management, by minimizing the volume of colloids transfused intraoperatively to combat intraoperative hemodynamic instability or positioning-related hypotension [19].

Question 9:
What is the role of IONM in patients undergoing posterior fossa craniotomy?

Answer:
IONM techniques, primarily comprising of somatosensory evoked potentials (SSEPs), transcranial electrical motor evoked potentials (MEPs); brainstem auditory evoked responses (BAERs); direct electrical stimulation and spontaneous free-running electromyography (EMG) play an important role in ensuring the safety of patient positioning and preserving critical neural structures during neurosurgical procedures.

As discussed previously (in Question 3), the posterior fossa neurosurgical procedures are associated with a high risk of devastating neurological deficits. The CN nuclei and pathways may be compromised at any step of surgery either by their direct or indirect injury (via stretching or compression, irrigation, temporal bone drilling, use of bipolar electrocauterization, tumor removal with a Cavitron ultrasonic surgical aspirator) or by their vascular compromise (vessel injury, occlusion, or vasospasm). IONM signal alterations provide immediate warning signs to allow timely changes in the surgical strategy or patient's hemodynamics, such as stopping surgical stimulus, saline irrigation of operative field to dissipate heat, installing local nimodipine to relieve vasospasm, or increasing the blood pressure [9]. IONM signal alterations also help to identify the course of CNs in patients with grossly large tumors and severely distorted surgical anatomy by providing immediate feedback during dissection and thus facilitate gross total tumor resection with minimal neural morbidity.

Facial nerve (CN VII) and vestibulocochlear nerve (CN VIII) are specifically at risk during cerebellopontine angle, posterior fossa, or brain stem surgery and thus need to be monitored continuously. The current standard techniques for intraoperative facial nerve monitoring includes direct electrical stimulation over the posterior fossa structures generating the compound muscle action potentials (CMAP) in the ipsilateral facial muscles, free-running EMG, and transcranial facial nerve motor evoked potentials (FNMEP) [20, 21]. Song et al. have demonstrated that a high delta FNMEP (delta FNMEP = postoperative stimulus threshold level-preoperative stimulus threshold level) of 75 V has 100% sensitivity and 98.8% specificity for predicting short- and long-term facial nerve function damage after a cerebellopontine angle tumor surgery [21]. CN VIII monitoring can be successfully achieved by using BAERs, electrocochleography, and compound nerve action potentials of the cochlear nerve [22].

Lower CN monitoring is employed more frequently in patients with larger posterior fossa

tumors, skull base tumors, and in cases of recurrences where significant adhesions are anticipated. Spinal accessory nerve and the hypoglossal nerve can be monitored intraoperatively via EMG and CMAP after electrical stimulation from relevant muscles (trapezius or sternocleidomastoid muscle for spinal accessory nerve and the lateral aspect of the anterior third of the tongue for hypoglossal nerve) [23]. In comparison, vagus nerve monitoring is highly demanding and complex in nature and requires either a special monitoring ETT or esophageal electrodes. Recently, Sinclair et al. have described a novel methodology for intraoperative neuro-monitoring of laryngeal and vagus nerves by utilizing the laryngeal adductor response. This brainstem reflex protects the larynx from aspiration which is highly relevant in patients undergoing posterior fossa/brain stem tumor surgery [24].

Slotty et al. have revealed that surgery of tumors located at the petroclival face of the posterior fossa or at the tentorium is associated not only with a higher incidence of CN deficits, but also with alterations in MEPs/SSEPs, which are likely to be followed by devastating neurological sequelae in a high percentage of cases [9]. MEP/SSEP monitoring also provides information regarding depth of anesthesia and rare incidents outside of the surgical field such as stroke, remote bleeding, or nerve damage caused by patient positioning. SSEP may also help to monitor cerebral and/or spinal cord hypoperfusion and ischemia related to hypotension in the sitting position and should be monitored continuously during neck flexion and patient positioning.

Question 10:
Any other specific monitoring which you would consider in this patient?

Answer:
Considering high risk of intraoperative VAE (because of seated position and high vascularity of tumor), monitoring for its timely detection is of paramount importance during this surgery. The three most commonly recommended monitors for VAE detection during neurosurgical procedures (in order of decreasing sensitivity) include the TEE, PCD and monitoring end-tidal carbon dioxide ($EtCO_2$) by capnography [4] (Table 16.4).

As no single monitor is 100% sensitive or specific, it is recommended to use more than one monitoring modality during posterior fossa surgery, especially during sitting position. Currently, TEE is considered the gold standard monitoring modality to detect VAE as well as PAE. However, it tends to overestimate the incidence of VAE by detecting even small amounts of air emboli that have no clinical significance [5, 25]. Furthermore, it is more invasive and not necessarily specific for VAE as even rapid intravenous infusion can be confused with VAE. On contrary, PCD is the most sensitive noninvasive monitor for VAE and is mostly used in combination with $EtCO_2$ monitoring as a standard of care for VAE detection. The Doppler probe is placed at the left or right parasternal positions between the third and sixth intercostal space to assess any change in the quality of sound (a chirping or roaring sound), possibly indicating the occurrence of VAE.

Capnography detects the impairment in pulmonary gas exchange as a result of air entering the pulmonary circulation via the right heart, and thus filling the pulmonary capillaries leading to a decline in end-expiratory CO_2. Though non-specific for VAE, Pandia et al. have suggested that continuous capnography alone is sensitive enough to provide an early warning of any potentially clinically significant VAE [25]. However, in a recent large retrospective study of clinically diagnosed VAE during sitting neurosurgical procedures, Kapurch et al. have shown that occasionally some patients with significant hemodynamic changes have minimal to no change in $EtCO_2$ while some with minimal hemodynamic changes have large reductions in $EtCO_2$ during VAE [26]. Hence, in absence of specific monitors for VAE detection, intraoperative VAE should still be considered as a diagnostic probability in patients who experience significant but unexplained events of hypotension despite minimal changes in $EtCO_2$.

Table 16.4 Monitors for detection of venous air embolism

Modality	Sensitivity	Advantages	Disadvantages
Transesophageal echocardiography	Highest (0.02 mL/kg)	Gold standard for VAE and PAE monitoring Most sensitive monitor Objective monitoring of VAE Gives information about the size of the embolus and its progression Helps in intraoperative detection of a PFO or other possible pulmonary-systemic shunt before placing the patient in the sitting position Assists in optimal positioning of the tip of CVC	Invasive Expensive Requires operator expertise and constant vigilance Non-quantitative Can cause laryngeal and oral trauma Almost too sensitive (detecting even small amounts of air emboli that have no clinical significance) Rapid intravenous infusion can be confused with VAE (differentiation between the two can be done by slowing the infusion)
Precordial Doppler	High (0.05 mL/kg)	Considered standard of care for VAE (along with $EtCO_2$ monitoring) Noninvasive High sensitivity (small emboli can be detected) Detects air before it enters the pulmonary circulation	Non-specific Changes in audible sound may also occur with changes in heart rhythm (atrial premature contraction, ventricular premature contraction, changes from sinus to junctional rhythm, etc.), and even rapid intravenous injection of small amounts of fluid/mannitol crystals Non-quantitative Electrical interference due to the activation of the electrocautery equipment False negative results in approximately 10% of cases where air does not pass beneath ultrasonic beam Continuous embolism is easily missed, as the ear detects changes in sound more readily than an "abnormal" sound Difficult to position the probe accurately in obese patients, patients with chest wall deformity and during prone and lateral patient positioning
End-tidal CO_2 monitoring by capnography	Moderate (0.15 mL/kg)	Continuous objective monitoring Useful quantitative indication of the severity of VAE Noninvasive	Less sensitive Not specific Not reliable in the event of systemic hypotension, tachypnea, patients with chronic obstructive pulmonary disease and blocked or kinked sampling line

Question 11:
The surgery is planned in a semisitting position. How will you position your patient and what precautions would you take?

Answer:
Patient positioning in semisitting position for a neurosurgical procedure involves an excellent teamwork by the neurosurgeons, neuroanesthesiologists, and operating room (OR) technicians. Prior to positioning, all the necessary equipment and table fixtures are to be kept inside the OR and the operating table is covered with a full-length viscoelastic foam mattress or flat, large, silicone pads to reduce the possibility of pressure sores during the lengthy surgical procedure.

All aspects of positioning should be discussed in detail with the entire team and specific tasks should be assigned to the appropriate person.

Since sitting position is associated with major physiological changes throughout the cardiorespiratory and central nervous system (Table 16.5), it should be achieved in a stepwise manner with minimal interruptions in monitoring. Prepositioning controlled fluid loading is a prerequisite to prevent positioning-related hypotension [15, 19]. In general, intravenous fluids should be infused to achieve a mean arterial pressure higher than 60 mm Hg or, in the case of patients at high cardiac risk, to achieve a stroke volume > 60 mL per beat [13].

Table 16.5 Changes of physiologic parameters in cardiovascular, respiratory, and central nervous system in anesthetized patient in sitting position

Cardiovascular changes	• Decrease in venous return because of hydrostatic effect of gravity • Increase in heart rate • Decrease in stroke volume along with little less fall in cardiac output (compensated by an increase in heart rate) • Fall in systolic blood pressure and mean arterial pressure • Decrease in pulmonary capillary wedge pressure • Increase in systemic and pulmonary vascular resistance
Respiratory changes	• Increase in total lung capacity and functional residual capacity because of a downward shift of the diaphragm • Lower airway pressures • Decrease in intrapulmonary shunt • Decrease in ventilation/perfusion mismatch • Less basal atelectasis with improved ventilation of dependent zones • Hypovolemia may affect oxygenation by decreasing pulmonary perfusion pressure • Arterial oxygenation may also decrease because of low cardiac output
Central nervous system changes	• Decrease in intracranial pressure • Gravity assisted increase in cerebral venous and cerebrospinal fluid drainage • Cerebral perfusion pressure is maintained (provided hypotension is avoided and/or treated timely)

The important steps of sitting/semisitting positioning include:

(a) Once the patient is intubated and all monitoring modalities are in place, the Mayfield-Kees head clamp is applied by the surgeon, with the patient in supine position. Patient is then gradually moved upwards on the table to place his/her hips at the level of the surgical table flexing place, so that the shoulders remain 10–15 cm above the cranial edge of the table.

(b) The head end of the OR table is elevated slowly first followed by the Trendelenburg tilt of table alternatively in a graded manner, finally elevating the patient's head by 30°–45°. As the increase in the degree of head elevation is directly related to the amount of air entrainment into bloodstream, elevating patients head by just 30° only seems a safer option with a lower incidence of VAE as compared to that with 45° head elevation [27].

(c) In the modified semisitting position, the upper body and legs are elevated by bending the operating table to a position in which the hip is flexed to a maximum of 90° [15]. A 30° flexion of the knees is maintained by placing pillows beneath the knees to avoid sciatic neuropathy or tendon injuries to the lower limbs [28]. The inclination of the whole operating table is then changed to a lower head and higher legs position (as high as the vertex), to achieve a positive venous pressure at the operation site, thereby reducing the risk of an air embolism [3, 5, 15].

(d) The head holder is then fixed to the Mayfield crossbar adaptor with the patient's head straight and flexed, keeping in mind the physiological range of neck movements noted previously during PAC. While flexing the neck, a minimum two-finger breadth (approx. 3–4 cm) distance is to be maintained between the chin and the sternal manubrium to prevent: (1) obstruction of venous outflow at the level of the internal jugular veins (which may

cause an increase in ICP), (2) obstruction of arterial inflow (which may cause cerebral hypoperfusion), (3) potential kinking of the ETT, (4) pressure at the tongue (which may cause macroglossia), and (5) cervical cord ischemia caused by prolonged focal pressure on the spinal cord.

Extra caution is advised if TEE is used for VAE monitoring, because the esophageal probe lies between the flexed spine and the airway and ETT, adding to the potential for compression of laryngeal structures and the tongue. Ideally, head flexion should be done under SSEP monitoring to monitor for cervical cord ischemia, especially in elderly and high-risk cases with limited range of neck movements.

(e) Since flexing the head results in inward migration of ETT towards the carina, correct positioning of tip of ETT should be reconfirmed by chest auscultation and readjusted accordingly [29].

(f) The crossbar adaptor (and armrests) is then fixed to the back or upper section of the operating table rather than the seat/lower section. This step is very crucial to allow a rapid change in position from sitting to supine in case of an emergency.

(g) The arms of the patient are either rested in the lap over the pillows or may be placed on armrests to avoid traction on the shoulder muscles and potential stretching of upper extremity neurovascular structures. All peripheral and central invasive monitoring lines and IONM monitoring wires in the upper extremity are then safely secured and taped to prevent accidental disconnection.

(h) The "praying position," as described by Choque-Velasquez J et al., is essentially a steeper sitting position with the upper torso and the head bent forward and downward [14]. The patient's upper torso is properly elevated and head is tilted about 30° making the tentorium almost horizontal, thus providing good viewing angle and at the same time allowing the surgeon to support his/her arms on the shoulders of the patient while performing the procedure.

(i) A flat board against the feet or a safety belt around the pelvis prevents any accidental caudal movement of the patient, especially when the position is changed forwards during the surgery.

(j) All pressure points including buttocks, legs, arms, and heels are adequately padded to prevent pressure ulcers and any direct contact with operating table or positioning devices [28]. Legs should be kept free of any pressure at the level of the common peroneal nerve just distal and lateral to the head of the fibula.

(k) Either pneumatic intermittent sequential compression devices or elastic bandages or G-suit trousers are applied to the patient's legs to minimize venous pooling [2, 14, 19]. Use of intermittent sequential compression device on the lower extremities has been proven to effectively decrease intraoperative hypotensive episodes as well as improve regional cerebral oxygen saturation [30].

(l) When a patient is changed from the supine to the sitting/semisitting position, the relationship of the heart to the thoracic contents changes, thereby resulting in migration of the catheter tip from the RA to the right ventricle or the inferior vena cava. Hence, CVC catheter tip should be readjusted after final patient positioning.

(m) Similarly, the position of PCD or the TEE probe should be readjusted after confirmation by injecting 10 mL of agitated isotonic saline solution through the CVC, which should cause either detectable changes in Doppler sound or visible bubbles on the mid-esophageal four-chamber view or mid-esophageal bicaval view on the TEE monitor. During this examination, the airway pressure should be kept at 25–30 cm H_2O with a positive end-expiratory pressure (PEEP) of 5 cm H_2O to further exclude a right-to-left cardiac shunt.

(n) The arterial transducer should be mounted high up on a pole and zeroed at the level of tragus for correct estimation of cerebral perfusion pressure.

(o) After patient positioning, the final draping of patient is to be done in a manner to keep patient's

face and arms visible to the anesthesiologist all the time and for emergency airway access.

In the end, the entire checklist is double-checked by both surgeon and the anesthesiologist to maximize patient's safety.

Question 12:
How will you like to maintain anesthesia intraoperatively?

Answer:
Total intravenous anesthesia (TIVA) is the preferred intraoperative anesthetic maintenance technique during posterior fossa craniotomy in the sitting position. Anesthesia is maintained by using a continuous infusion of propofol (6–8 mg/kg/h) with supplemental administration of opioids. When using balanced anesthetic technique, use of nitrous-oxide (N_2O) is controversial, considering its inherent risk of expansion of gas-filled spaces, leading to increase in the size of VAE and conversion of pneumocephalus into tension pneumocephalus. However, there is an abundance of literature to suggest that the severity of VAE is most likely associated with surgical and anatomical issues, rather than with intraoperative N_2O use [17, 31–33]. Hence, it can be safely used during posterior fossa craniotomies.

If the intraoperative use of IONM is contemplated, then the anesthetic maintenance technique needs to be modified accordingly. TIVA is preferred for SSEP monitoring and muscle relaxants are to be avoided during MEP and facial nerve monitoring [20].

Normovolemia is to be maintained at all times and intraoperative hypotension should be immediately managed with either fluid boluses and/or vasopressors (ephedrine and/or phenylephrine).

Question 13:
What will be your ventilation goals intraoperatively?

Answer:
The ventilation parameters should be adjusted to maintain normocapnia with fraction of inspired oxygen (FiO_2) kept between 0.4 and 1.26 [2]. However, mild hypercapnia has also been recommended in patients with a high risk of VAE, so that a fall in $EtCO_2$ in the event of a VAE becomes easily appreciable. Moreover, sitting position is associated with positioning-related decrease in ICP and thus, cerebral vasodilatory effects of hypercapnia are not a major concern. Similarly, for patients with high risk of PAE via intrapulmonary right-to-left air transmission, higher levels of FiO_2 should be maintained as hyperoxia may prevent or reduce blood flow through arteriovenous pathways bypassing the capillary system [34].

PEEP has a controversial role to play during sitting position craniotomies. Some advocates its use (from 6 to 10 cm H_2O), citing its preventive role in VAE by increasing the RA pressure [3, 15, 35, 36]. It may also be applied after VAE has occurred to help identify the source of air entrainment [13]. An earlier study by Zasslow et al. has found it to be safe up to 10 cm H_2O in terms of non-alteration of interatrial pressure difference [36]. In patients with proven PFO, Ammirati et al. have suggested biphasic PEEP (7–10 cm H_2O) to increase the intrathoracic pressure, thus decreasing VAE incidence [3].

Few centers, however, avoid it completely as it has the potential to cause hypotension, increases ICP, predisposes for VAE during its release and also increases PAE rate (by raising RA pressure which may possibly open a functionally closed foramen ovale) [14, 19, 37–40]. In an old study, Giebler et al. have observed that the incidence of VAE did not differ between patients undergoing conventional ventilation and those undergoing ventilation with 10 cm H_2O PEEP [38]. Hence, the decision to use PEEP is individualized and depends upon the choice of anesthesiologist and patient's VAE/PAE risk.

Question 14:
What are the main intraoperative complications that you should be watchful for during a sitting posterior fossa craniotomy?

Answer:
While undergoing posterior fossa craniotomy in a sitting/semisitting position, patients are prone for VAE along with its sequelae (cardiorespiratory compromise, PAE, coagulopathy) and hemody-

namic instability, consequent to the gravitational effects of sitting position and surgical manipulation close to brainstem [2, 4, 5, 7, 13, 14, 40–43].

Positioning the patient in a semisitting position leads to negative intracranial venous pressure, which may allow air to enter the venous system during surgery, potentially leading to air embolism. This phenomenon is compounded by the fact that dural veins and sinuses are noncollapsible and are highly prone for injury during craniotomy. Hence, VAE can occur at any step during craniotomy with maximum incidence during placement of the 3-pin head holder; incision on the skin, subcutaneous tissue, or muscle; craniotomy; opening of the dura mater; resection of the lesion; and closure. Essentially, during a sitting craniotomy the risk for VAE is directly related to an intraoperative accidental venous structures laceration and to a low cardiac preload due to the surgical position [14].

Commonly recommended measures to avoid or detect air embolism include placement of a CVC, achieving optimal intravascular volume, patient positioning with the toes above the level of the head, rapid surgical hemostasis, continuous intraoperative monitoring of $EtCO_2$, and confirmation of possible air bubbles by PCD or TEE.

The reported incidence of VAE during a sitting craniotomy varies from 21 to 38.6% (depending on the method of detection and clinical definition of VAE) [6, 13, 14, 26]. However, the actual incidence of clinically significant VAE (meaning a VAE resulting in hemodynamic or respiratory compromise, or alteration of the course of the case) is reportedly very low (0–3.3%) [5, 17, 41]. In a recent retrospective review of 1698 patients who underwent intracranial neurosurgical procedures in the seated position, extreme VAE (characterized by progressive hemodynamic instability, evolving malignant arrhythmias, persistent VAE, PAE or significant impairment of pulmonary gas exchange with persistent hypoxemia or hypercarbia; or significant clinical change in neurological symptoms) was found to occur in only 8 patients (6/404 during posterior fossa and suboccipital craniotomies and 2/324 during DBS implantations) with an overall incidence of only 0.47% [17].

PAE may occur across intracardiac and intrapulmonary shunts, resulting in arterial air embolism to coronary and cerebral circulation with resultant myocardial ischemia, arrhythmia, and possible cerebral ischemia and stroke, respectively. VAE is also associated with significant thrombocytopenia with a linear relationship between VAE grade and fall in platelet count [43]. Thus, in the event of a severe VAE one should reassess coagulation parameters and platelet count intraoperatively to timely manage any coagulopathy.

Hemodynamic instability, most notably intraoperative hypotension, is common during sitting craniotomies secondary to venous pooling of blood in lower extremities, vasodilator effects of anesthetic agents, intraoperative VAE, massive blood loss, and CN manipulation close to brainstem. Even a brief period of intraoperative hypotension may cause cerebral ischemia and stroke, especially in patients with disturbed autoregulation. Hence, any hemodynamic instability should be aggressively managed with intravascular volume resuscitation and/or vasoactive agents.

Question 15:
Intraoperatively, there is profuse bleeding from the surrounding venous sinuses with a change in the audible sound of PCD and a sudden drop in $EtCO_2$ from 27 mmHg to 20 mmHg? What do you think has happened and how will you manage?

Answer:
Change in the audible sound of PCD and a sudden drop in $EtCO_2$ of more than 5 mmHg are indicative of an intraoperative episode of VAE, which necessitates an immediate and collaborative treatment approach by both surgeon and anesthesiologist [4].

The main goals of treatment of VAE include limiting further air entrainment, supporting hemodynamics and respiratory parameters, and treating complications. The surgeon is immediately notified and further air entrainment can be minimized by flooding the surgical field with saline (so that saline will be aspirated into the vein rather than air), application of bone wax

over the bony edges, and moistened cotton pledgets, gelatin foam, or fibrin glue or Surgicel over susceptible air entrances [42].

Patient should be ventilated with 100% oxygen and N_2O, if being used, should be discontinued. Intravascular fluids should be administered to increase the central venous pressure and any hemodynamic compromise should be immediately managed pharmacologically as needed (inotropes, vasopressors, and/or antiarrhythmics) [17].

Amidst the ongoing measures preventing further air entry and supporting the hemodynamics, the source of air entry should be identified and repaired by the surgeon as early as possible. When the source is not immediately identifiable or time is required to repair the venous injury, some centers recommend bilateral jugular compression and/or intraoperative position change with head under or at the same level as the feet, to increase cerebral venous pressure and help to identify the source of air emboli, as well as to counteract further air aspiration [5, 13, 17]. However, bilateral compression of the jugular veins should be done with caution as it has the potential to increase ICP by decreasing cerebral venous outflow. In addition, it may also decrease cerebral blood flow along with an increased risk of carotid artery atheromatous plaque rupture and severe bradycardia secondary to the simultaneous compression of the carotid artery and carotid sinus stimulation.

As a definitive treatment modality, the anesthesiologist must attempt to aspirate air from the RA cavity via the CVC, with a reported clinical efficacy ranging from 43 to 52% [44, 45]. However, Abcejo et al. have shown a questionable role of CVC air aspiration as the primary factor improving hemodynamics over the administration of pressors or temporary occlusion of the VAE site [17]. Authors speculate the short stay and small volume of entrained air bubbles at the cavoatrial junction en route to the pulmonary circulation as a probable cause of failure of air aspiration via a CVC catheter in majority of cases with extreme VAE.

Urgent repositioning of the patient from the seated to a level position (ranging from supine to lateral decubitus to prone) collapses the pressure gradient between the VAE source and the central venous circulation, and has been shown to successfully terminate all episodes of extreme VAE over a relatively short period of time [17]. However, this maneuver carries risk of infection, neurological deficits and interruption and/or postponement of surgery and should be opted in vasopressor-refractory cases with utmost caution.

If patient suffers sudden cardiac arrest, immediate cardiac compressions should be initiated which can help to break down large air bubbles obstructing the right ventricular outflow tract [40].

Question 16:
During tumor resection, there is sudden bradycardia with a heart rate of 38 beats per minute. What do you think has happened and how will you manage?

Answer:
During posterior fossa surgery, surgical manipulation of the lower pons, upper medulla, floor of the fourth ventricle, and the CN nuclei may result in sudden hemodynamic responses in the form of either bradycardia, tachycardia, hypotension or hypertension and arrhythmias. The majority of these events occur during tumor manipulation, mostly secondary to activation of neurogenic reflexes including trigeminocardiac reflex and glossopharyngeal vagal reflex; direct stimulation of the vagus nerve itself, brainstem stimulation and occasionally due to PAE involving the coronary arteries [46].

These responses basically serve as a warning sign of surgical encroachment on the vital medullary and pontine structures, and subside immediately after the surgical stimulus is removed. Hence, in the event of sudden bradycardia, the surgeon should be notified immediately. Nonetheless, in few cases with persistent bradycardia or the one progressing to asystole, pharmacological measure (such as application of topical or intravenous local anesthetic, as well as preemptive atropine administration) should be done immediately. Though most of

cardiac rhythm disturbances subside after brief periods of surgical interruption and atropine, prophylactic transcutaneous pacing may be considered in high-risk cases with coexisting cardiac comorbidities, prior to sitting position craniotomy.

Question 17:
The surgery has lasted for nearly 5 h with a blood loss of approximately 500 mL, an intraoperative episode of VAE, and two episodes of bradycardia during tumor resection, which were managed effectively without major hemodynamic compromise. What would be your extubation plan for this patient?

Answer:
The decision to extubate the patient after a pineal region tumor surgery in sitting position depends upon the preoperative conditions of the patient, the intraoperative course, and the predictable postoperative neurological deficits depending upon the extent of surgical resection [2, 4]. The clinical effect of intraoperative VAE on overall neurological outcome is still not clear. Ganslandt et al. have found no difference in the rate of immediate postoperative extubation, postoperative duration of ventilation, length of ICU stay, length of hospital stay, reoperation rate, and in-hospital mortality in patients with and without VAE operated upon in sitting position for different posterior fossa and cervical spine pathologies [41]. Hence, episodes which are without major hemodynamic compromise should not be a contraindication for extubation.

Considering that the patient was neurologically intact preoperatively and no major intraoperative hemodynamic instability was observed, patient may undergo careful extubation after adequate return of protective airway reflexes. However, in cases with large tumors, with signs of brainstem compression, preoperative lower CN involvement, prolonged surgical duration and inadvertent lower CN injury, elective postoperative sedation and ventilation should be opted, to allow gradual awakening of patient.

16.3 Postoperative

Question 18:
What all postoperative complications may occur in the immediate postoperative period?

Answer:
Compared to supratentorial craniotomy, an infratentorial posterior fossa surgical procedure is associated with a higher risk of postoperative respiratory failure and death. Hence, all patients require close monitoring in the NICU in the immediate postoperative period [47].

Positioning-related postoperative complications may include tension pneumocephalus, airway edema (macroglossia), quadriplegia (due to cervical cord ischemia and/or compression), and compressive peripheral neuropathy (sciatic nerve injury) [13, 28, 41, 42, 44]. Though the reported incidence of most of these complications is very low in modern literature, their consequences are devastating, thus mandating utmost care while patient positioning.

The surgery-related complications include subdural/remote hematoma, hydrocephalus, cerebellar edema, venous infarcts, wound infection, CSF leak followed by meningitis, CN palsies, cerebellar syndrome, and transient Parinaud's syndrome [13, 42, 44]. In their analysis of intraoperative and perioperative complications of neurosurgical procedures performed in the sitting position, Himes et al. reported an overall complication rate of 3.3% [incidence of clinically significant VAE, tension pneumocephalus, and hemorrhage (1 subdural and 1 remote) were 2.7%, 0.2%, and 0.4%, respectively] among 450 cases who underwent sitting suboccipital procedures [42]. Few very rare complications that have been reported in literature after sitting procedures include acute parotitis, piriformis syndrome, tension pneumoventricle, delayed lateral rectus palsy, and anosmia [42].

Potential postoperative complications resulting from an episode of severe intraoperative VAE may include the sequelae of severe intraoperative hypotension/shock with end-organ damage, PAE, and ongoing coagulopa-

thy [4, 40, 48]. Neurological complications may include postoperative mental status changes, appearance of new neurologic deficits and stroke secondary to cerebral hypoperfusion and/or cerebral air embolism. Similarly, cardiovascular complications may range from new onset ST-T wave changes, progressive right ventricular failure as a result of pulmonary hypertension, myocardial ischemia from coronary air embolism or coronary hypoperfusion secondary to shock, to sudden cardiac arrest. Raimann et al. described an uncommon case of right heart decompensation, followed by resolution and development of a typical left-ventricular Takotsubo or stress-induced cardiomyopathy on the first postoperative day caused by VAE during a craniotomy in sitting position [49]. Pulmonary edema after VAE occurs as a result of leaky capillaries in pulmonary vasculature and is characterized by its rapid development, diffuse involvement, and rapid resolution [50].

Multiple Choice Questions

1. Sitting position is associated with the following physiological changes, except
   (a) Decrease in stroke volume
   (b) Increase in heart rate
   (c) Increase in systemic vascular resistance
   (d) Decrease in systemic vascular resistance
   Answer: d
2. Which is the most sensitive noninvasive monitor for detecting intraoperative VAE?
   (a) Transesophageal echocardiography
   (b) End-tidal nitrogen by mass spectrometer
   (c) Precordial Doppler
   (d) End-tidal carbon dioxide by capnography
   Answer: c
3. Patients undergoing posterior fossa surgery are prone for all of the following complications, except
   (a) Tension pneumoventricle
   (b) Sciatic nerve injury
   (c) Optic ischemic retinopathy
   (d) Macroglossia
   Answer: c
4. Which of the following is an absolute contraindication for posterior fossa craniotomy in a sitting position?
   (a) PFO of size 3 mm
   (b) Patent ventriculoatrial shunt
   (c) Cervical cord stenosis
   (d) Right carotid artery insufficiency of >80%
   Answer: b
5. Which is not a treatment recommendation during an intraoperative episode of VAE?
(a) Bilateral jugular venous compression
(b) Trendelenburg tilt of operating table
(c) Ventilation with 100% oxygen
(d) Increasing depth of anesthesia
   Answer: d

References

1. Porter JM, Pidgeon C, Cunningham AJ. The sitting position in neurosurgery: a critical appraisal. Br J Anaesth. 1999;82(1):117–28.
2. Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. Curr Opin Anaesthesiol. 2014;27(5):474–83.
3. Ammirati M, Lamki TT, Shaw AB, Forde B, Nakano I, Mani M. A streamlined protocol for the use of the semisitting position in neurosurgery: a report on 48 consecutive procedures. J Clin Neurosci. 2013;20(1):32–4.
4. Sandhu K, Gupta N. Anaesthesia for posterior fossa surgery. In: Prabhakar H, editor. Essentials of neuroanaesthesia. San Diego: Academic Press, Elsevier; 2017. p. 255–73.
5. Feigl GC, Decker K, Wurms M, Krischek B, Ritz R, Unertl K, et al. Neurosurgical procedures in the semisitting position: evaluation of the risk of paradoxical venous air embolism in patients with a patent foramen ovale. World Neurosurg. 2014;81:159–64.
6. Fathi AR, Eshtehardi P, Meier B. Patent foramen ovale and neurosurgery in sitting position: a systematic review. Br J Anaesth. 2009;102:588–96.
7. Klein J, Juratli TA, Weise M, Schackert GA. Systematic review of the Semisitting position in neurosurgical patients with patent foramen ovale: how frequent is paradoxical embolism? World Neurosurg. 2018;115:196–200.
8. Yamamoto I. Pineal region tumor: surgical anatomy and approach. J Neurooncol. 2001;54:263–75.
9. Slotty PJ, Abdulazim A, Kodama K, Javadi M, Hänggi D, Seifert V, Szelényi A. Intraoperative neurophysiological monitoring during resection of infratentorial lesions: the surgeon's view. J Neurosurg. 2017;126(1):281–8.

10. Black S, Ockert DB, Oliver WC Jr, Cucchiara RF. Outcome following posterior fossa craniectomy in patients in the sitting or horizontal positions. Anesthesiology. 1988;69(1):49–56.
11. Spektor S, Fraifeld S, Margolin E, Saseedharan S, Eimerl D, Umansky F. Comparison of outcomes following complex posterior fossa surgery performed in the sitting versus lateral position. J Clin Neurosci. 2015;22(4):705–12.
12. Leonard IE, Cunningham AJ. The sitting position in neurosurgery—not yet obsolete! Br J Anaesth. 2002;88(1):1–3.
13. Saladino A, Lamperti M, Mangraviti A, Legnani FG, Prada FU, Casali C, et al. The semisitting position: analysis of the risks and surgical outcomes in a contemporary series of 425 adult patients undergoing cranial surgery. J Neurosurg. 2017;127(4):867–76.
14. Choque-Velasquez J, Colasanti R, Resendiz-Nieves JC, Gonzáles-Echevarría KE, Raj R, Jahromi BR, et al. Praying sitting position for pineal region surgery: an efficient variant of a classic position in neurosurgery. World Neurosurg. 2018;113:e604–11.
15. Jadik S, Wissing H, Friedrich K, Beck J, Seifert V, Raabe A. A standardized protocol for the prevention of clinically relevant venous air embolism during neurosurgical interventions in the semisitting position. Neurosurgery. 2009;64(3):533–8.
16. Laban JT, Rasul FT, Brecker SJ, Marsh HT, Martin AJ. Patent foramen ovale closure prior to surgery in the sitting position. Br J Neurosurg. 2014;28(3):421–2.
17. Abcejo AS, Pasternak JJ, Perkins WJ. Urgent repositioning after venous air embolism during intracranial surgery in the seated position: a case series. J Neurosurg Anesthesiol. 2019;31(4):413–21.
18. Bunegin L, Albin MS, Helsel PE, Hoffman A, Hung TK. Positioning the right atrial catheter: a model for reappraisal. Anesthesiology. 1981;55(4):343–8.
19. Lindroos AC, Niiya T, Silvasti-Lundell M, Randell T, Hernesniemi J, Niemi TT. Stroke volume-directed administration of hydroxyethyl starch or Ringer's acetate in sitting position during craniotomy. Acta Anaesthesiol Scand. 2013;57(6):729–36.
20. Acioly MA, Liebsch M, de Aguiar PH, Tatagiba M. Facial nerve monitoring during cerebellopontine angle and skull base tumor surgery: a systematic review from description to current success on function prediction. World Neurosurg. 2013;80(6):e271–300.
21. Song H, Ma C, Xu D, Yu M, Feng J, Sun L. Prognostic value of transcranial facial nerve motor-evoked potentials in predicting facial nerve function following cerebellopontine angle tumorectomy. Medicine (Baltimore). 2018;97(40):e12576.
22. Simon MV. Neurophysiologic intraoperative monitoring of the vestibulocochlear nerve. J Clin Neurophysiol. 2011;28(6):566–81.
23. Topsakal C, Al-Mefty O, Bulsara KR, Williford VS. Intraoperative monitoring of lower cranial nerves in skull base surgery: technical report and review of 123 monitored cases. Neurosurg Rev. 2008;31(1):45–53.
24. Sinclair CF, Téllez MJ, Tapia OR, Ulkatan S, Deletis V. A novel methodology for assessing laryngeal and vagus nerve integrity in patients under general anesthesia. Clin Neurophysiol. 2017;128(7):1399–405.
25. Pandia MP, Bithal PK, Dash HH, Chaturvedi A. Comparative incidence of cardiovascular changes during venous air embolism as detected by transesophageal echocardiography alone or in combination with end tidal carbon dioxide tension monitoring. J Clin Neurosci. 2011;18(9):1206–9.
26. Kapurch CJ, Abcejo AS, Pasternak JJ. The relationship between end-expired carbon dioxide tension and severity of venous air embolism during sitting neurosurgical procedures—a contemporary analysis. J Clin Anesth. 2018;51:49–54.
27. Türe H, Harput MV, Bekiroğlu N, Keskin Ö, Köner Ö, Türe U. Effect of the degree of head elevation on the incidence and severity of venous air embolism in cranial neurosurgical procedures with patients in the semisitting position. J Neurosurg. 2018;128(5):1560–9.
28. Practice Advisory for the Prevention of Perioperative Peripheral Neuropathies 2018: an updated report by the American Society of Anesthesiologists Task Force on prevention of perioperative peripheral neuropathies. Anesthesiology. 2018;128(1):11–26.
29. Kim JT, Kim HJ, Ahn W, Kim HS, Bahk JH, Lee SC, Kim CS, Kim SD. Head rotation, flexion, and extension alter endotracheal tube position in adults and children. Can J Anaesth. 2009;56(10):751–6.
30. Kwak HJ, Lee D, Lee YW, Yu GY, Shinn HK, Kim JY. The intermittent sequential compression device on the lower extremities attenuates the decrease in regional cerebral oxygen saturation during sitting position under sevoflurane anesthesia. J Neurosurg Anesthesiol. 2011;23(1):1–5.
31. Losasso TJ, Muzzi DA, Dietz NM, Cucchiara RF. Fifty percent nitrous oxide does not increase the risk of venous air embolism in neurosurgical patients operated upon in the sitting position. Anesthesiology. 1992;77(1):21–30.
32. Friedman GA, Norfleet EA, Bedford RF. Discontinuance of nitrous oxide does not prevent tension pneumocephalus. Anesth Analg. 1981;60(1):57–8.
33. Hernandez-Palazon J, Martinez-Lage JF, de la Rosa-Carrillo VN, Tortosa JA, Lopez F, Poza M. Anesthetic technique and development of pneumocephalus after posterior fossa surgery in the sitting position. Neurocirugia (Astur). 2003;14(3):216–21.
34. Schlundt J, Tzanova I, Werner C. A case of intrapulmonary transmission of air while transitioning a patient from a sitting to a supine position after venous air embolism during a craniotomy. Can J Anaesth. 2012;59(5):478–82.
35. Meyer PG, Cuttaree H, Charron B, Jarreau MM, Perie AC, Sainte-Rose C. Prevention of venous air embolism in paediatric neurosurgical procedures performed

in the sitting position by combined use of MAST suit and PEEP. Br J Anaesth. 1994;73(6):795–800.
36. Zasslow MA, Pearl RG, Larson CP, Silverberg G, Shuer LF. PEEP does not affect left atrial-right atrial pressure difference in neurosurgical patients. Anesthesiology. 1988;68(5):760–3.
37. Perkins NA, Bedford RF. Hemodynamic consequences of PEEP in seated neurological patients—implications for paradoxical air embolism. Anesth Analg. 1984;63(4):429–32.
38. Giebler R, Kollenberg B, Pohlen G, Peters J. Effect of positive end-expiratory pressure on the incidence of venous air embolism and on the cardiovascular response to the sitting position during neurosurgery. Br J Anaesth. 1998;80(1):30–5.
39. Schmitt HJ, Hemmerling TM. Venous air emboli occur during release of positive end-expiratory pressure and repositioning after sitting position surgery. Anesth Analg. 2002;94(2):400–3.
40. Mirski MA, Lele AV, Fitzsimmons L, Toung TJ. Diagnosis and treatment of vascular air embolism. Anesthesiology. 2007;106(1):164–77.
41. Ganslandt O, Merkel A, Schmitt H, Tzabazis A, Buchfelder M, Eyupoglu I, Muenster T. The sitting position in neurosurgery: indications, complications and results. A single institution experience of 600 cases. Acta Neurochir. 2013;155(10):1887–93.
42. Himes BT, Mallory GW, Abcejo AS, Pasternak J, Atkinson JLD, Meyer FB, et al. Contemporary analysis of the intraoperative and perioperative complications of neurosurgical procedures performed in the sitting position. J Neurosurg. 2017;127(1):182–8.
43. Schäfer ST, Sandalcioglu IE, Stegen B, Neumann A, Asgari S, Peters J. Venous air embolism during semi- sitting craniotomy evokes thrombocytopenia. Anaesthesia. 2011;66(1):25–30.
44. Young ML, Smith DS, Murtagh F, Vasquez A, Levitt J. Comparison of surgical and anesthetic complications in neurosurgical patients experiencing venous air embolism in the sitting position. Neurosurgery. 1986;18(2):157–61.
45. Girard F, Ruel M, McKenty S, Boudreault D, Chouinard P, Todorov A, Molina-Negro P, Bouvier G. Incidences of venous air embolism and patent foramen ovale among patients undergoing selective peripheral denervation in the sitting position. Neurosurgery. 2003;53(2):316–9. discussion 319–20.
46. Chowdhury T, Petropolis A, Cappellani RB. Cardiac emergencies in neurosurgical patients. Biomed Res Int. 2015;2015:751320.
47. Flexman AM, Merriman B, Griesdale DE, Mayson K, Choi PT, Ryerson CJ. Infratentorial neurosurgery is an independent risk factor for respiratory failure and death in patients undergoing intracranial tumor resection. J Neurosurg Anesthesiol. 2014;26(3):198–204.
48. Moningi S, Kulkarni D, Bhattacharjee S. Coagulopathy following venous air embolism: a disastrous consequence—a case report. Korean J Anesthesiol. 2013;65(4):349–52.
49. Raimann F, Senft C, Honold J, Zacharowski K, Seifert V, Mersmann J. Takotsubo cardiomyopathy triggered by venous air embolism during craniotomy in the sitting position. World Neurosurg. 2017;107:1045.e1–4.
50. El Kettani C, Badaoui R, Fikri M, Jeanjean P, Montpellier D, Tchaoussoff J. Pulmonary oedema after venous air embolism during craniotomy. Eur J Anaesthesiol. 2002;19(11):846–8.

17 Management of Patient with Supratentorial Tumor

Rashmi Vandse, Donna Lien, and Promod Pillai

Stem Case Terminology

A 68-year-old right-handed man is brought to the operating room for craniotomy and resection of a right fronto-parietal tumor. He has a 2- to 3-month history of intermittent headaches that has worsened over the past month, which is associated with gradually worsening left-sided weakness. He was brought to emergency department (ED) after an episode of seizure 3 days ago.

Past Medical History: Hypertension for the last 20 years that is well controlled. Had good functional capacity until 2 months ago but is limited recently due to left-sided weakness, mild COPD.

Social History: 25 pack-year history of smoking, social drinking. No other drug abuse.

Past Surgical/Anesthetic History: Inguinal hernia repair 2 years ago under general anesthesia, no past anesthetic problems.

Home Medications: Losartan, Albuterol inhaler PRN.

Physical Examination: Height—70 in., weight—100 kg, anxious-appearing man.

Neurological Examination: CN II–XII intact, left hemiparesis, strength—3/5.

Vitals: BP 168/99, HR 88, RR 16, RR 17, T 37 °C.

Labs: Hemoglobin 14 g/dL, Sodium 138 mEq/L, Potassium 4.0 mEq/L, Glucose 130 mg/dL, HCO_3—28 mEq/L. ECG—normal sinus rhythm, left ventricular hypertrophy, left axis deviation.

Imaging: Brain MRI shows a right fronto-temporal 4.2 cm tumor with well-circumscribed borders, peritumoral edema, and 6 mm midline shift.

Question 1:

Describe the epidemiology and pathophysiology of supratentorial brain tumors.

Answer:

Supratentorial brain tumors constitute a distinct group of neoplasms arising from different cells within the central nervous system (CNS) like the meninges, neuroepithelial tissues, pituitary and related structures, cranial nerves, germ cells and blood-forming organs (primary brain tumors) or from systemic cancers that have metastasized to the CNS (secondary brain tumors).

Supratentorial tumors account for approximately 80% of all brain tumors in adults and 40% in children [1]. The average annual age-adjusted incidence rate for all primary brain and other CNS tumors was 23.03 per 100,000

R. Vandse (✉) · D. Lien
Department of Anesthesiology, Loma Linda University Medical Center, Loma Linda, CA, USA
e-mail: DLien@llu.edu

P. Pillai
Department of Neurologic Surgery, Loma Linda University, Loma Linda, CA, USA

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_17

population. Glioblastomas (47.7%) are the most common malignant tumors, whereas meningiomas (53.1%) account for the most common nonmalignant tumors. Nearly 30% of patients with systemic solid cancers will develop cerebral metastases during their lifetime. These secondary brain tumors occur with equal frequency in adults, but primary tumors are far more common in children. The most common cancers to metastasize to the brain are lung, breast, melanoma, renal, and colorectal cancers [1, 2].

Primary CNS tumors are currently classified by the World Health Organization into a broad range of distinct categories based upon histologic morphology, molecular biomarkers, and clinical phenotype [3] (Fig. 17.1).

Most primary brain tumors in adults are sporadic with no identifiable risk factors. Apart from the rare genetic syndromes such as neurofibromatosis, tuberous sclerosis complex (TSC), and cancer predisposition syndromes such as Li–Fraumeni, the only well-confirmed risk factor for primary brain tumors is exposure to ionizing radiation. There is a 2.3% incidence of primary brain tumors in children treated with prophylactic cranial irradiation for acute leukemia [1].

Question 2:
Briefly discuss the anatomy of the supratentorial region relevant to the care of the patient.

Answer:
The supratentorial region is the part of the brain that lies above the tentorium cerebelli, bounded superiorly and laterally by the skull and dura mater. The anterior cranial fossa, middle cranial fossa, posterior cranial fossa, and tentorium cerebelli together constitutes the inferior border. The falx cerebri divides the supratentorial compartment into two equal right and left parts which contains the paired cerebral hemispheres. Each cerebral hemisphere is divided into frontal, temporal, parietal, and occipital lobes.

Eloquent cortical areas are generally considered to be regions responsible for gross motor function and language. The primary motor and somatosensory areas lie adjacent to the central sulcus in the frontal and parietal lobes, respectively, and extend inferiorly to the Sylvian fissure. Broca's area, an area responsible for language formation, is located in the premotor frontal cortex and Wernicke's area, an area required for language acquisition, is located in the posterior superior temporal cortex [4]. Lesions in Broca's area lead to expressive aphasia, whereas those in Wernicke's area cause receptive aphasia.

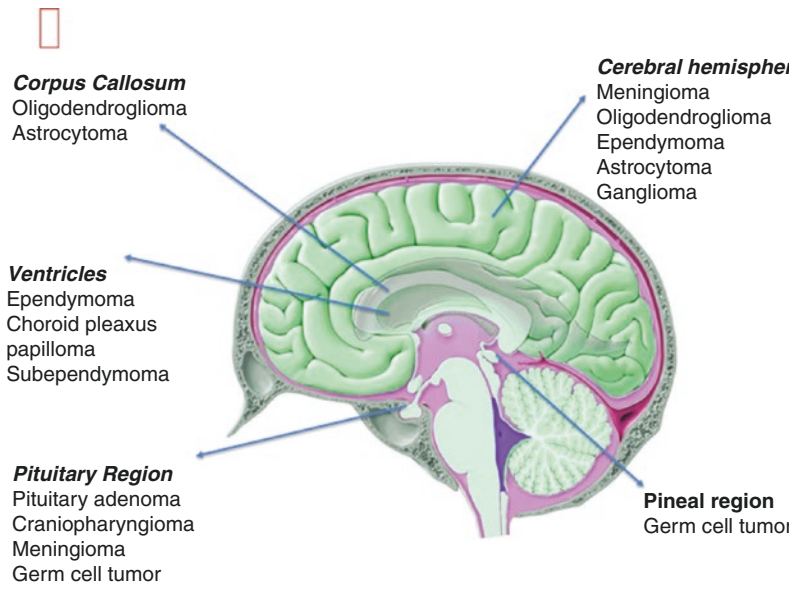


Fig. 17.1 Location of various primary supratentorial brain tumors

The supratentorial compartment also includes the basal ganglia, which is part of the extrapyramidal system, thalamus, hypothalamus, lateral ventricles, and corpus callosum. The thalamus is the main sensory and motor "relay station" that functionally and physically links the cortex with the rest of the nervous system. The hypothalamus, which lies below the thalamus, has autonomic and endocrine functions and is connected to the pituitary gland via the infundibulum. The hippocampus, amygdala, part of the hypothalamus, and some regions of the cortex (e.g., insular region) constitute the limbic system which play a role in cognitive function, memory, and emotion. Tumors can arise from any of these locations.

Question 3:
What are the effects of supratentorial tumors on the intracranial physiology?

Answer:
The supratentorial tumors affect intracranial homeostasis by the following:

A. Increasing the intracranial pressure (ICP) due to direct mass effect of the tumor and/or tumor-related edema
B. Impairing autoregulation
C. Disruption of the blood–brain barrier (BBB)
D. Functional alteration in the surrounding non-neoplastic brain cells

A. The effect on ICP: The ICP within the different compartments of the brain is in equilibrium and is normally 7 to 15 mmHg for a supine adult [5]. The key intracranial components of the brain (tissue, intravascular blood, and cerebrospinal fluid [CSF]) are enclosed within a noncompliant cranium. According to the Monro–Kellie hypothesis, "an increase in the volume of one intracranial compartment leads to a rise in ICP unless it is matched by an equal reduction in the volume of another compartment [5, 6]." In patients with intracranial tumors, an initial raise in the intracranial volume by the growing tumor is compensated by the translocation of CSF and venous blood to the spinal CSF space and the extracranial veins, respectively.As shown in the pressure–volume curve (Fig. 17.2), these compensatory mechanisms keep the ICP under check during the initial period of slow-growing tumors. When these compensatory mechanisms are exhausted (phase 2), a slight surge in the volume leads to significant rise in the ICP with the potential for ischemic injury due to impairment of the cerebral circulation and, ultimately, *brain herniation* (phase 3 and 4).

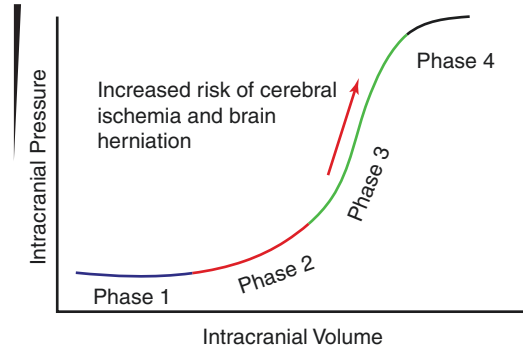


Fig. 17.2 Intracranial compliance curve (pressure–volume curve)

Brain Herniation The ability of these homeostatic mechanisms to compensate in the presence of an expanding mass depends not only on the volume of the mass, but also on the rate of growth. At first, there is ***subfalcine herniation*** causing a "midline shift" due to discordance in ICP between the two halves of the supratentorial compartments (Figs. 17.3 and 17.4). A midline shift of more than 5 mm is usually considered as significant [5, 7]. Further shifts in the brain structures can lead to downward ***central* and *transtentorial herniation (TTH)*** (Figs. 17.3, 17.5, and 17.6). Initially, the laterally directed compressive forces lead to asymmetric herniation of the *uncus of the temporal lobe* between the rostral brain stem and tentorial edge into the posterior fossa, resulting in a clinical syndrome of progressively impaired consciousness, dilated ipsilateral pupil, and contralateral hemiplegia (compression of the cortical spinal tract in the midbrain) [5, 8]. Loss of reactivity of the contralateral pupil usually indicates midbrain damage [9]. Radiologically this is manifested as obliteration of basal cisterns. This can be rapidly fatal. This is the time when surgical procedure for decompression of

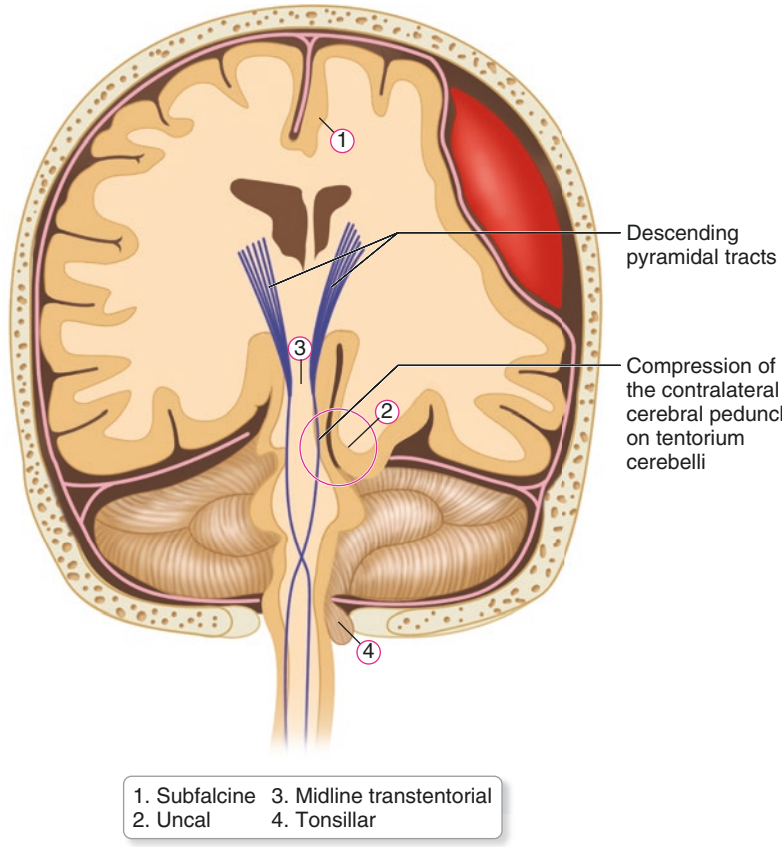


Fig. 17.3 Patterns of brain herniation in response to intracranial mass

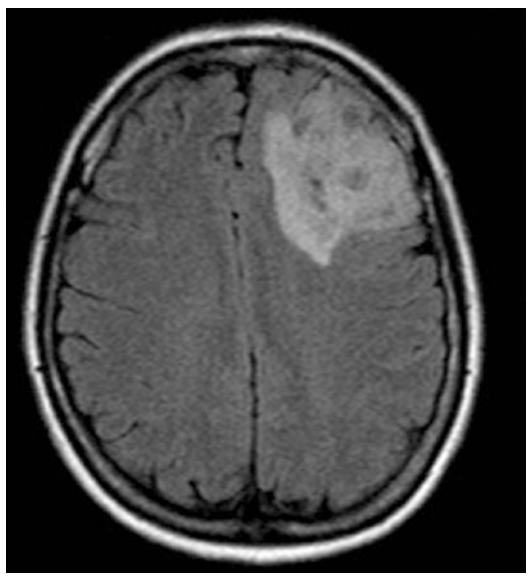


Fig. 17.4 MRI axial FLAIR image showing a left frontal intra-axial tumor—oligodendroglioma

mass lesion is an absolute emergency. Compression of foramen of Monro or third ventricle can result in hydrocephalus.

Tonsillar Herniation The tonsils of the cerebellum herniate through the foramen magnum into the upper spinal canal, compressing the medulla (Fig. 17.3). Clinically, this may result in cardiorespiratory impairment, hypertension, high pulse pressure, Cheyne–Stokes respiration, neurogenic hyperventilation, impaired consciousness, and death. The Cushing's response consisting of hypertension and bradycardia may be seen.

Tumor-associated Edema Despite their diverse histological types, most brain tumors cause vasogenic brain edema, which is a significant cause of patient morbidity and mortality by aggravating

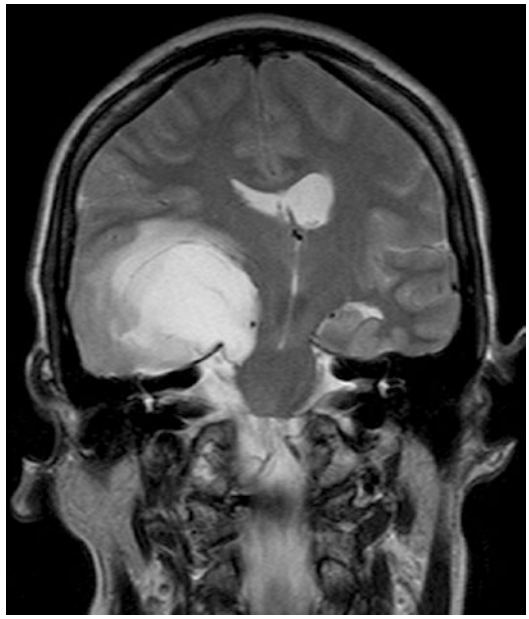


Fig. 17.5 Midocoronal section MRI view showing a medial temporal lobe tumor with mass effect, uncal herniation, distortion of midbrain

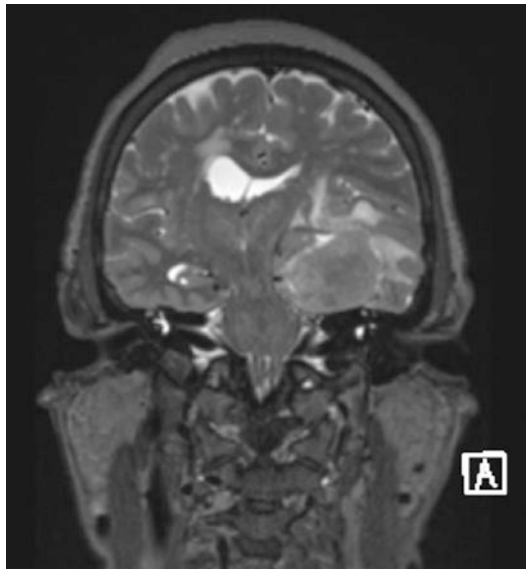


Fig. 17.6 Midocoronal section MRI view showing a middle cranial fossa meningioma with mass effect, subfalcine herniation, distortion of midbrain

the mass effect induced by the tumor and causing ischemia of the normal peritumor tissue [10, 11]. It is a complex process involving not only peritumoral edema but also rise in the water content of the tumor itself. The incompetent BBB due to defective endothelial tight junctions and excessive secretion of angiogenic factors leads to the leakage of fluid into the extracellular space (ECS) of the brain parenchyma [10, 11]. Peritumoral edema is particularly marked around fast-growing tumors as it is believed to facilitate tumor cell invasion [11]. It generally responds well to corticosteroid therapy, and can persist or even rebound after surgical excision of the tumor.

B. Impaired autoregulation: The presence of intracranial tumor can adversely affect the regional blood flow, autoregulation, and carbon dioxide (CO_2) reactivity in the regions of brain both ipsilateral and contralateral to the lesion [12, 13]. Preoperative cerebral autoregulation was impaired in a significant number of patients with large supratentorial tumor and midline shift of more than 5 mm which lasted for up to 24 h after surgery [12].

C. The blood–brain barrier (BBB) and edema: It has been suggested that BBB integrity is compromised in brain tumors [14, 15]. The change in the BBB permeability is heterogeneous within the tumor and is dependent on the type and stage of tumor development [14, 15]. Significant increases in BBB permeability only occur during the later stages as the tumor mass increases [14].

D. Functional alteration in the non-neoplastic brain cells: Infiltrating tumor cells also cause functional alteration in the non-neoplastic brain cells, most notably neurons, triggering many of the clinical symptoms [16]. For example, epileptogenesis associated with tumors is believed to be due to changes in peritumoral microenvironment, changes in the synaptic neurotransmitter release and reuptake, and the exitotoxic effect of glutamate [17].

Question 4:
What are the clinical signs and symptoms of supratentorial tumors?

Answer:
The presenting symptoms and signs in patients with supratentorial tumors depend on the location of the tumor (localizing signs), its size and mass effect (non-localizing), and its speed of growth.

Low-grade tumors often present with site-specific and focal signs due to tissue destruction or compression of specialized regions. The lesion affecting the motor cortex may be associated with contralateral hemiparesis, tumors near the speech area present with aphasia, vision change for tumors of the optic apparatus, and endocrinopathies for tumors involving the hypothalamic-pituitary axis. They progress to generalized signs and symptoms as the tumor increases in size and spreads [18, 19]. Patients often present with features of raised ICP such as headache, nausea, projectile vomiting, papilledema, cognitive decline, and change in the consciousness [20, 21]. There can be changes in the heart rate and blood pressure due to compensatory autoregulatory responses to decreased cerebral blood flow (CBF) caused by the raised ICP. They may present with herniation symptoms as were described in question 2.

Slow-growing tumors often have an insidious onset with a gradual, progressive course in contrast to rapidly expanding masses. Similarly, a bleed into the tumor may result in an acute presentation. A TTH is representative of an acute neurological deterioration.

Question 5:
What are the determinants of CBF? How are they altered in patients with supratentorial brain tumors?

Answer:
The brain has very high metabolic demand and receives a disproportionately high percentage of cardiac output (50 mL/100 g brain tissue/min). CBF depends on the pressure gradient across the vessel wall, also called as cerebral perfusion pressure (CPP). CPP is the difference between mean arterial pressure (MAP) and either ICP or central venous pressure (CVP), depending on which is higher. The cerebral autoregulation keeps the CBF constant over a wide range of MAP estimated at 65 to 150 mmHg, given normal venous pressure (Fig. 17.7).

CBF becomes pressure passive when MAP is outside this autoregulatory range. Below the lower limit of autoregulation (LLA), cerebral ischemia can result as the vessels are already vasodilated and above the upper limit of autoregulation, cerebral vessels are maximally vasoconstricted and increases in perfusion pressure may lead to disruption of the BBB, cerebral edema, or cerebral hemorrhage [22]. However, substantial inter-subject variability exists and the LLA may be as high as 80 mmHg in some healthy individuals [23]. This curve might shift to right in patients with chronic untreated hypertension [23]. However, in the last decade significant evidence has accumulated to indicate that hypertension may be associated with impairment in autoregulation with loss of the plateau phase [23, 24], which means that CBF is dependent on systemic blood pressure.

Besides MAP, other physiologic parameters play an important role in regulating CBF. First and foremost, CBF is controlled by "**flow-metabolism coupling**," whereby changes in regional neuronal electrical activity bring corresponding alteration in regional blood flow. Such coupling occurs on the order of seconds by alterations in cerebral vasomotor tone that is regulated at the level of the cerebral arteriole [22, 25]. There are several factors that play a role in regulating CBF as shown in Table 17.1.

Arterial carbon dioxide ($PaCO_2$) tension [22]: CBF is linearly linked with $PaCO_2$ between 20 and 80 mmHg. The change in the CBF occurs by 1 to 2 mL/100 g/min for each 1 mmHg change in $PaCO_2$. This response occurs quickly due to swift diffusion of carbon dioxide (CO_2) across the cerebrovascular endothelium causing alterations in pH of the extracellular fluid; however, it lasts only for about 6–8 h as the pH of the CSF will consequently re-normalize due to extrusion of bicarbonate. Consequently, a patient who has had a sustained period of hyper- or hypoventilation deserves special consideration. Acute restoration of a normal $PaCO_2$ value will result in increased CBF with a concomitant increase in

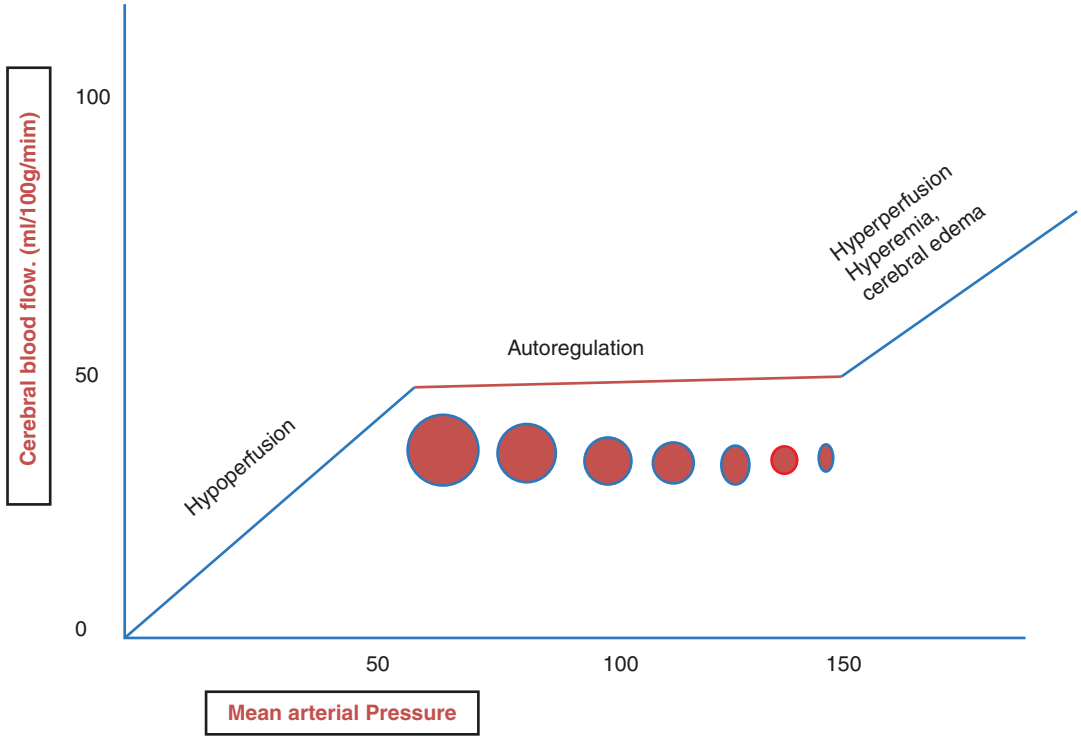


Fig. 17.7 Cerebral autoregulation curve

Table 17.1 Factors that influence cerebral blood flow

1. *Modulating cerebral metabolic rate*
Awakening/pain, seizures
Temperature, anesthetics
2. *Changing cerebral blood volume*
PaO_2 and $PaCO_2$
Blood pressure/status of autoregulation
Vasoactive agents
Anesthetics
Vasodilators
Blood viscosity
3. *Neurogenic pathways* (intra- and extra-axial)

ICP (after hypocapnia) and risk for cerebral ischemia (after hypercapnia). Hyper- and hypoventilation thus play critical roles in decreasing or increasing CBF, respectively.Changes in oxygen tension in the arterial blood (PaO_2) from 60 to more than 300 mmHg have little influence on CBF. When PaO_2 is less than 60 mmHg, CBF increases dramatically. When PaO_2 is greater than 350 mmHg, slight cerebral vasoconstriction can occur [25].

Temperature: Temperature is another important determinant of CBF [22, 26], with a 6–7% decrease in CBF per 1 °C decrease in core temperature primarily by suppression of cerebral metabolism. The complete suppression of the electroencephalogram (EEG) occurs at approximately 18–20 °C [22, 26]. Further reduction in temperature does produce a further decrease in the cerebral metabolic rate (CMR), as hypothermia decreases the rate of energy utilization associated with both electrophysiologic function and the basal component associated with the maintenance of cellular integrity [22, 26]. This explains the brain's tolerance for moderate periods of circulatory arrest at cooler temperatures. However, clinical studies have not demonstrated any beneficial effect of hypothermia in neurosurgical patients. Hence, normothermia should be a major goal of neuroanesthetic management. In addition, hypothermia also increases the risk of bleeding, surgical infection, prolonged recovery, and shivering [26].

Effect of anesthetic agents on CBF: Various anesthetics can have profound effects on CBF and intracranial homeostasis. The net effect on the CBF depends on the interaction of several factors including the concentration of the anesthetic, underlying CMR depression, blood pressure changes, any autoregulation abnormalities, and simultaneous changes in $PaCO_2$, which works in combination with any disease-related impairment in CO_2 responsiveness and various other factors that affect the CBF.

Volatile Anesthetics Potent volatile anesthetics such as isoflurane, sevoflurane, and desflurane are direct cerebral vasodilators [26]. However, this direct vasodilation is offset due to drug-induced decrease in CMR and subsequent vasoconstriction via flow-metabolism coupling. EEG burst suppression is obtained at around 2 minimum alveolar concentrations (MAC). At low concentrations (less than 1 MAC), CBF is lower than in the awake person. However, at high doses where maximal suppression of CMR has occurred, direct vasodilatory effects lead to a dose-dependent increase in CBF and cerebral blood volume [27, 28]. For the normal brain and at less than 1 MAC concentration, autoregulation and CO2 reactivity remain intact, enabling control of vasodilation by hyperventilation [26]. $PaCO_2$ reactivity and autoregulation are impaired or even abolished with a pathologic brain condition like brain tumors or high concentration of volatile anesthetic [29, 30].

Nitrous Oxide Nitrous oxide increases CBF, CMR, and sometimes ICP [30]. Increase in the CBF was noted when nitrous oxide was replaced for an equipotent concentration of a volatile anesthetic agent [31]. For the normal brain, the resulting cerebral vasodilation can be controlled by hypocapnia or the addition of an intravenous (IV) anesthetic [30, 31]. Even though autoregulation was preserved when nitrous oxide was combined with propofol anesthesia, combination of nitrous oxide and sevoflurane resulted in impaired autoregulation [32]. The potential for nitrous oxide to diffuse and expand hollow spaces must be considered as it could cause tension pneumocephalus in patients with intracranial air [33].

Intravenous (IV) Anesthetics All IV anesthetics such as barbiturates, propofol, and etomidate (with the exception of ketamine) reduce the CMR, CBF, preserve autoregulation, and maintain flow-metabolism coupling and CO_2 reactivity [30, 34, 35]. However, CMR reduction reaches a ceiling effect once the EEG burst suppression is achieved.Propofol anesthesia results in a lower ICP than sevoflurane or isoflurane anesthesia, suggesting improved operating conditions with a total intravenous anesthetic (TIVA) technique [36]. The evidence regarding the effect of ketamine on cerebral physiology is contradictory. Several studies have reported that ketamine increases CBF, CMR, and ICP while preserving autoregulation or $PaCO_2$ responsiveness [30, 37] and is traditionally avoided in neurosurgical patients due to concerns of increasing ICP. However, recent studies have demonstrated that ketamine does not change or even decrease these parameters especially when combined with other anesthetics. Its use should therefore not be discouraged because of ICP-related concerns [38–40].Barbiturates, propofol, ketamine, volatile anesthetics, and xenon also have shown some neuroprotective efficacy and can reduce ischemic cerebral injury in experimental models. This anesthetic neuroprotection is sustained only when the severity of the ischemic insult is mild; with moderate-to-severe injury, long-term neuroprotection is not achieved.

Opioids Opioids have been shown to cause short-term increase in ICP, which is thought to be the result of reflex cerebral vasodilation following decreases in blood pressure [41, 42]. Generally, opioids cause modest decrease in CMR without affecting flow-metabolism coupling, autoregulation, or the carbon dioxide reactivity.

Systemic Vasodilators and Vasoconstrictors Systemic vasodilators like nitroglycerin, nitroprusside, hydralazine, and calcium channel blockers vasodilate the cerebral circulation and

can, depending on the MAP, increase CBF and ICP [43, 44]. Cerebral vasodilation may result from a normal autoregulation response or direct arterial vasodilation. Vasopressors such as phenylephrine, norepinephrine, ephedrine, and dopamine do not have direct effects on the cerebral circulation. However, they can influence the CBF when outside the autoregulatory range (increasing systemic BP increases CBF) [22, 45]. The effect of phenylephrine on CBF is however contentious as some studies have showed decreased cerebral oxygenation induced by phenylephrine [46].

Question 6:
Describe the preoperative workup and preparations for supratentorial tumor resection surgery.

Answer:
Preoperative preparation should include

17.1 Preoperative

Preoperative assessment: An anesthesiologist may encounter a patient with a supratentorial tumor for an elective planned surgery, thus allowing adequate time for preoperative workup and optimization or for an emergent or urgent neurosurgical intervention secondary to hemorrhage or impending herniation. An anesthetic evaluation should entail comprehensive neurosurgical and systemic evaluation of the patient.

Thorough assessment of current *neurological status*, especially any signs of raised ICP (headache, nausea, vomiting, and altered consciousness) and focal neurological deficits (hemiparesis, sensory deficits, cranial nerve deficits, speech deficits, personality changes, and vision changes) must be documented. Any history of seizures (type and frequency), paraneoplastic syndromes, hormonal changes (especially in pituitary tumors), and electrolyte abnormalities (in conditions like syndrome of inappropriate antidiuretic hormone (SIADH) or diabetes insipidus (DI)) should be clarified.

As with all preoperative assessment, the evaluation of *coexisting medical conditions* that may impede with the patient's ability to undergo safe surgery is of paramount importance. Systematic assessment and optimization of the cardiopulmonary system, gastrointestinal system, genitourinary tract, as well as endocrine abnormalities should be done before any elective procedures. Infections, both past and present, should be investigated for choosing the perioperative antibiotic. Patients with malignant tumors are associated with an increased risk of thromboembolism, which can be as high as 21% in the first year after surgery [47], necessitating prophylactic anticoagulation postoperatively.

Patient should undergo routine *preoperative investigations,* which can include an electrocardiogram, chest X-ray depending on the age, urinalysis, complete blood count with differential, electrolyte panel, liver enzymes, and coagulation parameters including prothrombin time, plasma thromboplastin time, and international normalized ratio. Further tests can be added depending on the patient's comorbidities.

Imaging: computed tomography (CT) or magnetic resonance imaging (MRI): The patient's CT scan and MRI images should be examined for the size and location of the tumor (any proximity to the eloquent areas and major vessel), its vascularity, and for signs of raised ICP (midline shift, decreased size of the ventricles, and temporal lobe herniation). Although MRI is more sensitive than CT scans for evaluation of the tumors, patients presenting with acute neurological deterioration might come with just the CT scans. Positron emission tomographic (PET) scan gives the amount of metabolic activity in the brain, thus differentiating the tumors from inflammatory lesions. CT angiography is helpful in distinguishing arteriovenous malformations and giant aneurysm, which may present as mass lesions.

Imaging scans are extremely valuable in formulating the anesthetic plan. For example, patients with limited intracranial compliance might require interventions to decrease the ICP or tumors close to eloquent areas might otherwise need an awake resection. Location and size of the tumor give insights to the surgical position, any potential for blood loss, and can also reveal the risk for air embolism such as in patients with convexity meningioma close to dural sinus.

Our patient has preoperative hemiparesis and the tumor is in frontal area. It is important to rule out the proximity of tumor to eloquent area. There is a need for further testing like functional MRI or WADA test.

Question 7:
How will you prepare the patient for surgery? Should this patient receive premedication?

Answer:
Preparing the patient for surgery consists of

Multidisciplinary discussion: It is important to have a multidisciplinary discussion with the surgeon, intensivist, nursing, and recovery staff to make proper preoperative preparation and planning as well as postoperative recovery. It is important to clarify with the surgeon, the size and location of the tumor, diagnosis, surgical approach, need for ICP reduction, neuromonitoring, expected complications, and goals of surgery (e.g., radical excision versus decompression). The surgical approach determines patient positioning and intrinsic problems; common approaches to supratentorial masses are either parietal or temporal and frontal craniotomies. In a bi-frontal approach, the sagittal venous sinus is navigated, thereby increasing the risk of bleeding and venous air embolism (VAE).

For example, meningiomas can be quite large at the time of diagnosis and they are often highly vascular and are located in difficult to access areas like skull base, tentorial notch, or ventricles. This requires maximal brain relaxation to facilitate surgical access. All these factors make for a long duration of surgery that is often associated with significant bleeding. Preoperative embolization may be helpful to reduce intraoperative bleeding in certain situations. In contrast, gliomas are often easily accessible and have low propensity for bleeding. The non-pituitary supratentorial lesions like colloid cysts of the third ventricle and epidermoid tumors arising in the basal cisterns may be accompanied by obstructive hydrocephalus.

Premedication: All the current medications must be reviewed and continued as needed.

Anxiolytics In patients with elevated ICP, preoperative sedatives or anxiolytics must be used judiciously in small incremental doses or avoided completely because of the concern about producing CO_2 retention in a patient whose intracranial compliance is already compromised. Even a small dose of benzodiazepines or narcotics has shown to unmask or worsen a pre-existing compensated neurologic deficit [48, 49]. Complications of preoperative sedation however must be weighed against the complications associated with perioperative stress, which can cause increased CMR, CBF, and hypertension [50]. The decision to use anxiolytic premedication must be done on an individual basis after full consideration of the patient's expected risks and benefits. In elderly patients, the use of benzodiazepines is associated with an increased rate of postoperative delirium. In patients with tumors without signs of increased ICP, a small dose of benzodiazepine can help decrease the level of anxiety. Even though, our patient appears anxious, he also has a relatively large tumor and evidence of midline shift on imaging. For this reason, it may be best to avoid a premedication. A professional, reassuring visit by the anesthesiologist is invaluable as a preoperative anxiolysis itself.

Antiepileptics Antiepileptic drugs are generally continued throughout the perioperative period unless seizure focus mapping is anticipated. Antiepileptics can induce liver enzymes and increase the metabolism of muscle relaxants, opioids, and dexmedetomidine, which may require higher dosing [51]. Evidence for prophylactic use of anticonvulsants in seizure-naive patients is not compelling [52]. Sedative effects of anticonvulsants must also be considered during preoperative evaluation and premedication. Perioperative variations in antiepileptic medications may occur, contributing to perioperative development of seizures [53, 54]. Monitoring of plasma levels or temporary augmentation of dosage of such medications may be necessary.

Steroids Patients with a significant tumor-related mass effect, especially if there is tumor-related edema, are usually started on preoperative steroids. Although 48-h course is ideal, clinical effect is usually apparent within 24 h. Dexamethasone is the most commonly used agent. The initial bolus dose of 10 mg followed by 4 mg every 6 h is usually effective and is continued during the perioperative period [55].

Other Medications All blood thinners must be stopped appropriately. All the other home medications must be reviewed and continued unless contraindicated. Histamine (H_2) blockers and gastric prokinetic agents should be considered to counteract the reduced gastric emptying and greater acid secretion associated with increased ICP and steroid therapy.

Question 8:
How would you monitor the patient? Do you require a central line?

Answer:
American Society of Anesthesiology recommends that *standard monitoring* of oxygenation, ventilation, circulation, and temperature is followed in all patients. Besides these, *invasive arterial pressure* transducing at the mid-ear level which corresponds to the circle of Willis is essential for strict control of blood pressure and CPP.

Frequent blood gas and electrolyte measurements are prudent to determine the adequacy of ventilation, electrolyte balance, and hematocrit assessment. Neurosurgical patients are at increased risk for developing disturbance in the serum osmolality and electrolytes secondary to drugs like mannitol, HS, or owing to the development of DI, SIADH, or cerebral salt wasting (CSW). Tumors with bone metastases can cause hypercalcemia which can precipitate arrhythmias.

Blood glucose levels should be monitored regularly as general anesthesia and steroid therapy both tend to increase the blood glucose levels; hyperglycemia worsens neuronal damage during ischemia hence must be avoided [56, 57].

Central venous pressure monitoring is not routinely done but should be individualized. Two large-bore peripheral IV lines are usually suggested for vascular access. Central venous access should be considered in patients with the following:

- Significant risk for VAE (surgery requiring significant head-up position and lesions close to dural sinus)
- Substantial bleeding risk (e.g., large vascular tumor, proximity to major vasculature, or extensive bone resection)
- Significant cardiorespiratory disease requiring vasoactive medication

Even though VAE risk is low with these procedures, rarely, patients might need a *precordial Doppler or transesophageal echocardiography* to monitor VAE.

A *urinary catheter* is placed to monitor *urine output.*

Neuromuscular block should be monitored in patients receiving muscle relaxants. Care should be taken to avoid using the paralyzed extremity for monitoring the neuromuscular transmission as this might result in overdosing of the muscle relaxants due to upregulation of the acetylcholine receptor [58].

Patients with brain tumors can have hemostatic abnormalities including both hypercoagulable and hypocoagulable states, which can get exacerbated by endothelial injury, ischemia, and secondary inflammatory reactions triggering the release of brain thromboplastins [59, 60]. They can present with thromboembolic complications, disseminated intravascular coagulation, hyperfibrinolysis, or hemorrhage [61, 62]. Antiepileptic drugs can also affect the hemostatic system. In addition to the *routine coagulation parameters, point-of care (POC) viscoelastic assays* (ROTEM® or TEG®) should be used as needed.

Intracranial pressure monitoring: Patients may have an extraventricular drain (EVD) placed prior to or during craniotomy which can be used to drain CSF and to monitor ICP.

Processed EEG: The processed EEG monitor (bispectral index [BIS] or SedLine) can be useful to help guide the anesthetic depth and to facilitate rapid emergence from anesthesia.

Central jugular venous bulb oxygen saturation and transcranial Doppler ultrasonography (TCD): Central jugular venous bulb oxygen and TCD, though not routinely used, are available for select, high-risk patient population. They can be used to determine the adequacy of cerebral perfusion. TCD also allows for the assessment of pressure autoregulation, CO_2 reactivity, and to assess vessel patency during challenging dissection from the tumor [63].

17.2 Intraoperative

Intraoperative neuromonitoring: Surgical resection near the eloquent areas might necessitate brain mapping and *evoked potential* monitoring for more precise localization and dissection; EEG and evoked potential monitoring are also useful for surgeries at risk for cerebral hypoperfusion.

Need for neuromonitoring or awake resection must be clarified in our case as he presented with hemiparesis and the tumor is in frontal area.

Question 9:
What are the anesthetic goals for this case? Which anesthetic agents should be employed to accomplish these goals? How will you induce anesthesia? Are you worried about patient's blood pressure? Will you treat it before induction?

Answer:
The perioperative goals for supratentorial tumor resection are to optimize cerebral perfusion, oxygenation, and operative conditions, bestow neuroprotection, facilitate rapid and smooth awakening for postoperative neurological evaluation, minimize postoperative pain, and improve the oncological outcomes. It is important to avoid any secondary systemic insults. An ideal anesthetic regimen should deliver adequate amnesia and analgesia while maintaining systemic and cerebral milieu along with reduction in CMR and ICP.

Induction and airway management are critical stages of general anesthesia, especially in patients with elevated ICP. Following adequate preoxygenation and moderate hyperventilation, slow and controlled induction with constant attention to hemodynamics and ventilation is essential in order to maintain CPP [64, 65]. Both hypo- and hypertension can be detrimental particularly in patients with autoregulatory failure. Even cerebral autoregulation requires approximately 20–30 s to activate; any sharp change in the blood pressure needs to be treated immediately.

The commonly used induction agents are propofol, thiopentone sodium, and etomidate in combination with opioids. The combination of propofol (1–3 mg/kg), opioids like fentanyl (2–3 μg/kg), remifentanil (0.5–1 μg/kg) or sufentanil (0.5–1.5 μg/kg), and lidocaine (1.5 mg/kg) achieves adequate depth of anesthesia to blunt the sympathetic response to intubation. In patients with frailer cardiovascular systems, etomidate (0.2–0.4 mg/kg) may be used instead of propofol. Ketamine is usually avoided because of its propensity to increase ICP and postoperative delirium [65]. The effect of the various anesthetic agents on hemodynamics, CBF, CMR, and ICP has been reviewed in detail in question 5.

The commonly used muscle relaxants to facilitate intubation are rocuronium and vecuronium which have minimal effects on intracerebral hemodynamics. Succinylcholine has the potential to raise the ICP and should preferably be avoided although its effect on the ICP is transient and the clinical significance is debatable [66]. Caution must be exercised while using succinylcholine in patients with pre-existing motor deficits because of the increased risk of hyperkalemia. The need to increase the dosage by as much as 50% for non-depolarizing muscle relaxants in patients on long-term phenytoin or carbamazepine treatment should be noted [64, 65]. Even though the preoperative blood pressure is higher in our patient, one must be careful while treating blood pressure in patients with raised ICP as this could lead to reduction in CPP.

Sequence of events during induction is listed in Table 17.2.

Table 17.2 Sequence of events during induction

1. Monitors: ASA monitors. Pre-induction arterial line for patients with raised ICP
2. Ensure availability of short-acting vasoactive agents like phenylephrine, esmolol, and nicardipine or nitroglycerine to rapidly control the hemodynamics during induction
3. Pre-oxygenation and voluntary hyperventilation
4. Slow induction with fentanyl 1–3 μg/kg or remifentanil 0.5–1 μg/kg, lidocaine 1–2 mg/kg, propofol 1–3 mg/kg or thiopentaone, or etomidate followed by non-depolarizing muscle relaxant. Treat any hypotension with small doses of phenylephrine. Controlled ventilation (end-tidal CO_2 around 30–35). For patients with increased ICP, hyperventilation to bring end-tidal CO_2 to around 30 before intubation
5. Attempt at intubation after ensuring adequate depth. Supplement with esmolol 0.25–0.5 mg/kg or small doses of remifentanil (0.5–1 μg/kg), propofol, or nicardipine as needed
6. Intubation
7. Treat any cardiovascular response appropriately

Question 10:
Describe intraoperative management after induction. How will you maintain anesthesia?

Answer:
Care should be taken during

Patient positioning: Patient positioning is done after induction. Application of the Mayfield skull pins is associated with maximal nociceptive stimulation. Hemodynamic activation can be prevented by deepening the depth of anesthesia and analgesia with a bolus of remifentanil 0.25 to 1 μg/kg or fentanyl 1 to 2 μg/kg, esmolol 0.25 to 0.5 mg/kg, or propofol 0.5 to 1 mg/kg just before pinning. Local anesthetic infiltration of the pin site can also mitigate adverse CNS and hemodynamic activation [67]. Scalp blockade, preferably prior to pinning, can provide intraoperative hemodynamic stability and postoperative analgesia [68].

Patient positioning must be done carefully with adequate padding of all pressure points. The slight head-up position is favorable. Excessive flexion, extension, or rotation of the neck should be avoided to maintain cerebral venous drainage. There should be at least two-finger space between the chin and the sternum/clavicle to prevent excessive reduction of the anterior-posterior diameter of the oropharynx as this can precipitate postoperative airway edema. The knees should be mildly flexed to avoid lumbosacral injury. In patients requiring to be in the lateral position, the axillary roll should be used to prevent brachial plexus stretch injury. The endotracheal tube and lines should be secured well to prevent accidental dislodgement.

Pre-incision preparation: After skull pinning, a light level of anesthesia is often required for a potentially extensive period of time during registration of the stereotactic guidance system, sterile skin preparation, and draping. Blood pressure needs to be supported to maintain CPP. Perioperative antibiotics must be administered.

Maintenance of anesthesia: Adequate anesthetic depth should be ensured pre-incision. Craniotomy and raising the scalp and bone flaps can be associated with significant bleeding; adequate brain relaxation should be provided prior to opening the dura. The parietal dura is rich in pain fibers which demands continuation of a relatively deep level of anesthesia.

The *perioperative goals* during the maintenance phase remain the same as described during the induction. In patients with large tumors or significant intracranial hypertension (ICH), efforts should be made to shrink the brain to facilitate surgical exposure and to minimize ischemia that occurs under the retractor [69]. Short-acting and easily titratable agents are preferred for maintenance. Various agents, both IV and inhalational techniques have been used and extensively studied in clinical trials.

There has been a long-standing debate surrounding the use of TIVA versus volatile anesthetics for intracranial procedures. To this point, no study comparing TIVA with volatile anesthesia has been able to establish strong outcome

benefit of one over the other [70–72]. The combination of volatile anesthetics (isoflurane, sevoflurane, and desflurane) and synthetic opioids (remifentanil and fentanyl) are still extensively used because of their controllability, predictability, and rapid recovery [72–74]. However, volatile anesthetics are not the most ideal agents for patients with reduced intracranial compliance because of their potential to adversely affect the cerebral autoregulation, CBF, and ICP [73–76].

Several prospective, randomized clinical trials have suggested that ICP is decreased and CPP is increased in patients receiving TIVA when compared with those receiving volatile anesthetics during elective craniotomy procedures [70, 71, 77]. In a meta-analysis [71] that included 14 studies and yielded 1819 patients, comparing the effects of propofol to volatile-based anesthesia in patients undergoing elective craniotomy, there were similarities between the two groups with regard to hemodynamic stability, emergence, early cognitive function, and perioperative complications; except the incidence of post-operative nausea and vomiting (PONV) was lower in the propofol group. However, the initial mean ICP values were lower and CPP values were higher with propofol-based anesthesia. Nevertheless, this ICP lowering effect was not associated with less brain swelling or better operative conditions after dural opening. Yet, results of this meta-analysis cannot be extrapolated to all neurosurgical patients as primary studies included only relatively healthy and neurologically intact patients undergoing supratentorial excision of tumors who probably had near normal preoperative ICP.

The clinical impact of these different techniques in patients with elevated ICP has yet to be evaluated [77]. Until then, TIVA should be used in complicated patients with substantial elevation in ICP where maximal brain relaxation is required. The concurrent use of nitrous oxide and volatile anesthetics is best avoided because of their synergistic effects in increasing CBF and ICP [76]. Intermediate acting muscle relaxants are usually used to maintain akinesia unless precluded by neuromonitoring.

Other anesthetic adjuvants that are useful for anesthetic maintenance are:

Dexmedetomidine Dexmedetomidine, which is an alpha-2 adrenergic receptor agonist, has gained popularity for use in neurosurgical procedures as it has shown to provide stable hemodynamics, while reducing anesthetic and analgesic requirements [78, 79] along with some neuroprotective properties [80]. Dexmedetomidine can also attenuate the hemodynamic response to tracheal intubation [81] and cranial pinning [82].

Remifentanil Remifentanil infusion has been shown to provide easily controllable hemodynamics during intense surgical stimulation while drastically reducing the amount of volatile anesthetic or propofol during craniotomy [83]. It also provides rapid and smooth emergence [84, 85] and is associated with the earliest cognitive recovery when compared with other opioids [86]. With its short half-life, remifentanil should be transitioned with another analgesic to prevent pain and hypertension during emergence from general anesthesia.

Question 11:
How will you modify your anesthetic if there is neuromonitoring?

Answer:
The use of neurophysiological monitoring will impact the choice of anesthetic agents administered. Volatile anesthetic agents are known to decrease the amplitude and increase the latency of somatosensory evoked potentials (SSEPs) and depress motor evoked potentials (MEP) in a dose-dependent manner. IV agents like propofol, dexmedetomidine, or remifentanil interfere least with electrophysiological monitoring, hence either combination of volatile anesthetics with IV agents or TIVA should be used depending on the type of neuromonitoring and intracranial pathology.

Question 12:
Once the bone plate is removed, the surgeon complains of a tense brain. How will you manage?

Answer:
One of the important objectives of anesthetic management is to facilitate the surgical exposure to the lesion by providing a slack surgical brain. This minimizes brain retraction and perilesional neuronal injury. Anesthesiologists can utilize a variety of methods to accomplish this goal. In cases of massive tumors, despite all the physiological, pharmacological, and mechanical methods advocated to reduce the ICP, the brain can still take the path of least resistance leading to transcalvarial herniation referred to as brain bulge. Details of prevention and treatment of increases in ICP and brain bulk are shown in Tables 17.2 and 17.3.

Question 13:
Describe your strategy to manage intraoperative ventilation.

Answer:
One should aim for normocapnia or mild hypocapnia ($PaCO_2$ of 30 to 35 mmHg) and low intrathoracic pressures. Even though there is not much data on lung protective ventilation in neurosurgical patients, it has shown to improve outcome in patients at risk of pulmonary complications after major surgery [87]. Hyperventilation must be used judiciously; one must balance the benefit of brain relaxation against the risk of cerebral hypoperfusion [88]. Our patient has COPD. Hence it is important to know his baseline $PaCO_2$ and end-tidal CO_2 to $PaCO_2$ gradient. Care must be exercised while using high positive-end expiratory pressure (PEEP). However, several studies indicate that PEEP has only minimal effect on CBF or ICP when used at less than 10 cmH_2O in neurosurgical patients [89].

Question 14:
Will you use diuretics and osmotic agents routinely for all the cases?

Answer:
Hyperosmolar solutions such as mannitol and hypertonic saline (HS) are widely used in neurosurgery to reduce brain volume and facilitate surgical exposure during tumor resection. Both HS and mannitol cause acute increase in the blood osmolality, which in the presence of an impermeable BBB causes movement of water from brain parenchyma to the intravascular

Table 17.3 Stepwise approach to address the brain bulge

1. Decrease the cerebral venous pressure by:
(a) Head-up position, avoid extreme neck flexion or rotation
(b) Discontinuing use of any venodilators like nitroglycerin, nitroprusside
(c) Decreasing airway pressure: treat any bronchospasm, avoid excessive (PEEP), treat any coughing or straining on tube, and consider other lung pathologies like pneumothorax
(d) Decrease the cerebral blood volume (CBV) and CBF by:
(i) *Maintaining moderate hyperventilation and adequate oxygenation*
(ii) *Maintaining hemodynamics; treat hypertension, hypotension, and tachycardia*
(iii) *Conversion to TIVA (burst suppression as needed); control pain and arousal*
2. Decrease CMR by:
(a) Deepening anesthesia
(b) Controlling fever
(c) Maintaining moderate hypothermia
(d) Treating any seizure activity
3. Shrink the brain by:
(a) Osmotic agents like mannitol or hypertonic saline or
(b) Steroids for brain tumors
4. Drain CSF if a ventricular or lumbar catheter is in situ; 10 to 20 mL is usually adequate
5. Recognize and treat other mass effect like:
(a) Hematoma
(b) Air

compartment, thereby decreasing the brain bulk and ICP [90–92].

It is recommended to administer these medications before opening the dura to ensure adequate brain relaxation in patients with features of raised ICP [93]. By reducing the edema of the vascular endothelium and erythrocytes, they also improve the blood rheology [94, 95]. Mannitol usually is given as a bolus of 0.25 to 1 g/kg and HS has been used at 3 to 5 mL/kg bolus. The ICP reduction will usually be seen within 15 to 30 min and lasts for 2 to 6 h. At the same volume, 20% mannitol (1098 mOsm/L) and 3% HS (1024 mOsm/L) have almost equivalent osmolarity and have yielded comparable results on ICP reduction [90–92]. By contrast, a meta-analysis performed by Fang et al. [96], which involved 9 randomized controlled trials, suggested that HS provided better brain relaxation than mannitol.

Electrolyte abnormalities and increase in the serum osmolality are the adverse effects most commonly encountered with hyperosmolar therapy. Osmolality should be checked and maintained at less than 320 mOsm/kg. HS causes significantly higher levels of serum sodium, lasting for about 6 h, along with temporary reduction of potassium and a lesser diuretic effect compared with mannitol [91, 92, 97]. In contrast, mannitol results in a transient acute dilutional hyponatremia which normalizes over time as a result of the diuretic effects of mannitol and increase of potassium over time [91, 92, 97].

Great care should be taken in patients with congestive heart failure, pulmonary edema, or renal failure as the initial elevation in central circulatory volume may be detrimental [98]. Even though both the drugs have comparable effects in decreasing the ICP, HS may be recommended in hemodynamically unstable, hypovolemic patients as HS has shown to reduce the IV fluid replacement needs in patients undergoing surgery [99]. On the contrary, serum saline should be infused to replace urinary losses in order to avoid hypovolemia and maintain blood pressure after mannitol induced diuresis.

Question 15:
How will you manage intraoperative fluid requirement and hemodynamics? What is the best IV fluid for maintenance? Surgeon is requesting you to run the patient dry, do you concur?

Answer:
Neurosurgical patients can experience rapid changes in intravascular volume caused by hemorrhage, the administration of potent diuretics, or the onset of DI, CSW, or SIADH. Maintaining normovolemia and normotension is the goal for intracranial surgery. Careful ongoing monitoring of serum sodium levels, plasma osmolarity, urine output, and vascular volume status is imperative. The isotonic crystalloids and/or colloid, with target osmolality, 290 to 320 mOsm/kg, should be used for maintenance. Role of colloid oncotic pressure in brain edema is uncertain. Glucose-containing or hypo-osmolar solutions (e.g., 5% dextrose or lactated Ringer's) should be avoided as hyperglycemia has shown to worsen the consequences of cerebral ischemia and hypo-osmolality increases the brain edema, respectively [100, 101]. More prospective studies are needed to address optimal glucose management targets for patients with a specific type of neurologic injury or neurosurgical procedures. Until then, moderate glucose management with the goal of 140–180 mg/dL is recommended as hypoglycemia, which is a common side effect of intense insulin therapy, can trigger significant morbidity especially in the neurologically injured patient [101].

0.9% normal saline (NS) is the commonly used fluid in neurosurgical patients; however, large volumes of NS can result in normal anion gap hyperchloremic metabolic acidosis [102]. Despite the theoretical superiority of colloids, there is a limited scientific evidence to support their use [103]. In large volumes resuscitation, a combination of isotonic crystalloids (plasmalyte, 0.9% NS, and sodium acetate) and colloids may be the best choice.

Blood loss should be monitored closely. Both anemia and red blood cell (RBC) transfusion

may negatively influence the outcome. The need for intraoperative blood transfusion should be individualized taking into account expected blood loss, type of surgery, cardiorespiratory status, and clinical endpoints. The "dynamic" hemodynamic parameters (e.g., changes in stroke volume, arterial pulse pressure) provide a more accurate picture of volume status and responsiveness to fluid expansion than static hemodynamic parameters.

Blood pressure must be maintained by optimizing intravascular volume and if needed, using vasopressors like phenylephrine, norepinephrine infusion to counteract the vasodilation caused by anesthetic agents. Based on the patient's cardiac function and other comorbidities, agents like dopamine, dobutamine, or vasopressin can be used if hypotension is refractory to adrenergic agents.

17.3 Postoperative

Question 16:
How will you prepare the patient for emergence from anesthesia? Will you allow the patient to become hypercarbic to stimulate spontaneous ventilation? If the blood pressure elevates to 180/100 how will you manage?

Answer:
Emergence from anesthesia following craniotomy for tumor excision is a very crucial phase that requires meticulous planning, preparation, and skills. The two important goals are to achieve the following:

1. Smooth emergence without coughing/bucking and sympathetic stimulation
2. Rapid and complete awakening to facilitate the neurological examination

Emergence from anesthesia is often associated with significant sympathetic stimulation and catecholamine surge which gets further accentuated by the airway irritation from the endotracheal tube. The reported incidence of patient coughing during emergence is as high as 80–95% [104, 105]. Unfortunately, this can result in a number of detrimental side effects including hypertension, tachycardia, increased bleeding from the surgical site, and increased intracranial and intraocular pressures [106]. The incidence of hypertension during emergence has been reported to be more than 90% in neurosurgical patients [107, 108].

Perioperative hypertension has been directly linked with peri-resection bed hematoma, hematoma distant from the resection site, cerebral edema, and increased ICP [109, 110]. Given the potential morbidity, controlling this hemodynamic response is of extreme importance to preserve cerebral homeostasis. Various strategies have been employed to attenuate the airway and circulatory responses during extubation including extubating in a deep plane of anesthesia [111], administrating of IV agents like short-acting narcotics [112–114], IV and intra-cuff lidocaine [104, 115] or dexmedetomidine [116, 117] and various anti-hypertensives like esmolol [108, 118], nicardipine [119], and labetalol [108]. Each of these methods has its own limitations.

Adequate analgesia, prevention of hypothermia and shivering, adequate reversal of neuromuscular blockade, and timely tracheal extubation to avoid bucking against the tube are critical to limit catecholamine surge and hemodynamic changes. Esmolol, a short-acting beta-blocker has shown to improve hemodynamic stability during emergence and mitigate CBF changes [118]. Low dose remifentanil [112, 113] infusion continued during the emergence period has been successful in blunting the hemodynamic responses, but attention should be paid to avoid respiratory depression and hypercapnia.

Early awakening allows for neurological examination, as the awake patient is the best neurological monitor. This helps to diagnose any postoperative complications like postoperative hematoma. The anesthetic technique that can lead to early awakening have been addressed from time to time and as discussed earlier in question 10. Prospective, randomized clinical trials have failed to consistently prove that one

anesthetic technique is advantageous over another with regard to time to recovery, extubation, or postoperative cognitive function.

In certain situations, delayed emergence might be preferred [120] as respiratory drive and protective airway reflexes are expected to be impaired putting the patient at risk for secondary brain damage due to hypercapnia and hypoxia. Examples include prolonged procedures, large tumors requiring extensive dissection, surgery associated with significant brain ischemia (e.g., long vascular clipping times and extensive retractor pressure), significant cerebral edema, tight brain, proximity of the tumor to vital centers, hemodynamic instability, and significant intraoperative bleeding. If the patient was obtunded or had inadequate airway control preoperatively, the probability of successful early extubation becomes less likely. If delayed emergence is chosen, patient should be adequately sedated with easily titratable short-acting agents to avoid fighting the ventilator.

Hypertension needs to be treated immediately with short-acting agents, and CO_2 should be allowed to raise slowly to normal level especially after a period of hyperventilation. Acute restoration of a normal $PaCO_2$ value will result in increased CBF with a concomitant increase in ICP.

Question 17:
Patient is not waking up after the surgery. How will you evaluate?

Answer:
The majority of commonly used anesthetics have demonstrated acceptable emergence times without clinically significant difference in emergence. Nevertheless, prolonged duration of anesthesia can cause delayed emergence due to increased tissue uptake depending upon the concentration used and drug solubility. If the patient is not awake enough to obey simple verbal commands 20–30 min after complete cessation of anesthesia, non-anesthetic causes must be ruled out.

While the specific cause is being pursued, primary management is always support of airway, breathing, and circulation. A quick neurological examination, twitch monitor, vital signs including temperature, arterial blood gas including electrolytes and glucose can rule out most of the common causes followed by imaging. The possibility of acute intracranial event must be ruled out with CT or MRI especially after craniotomy. The causes for delayed emergence [121] are listed in Table 17.4.

Question 18:
Where will you recover the patient after surgery? Will you consider sending the patient to step down if intensive care unit (ICU) is full?

Answer:
The most feared postoperative complication is cerebral hemorrhage, which occurs most often in the first 6 h after surgery, hence close clinical monitoring in an ICU setting is recommended. In a retrospective analysis, factors associated with postoperative complications were tumor severity score (combining tumor location, mass effect, and midline shift), estimated blood loss, intraoperative fluids volume, longer duration of surgery, and postoperative ventilation [122]. However, because of the limited ICU resources, direct admission of low-risk patients to the ward has been proposed [123]. However, one should ensure adequate nurse and physician staffing, adequate monitoring, and the presence of a rapid response team in cases of neurological deterioration. Decision must be taken on an individualized basis after discussing with the surgeon. Our patient had significant midline shift and large tumor, thus it is safest to recover in the recovery unit until an ICU bed becomes available.

Question 19:
Patient is concerned about pain after surgery. How will you manage post-craniotomy pain?

Answer:
Pain after craniotomy is often moderate or severe and is greatest in the first 48 h after the procedure [124, 125] and is often undertreated. Strategies to overcome craniotomy pain requires interventions at all phases of patient care such as patient education, risk stratification, multimodal analgesia, and nonpharmacological and bio/behavioral

Table 17.4 Causes and workup for delayed emergence

1. *Effects of drugs:*
(a) **Residual anesthetic** after prolonged anesthesia: supportive therapy
(b) Excess **narcotics**: careful titration with small doses of **naloxone**
(c) Excessive preoperative **anxiolytics**: benzodiazepines can be reversed by **flumazenil 0.2 mg every minute up to 1 mg**
(d) **Central anticholinergic syndrome: precipitated by antihistamines, atropine, or antidepressants: Physostigmine 1.25 mg IV** can reverse cholinergic effects
(e) **Inadequate reversal of muscle relaxation** or **pseudocholinesterase deficiency**
(f) **Acute alcohol intoxication** or other **illicit drugs** rendering unconsciousness extending the length of the anesthetic
2. *Metabolic causes:*
(a) **Hypercarbia**; patients might need postoperative ventilation
(b) **Hypoxemia**; patients may require mechanical ventilation or supplemental oxygen
(c) **Acidosis**; correction of the underlying disorder will address the acidosis
(d) **Hypo-/hyperglycemia**; check blood gas, correct as indicated
(e) **Hypo-/hypernatremia**; correct slowly such as not to create central pontine myelinolysis
(f) **Hypo-/hyperthermia**; correct as indicated
(g) Underlying **metabolic disorder**; disorders can include liver disease, uremia, hypothyroidism
3. *Neurologic causes:*
(a) **Seizure:** a postictal state may well mimic unconsciousness
(b) **Cerebral edema**
(c) **Intracranial hematoma** or **pneumocephalus**
(d) New **ischemic** event

interventions. Multimodal analgesia is the gold standard for managing perioperative pain, which combines drugs with additive or synergistic effects resulting in reduced opioid consumption, side effects, and improving overall outcomes.

Various groups of drugs like lidocaine infusion, gabapentin, dexmedetomidine, ketamine, acetaminophen, and corticosteroids have been used successfully as part of the multimodal analgesia [125]. An increasing use of remifentanil during anesthesia necessitates an effective postoperative analgesic strategy. Limiting the dose of remifentanil to less than 0.2 μg/kg/min and combination with other analgesics has been suggested to mitigate acute opioid tolerance and opioid-induced hyperalgesia [126]. Scalp block or wound infiltration with local anesthetics administrated prior to craniotomy has been found to reduce intraoperative analgesic requirement as well as delay the onset of post-craniotomy pain [125]. Acetaminophen alone is not potent enough to control pain after craniotomy but is an ideal component of multimodal analgesia for acute post-craniotomy pain. Patient-controlled analgesia with various opioids can be used, but needs close postoperative monitoring to recognize any respiratory depression. Nonsteroidal anti-inflammatory drugs (NSAID) are not commonly used because of their potential to cause bleeding. However, the risk of bleeding due to NSAID has not been demonstrated after neurosurgery [125].

Question 20:
How will you manage post-craniotomy nausea and vomiting.

Answer:
Intracranial procedures per se carry high risk for PONV. The overall incidence of PONV within 24 h after craniotomy is approximately 50% [127]. Vomiting and retching could result in an increase in ICP and bleeding at the surgical site. It also puts the patient at risk for aspiration and electrolyte imbalance, compromising the outcome after intracranial procedures. Prophylaxis for PONV is therefore highly recommended. 5-HT_3 antagonists such as ondansetron are considered as agent of choice. Ondansetron and granisetron are considered safe with fewer side effects but are only partially effective [128]. However, dexa-

methasone routinely administered in neurosurgical patients for reduction of peritumoral edema increases the antiemetic efficacy of 5-HT_3 antagonists. Effective prevention of PONV in neurosurgical patients requires accurate risk stratification by means of a PONV scoring system. In the presence of more than 2 individual risk factors, multimodal method should be employed.

Multiple Choice Questions

1. Which of the following drugs is the BEST choice for lowering ICP while maintaining CPP in a patient with intracranial tumor with intact cerebral autoregulation?
   (a) Propofol
   (b) Thiopental
   (c) Hypertonic saline
   (d) Sevoflurane

   Answer: c

   Propofol and thiopentone decrease ICP but will decrease CPP due to decrease in blood pressure. Sevoflurane also decreases CPP. Hypertonic saline decreases ICP while maintaining CPP.
2. Which of the following value sets is MOST consistent with the SIAD secretion?
   (a) Serum [Na+] (mmol/L): 130, Serum Osmolality (mOsm): 270, Urine [Na+] (mmol/L): 18, CVP: 12
   (b) Serum [Na+] (mmol/L): 128, Serum Osmolality (mOsm): 267, Urine [Na+] (mmol/L): 40, CVP: 12
   (c) Serum [Na+] (mmol/L): 128, Serum Osmolality (mOsm): 268, Urine [Na+] (mmol/L): 40, CVP: 4
   (d) Serum [Na+] (mmol/L): 157, Serum Osmolality (mOsm): 334, Urine [Na+] (mmol/L): 18, CVP: 4

   Answer: b

   A has a pattern that is most consistent with water intoxication. C has a pattern that is most consistent with CSW syndrome. D has pattern that is most consistent with either central or nephrogenic diabetes insipidus.
3. Which statement about VAE during cranial surgery is MOST likely true?
   (a) The VAE can be decreased by keeping high PEEP during sitting craniotomy.
   (b) The VAE risk is increased when the head is more than 15° above the level of the heart.
   (c) A VAE is best detected with a precordial stethoscope.
   (d) A single-orifice central line provides the most effective treatment should a VAE occur.

   Answer: b

   High PEEP is not proven to decrease the incidence of VAE. It is not recommended as it can increase the risk of paradoxical air embolism. For choice C, transesophageal echocardiography is the most sensitive detector of air in the heart. A precordial Doppler is the next most sensitive detector. In choice D, a multiorifice central venous catheter placed at the junction of the superior vena cava and the right atrium has been shown to be effective in treating experimental VAEs.
4. Which of the following statements is TRUE about CBF and nitrous oxide?
   (a) Carbon dioxide causes a CBF response that is unchanged with nitrous oxide.
   (b) CBF is decreased with nitrous oxide use.
   (c) Nitrous oxide decreases blood flow through vasoconstriction.
   (d) The effects of nitrous oxide are the greatest with concomitant use of IV anesthetics.

   Answer: a

   Carbon dioxide causes CBF to change depending on the level and its response is not changed by the presence of nitrous oxide.
5. A 65-year-old man has quadriplegia after undergoing suboccipital craniotomy in the sitting position for posterior fossa tumor. Which of the following is the most likely cause?
   (a) Air embolism with the presence of probe patent foramen ovale
   (b) Postoperative pneumocephalus
   (c) Compression of the cervical cord due to excessive flexion of the neck
   (d) Increased CPP

   Answer: c

   VAE is a known complication in the sitting position; however, isolated quadriplegia is uncommon. Jugular venous obstruction can lead to raised ICP but does not produce quadriplegia by itself.

Pneumocephalus is one of the differential diagnoses of delayed awakening. Collection of air under the dura can increase ICP and neurological deficit but unlikely to cause isolated quadriplegia. It occurs because air enters the cranium when the patient is in a head-up position at a time when the volume of the intracranial contents has been reduced. When the cranium is closed and the patient is returned to the near supine position, CSF, venous blood volume, and extracellular fluid return or reaccumulate and the air pocket becomes an unyielding mass lesion. Supratentorial pneumocephalus (STP) can develop during procedures performed in the sitting position as CSF drains out of the cranial cavity at the durotomy site. The treatment can include in mild cases, supplemental oxygen is enough or a twist-drill hole followed by needle puncture of the dura can be performed for resistant cases. Tension pneumocephalus can result in delayed emergence from anesthesia, locked-in syndrome, and lateral rectus muscle palsy, and requires emergent evacuation.

References

Question 1

1. Ostrom QT, Gittleman H, Truitt G, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011–2015. Neuro Oncol. 2018;20(suppl_4):iv1–86.
2. Ellenbhogen R, Sekhar L, Kitchen N, et al. Principles of neurological surgery. Brain metastasis. 4th ed. Amsterdam: Elsevier. p. 586–592.e1.
3. Louis DN, Perry A, Reifenberger G, Von Deimling A, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol. 2016;131(6):803–20.

Question 2

4. Barash PG. Clinical anesthesia. Anesthesia for neurosurgery. 8th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2017. p. 1003.

Question 3

5. Dunn LT. Raised intracranial pressure. J Neurol Neurosurg Psychiatry. 2002;73(suppl 1):i23–7.
6. Macintyre I. A hotbed of medical innovation: George Kellie (1770–1829), his colleagues at Leith and the Monro–Kellie doctrine. J Med Biogr. 2014;22(2):93–100.
7. Ropper AH. Lateral displacement of the brain and level of consciousness in patients with an acute hemispheral mass. N Engl J Med. 1986;314(15): 953–8.
8. Simonetti F, Uggetti C, Farina L, et al. Uncal displacement and intermittent third nerve compression. Lancet. 1993;342(8884):1431–2.
9. Ropper AH. The opposite pupil in herniation. Neurology. 1990;40(11):1707.
10. Bruce JN, Criscuolo GR, Merrill MJ, et al. Vascular permeability induced by protein product of malignant brain tumors: inhibition by dexamethasone. J Neurosurg. 1987;67(6):880–4.
11. Tatagiba M, Mirzai S, Samii M. Peritumoral blood flow in intracranial meningiomas. Neurosurgery. 1991;28(3):400–4.
12. Sharma D, Bithal PK, Dash HH, et al. Cerebral autoregulation and CO2 reactivity before and after elective supratentorial tumor resection. J Neurosurg Anesthesiol. 2010;22(2):132–7.
13. Smith DR, Jacobson J, Kobrine AI, et al. Regional cerebral blood flow with intracranial mass lesions. Part II: autoregulation in localized mass lesion. Surg Neurol. 1977;7(4):238–40.
14. Wiranowska M, Gonzalvo AA, Saporta S, et al. Evaluation of blood–brain barrier permeability and the effect of interferon in mouse glioma model. J Neurooncol. 1992;14:225–36.
15. On NH, Mitchell R, Savant SD, et al. Examination of blood–brain barrier (BBB) integrity in a mouse brain tumor model. J Neurooncol. 2013;111(2): 133–43.
16. Torres D, Canoll P. Alterations in the brain microenvironment in diffusely infiltrating low-grade glioma. Neurosurg Clin N Am. 2019;30(1):27–34.
17. Liubinas SV, O'Brien TJ, Moffat BM, et al. Tumour associated epilepsy and glutamate excitotoxicity in patients with gliomas. J Clin Neurosci. 2014;21:899–908.

Question 4

18. Chang SM, Parney IF, Huang W, et al. Patterns of care for adults with newly diagnosed malignant glioma. JAMA. 2005;293(5):557–64.
19. Youland RS, Schomas DA, Brown PD, et al. Changes in presentation, treatment, and outcomes of adult low-grade gliomas over the past fifty years. Neuro Oncol. 2013;15(8):1102–10.
20. Grant R. Overview: brain tumour diagnosis and management/Royal College of Physicians guidelines. J Neurol Neurosurg Psychiatry. 2004;75(suppl 2):ii18–23.
21. Dunn LT. Raised intracranial pressure. J Neurol Neurosurg Psychiatry. 2002;73(suppl 1):i23–7.

Question 5:

22. Miller's anesthesia. Cerebral physiology and the effects of anesthetic drugs. 8th ed. Philadelphia, PA: Elsevier/Saunders; 2015. p. 387–422.
23. Sanders RD, Degos V, Young WL. Cerebral perfusion under pressure: is the autoregulatory 'plateau'a level playing field for all? Anaesthesia. 2011;66(11):968–72.
24. Hu K, Peng CK, Czosnyka M, et al. Nonlinear assessment of cerebral autoregulation from spontaneous blood pressure and cerebral blood flow fluctuations. Cardiovasc Eng. 2008;8(1):60–71.
25. Lebrun-Grandié P, Baron JC, Soussaline F, et al. Coupling between regional blood flow and oxygen utilization in the normal human brain: a study with positron tomography and oxygen 15. Arch Neurol. 1983;40(4):230–6.
26. Barash PG. Clinical anesthesia. Anesthesia for neurosurgery. 8th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2017. p. 1003.
27. Stullken EH Jr, Milde JH, Michenfelder JD, Tinker JH. The nonlinear responses of cerebral metabolism to low concentrations of halothane, enflurane, isoflurane, and thiopental. Anesthesiology. 1977;46:28–34.
28. Kuroda Y, Murakami M, Tsuruta J, et al. Preservation of the ration of cerebral blood flow/metabolic rate for oxygen during prolonged anesthesia with isoflurane, sevoflurane, and halothane in humans. Anesthesiology. 1996;84:555–61.
29. Strebel S, Lam AM, Matta BF, Newell DW. Impaired cerebral autoregulation after mild brain injury. Surg Neurol. 1997;47:128–31.
30. Bruder NJ, Ravussin P, Schoettker P. Cottrell and Patel's neuroanesthesia. Supratentorial masses: anesthetic considerations. In: Cottrell J, Patel P, editors. Neuroanesthesia. 6th ed. Amsterdam: Elsevier; 2016. p. 189–208.
31. Drummond JC, Scheller MS, Todd MM. The effect of nitrous oxide on cortical cerebral blood flow during anesthesia with halothane and isoflurane, with and without morphine, in the rabbit. Anesth Analg. 1987;66:1083–9.
32. Harrison JM, Girling KJ, Mahajan RP. Effects of propofol and nitrous oxide on middle cerebral artery flow velocity and cerebral autoregulation. Anaesthesia. 2002;57:27–32.20.
33. Yates H, Hamill M, Borel CO, Toung TJ. Incidence and perioperative management of tension pneumocephalus following craniofacial resection. J Neurosurg Anesthesiol. 1994;6(1):15–20.
34. Bekker AY, Mistry A, Ritter AA, Wolk SC, Turndorf H. Computer simulation of intracranial pressure changes during induction of anesthesia: comparison of thiopental, propofol, and etomidate. J Neurosurg Anesthesiol. 1999;11(2):69–80.
35. Renou AM, Vernhiet J, Macrez P, Constant P, BILLEEREY J, Khadaroo MY, Caille JM. Cerebral blood flow and metabolism during etomidate anaesthesia in man. Br J Anaesth. 1978;50(10):1047–51.
36. Petersen KD, Landsfeldt U, Cold GE, Petersen CB, Mau S, Hauerberg J, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. Anesthesiology. 2003;98(2):329–36.
37. Långsjö JW, Maksimow A, Salmi E, Kaisti K, Aalto S, Oikonen V, Hinkka S, Aantaa R, Sipilä H, Viljanen T, Parkkola R. S-ketamine anesthesia increases cerebral blood flow in excess of the metabolic needs in humans. Anesthesiology. 2005;103(2):258–68.
38. Zeiler FA, Teitelbaum J, West M, Gillman LM. The ketamine effect on intracranial pressure in nontraumatic neurological illness. J Crit Care. 2014;29(6):1096–106.
39. Wang X, Ding X, Tong Y, Zong J, Zhao X, Ren H, et al. Ketamine does not increase intracranial pressure compared with opioids: meta-analysis of randomized controlled trials. J Anesth. 2014;28(6):821–7.
40. Zeiler FA, Teitelbaum J, West M, Gillman LM. The ketamine effect on ICP in traumatic brain injury. Neurocrit Care. 2014;21(1):163–73.
41. Albanese J, Viviand X, Potie F, Rey M, Alliez B, Martin C. Sufentanil, fentanyl, and alfentanil in head trauma patients: a study on cerebral hemodynamics. Crit Care Med. 1999;27(2):407–11.
42. Jamali S, Ravussin P, Archer D, et al. The effects of bolus administration of opioids on cerebrospinal fluid pressure in patients with supratentorial lesions. Anesth Analg. 1996;82:600–6.
43. Nishikawa T, Omote K, Namiki A, Takahashi T. The effects of nicardipine on cerebrospinal fluid pressure in humans. Anesth Analg. 1986;65(5):507–10.
44. Pinaud M, Souron R, Lelausque JN, Gazeau MF, Lajat Y, Dixneuf B. Cerebral blood flow and cerebral oxygen consumption during nitroprusside-induced hypotension to less than 50 mmHg. Anesthesiology. 1989;70(2):255–60.
45. Strebel SP, Kindler C, Bissonnette B, et al. The impact of systemic vasoconstrictors on the cerebral circulation of anesthetized patients. Anesthesiology. 1998;89:67–72.
46. Nissen P, Brassard P, Jorgensen TB, et al. Phenylephrine but not ephedrine reduces frontal lobe oxygenation following anesthesia-induced hypotension. Neurocrit Care. 2010;12:17–23.

Question 6

47. Brandes AA, Scelzi E, Salmistraro G, et al. Incidence and risk of thromboembolism during treatment of high-grade gliomas: a prospective study. Eur J Cancer. 1997;33(10):1592–6.

Question 7

48. Lazar RM, Fitzsimmons BF, Marshall RS, Berman MF, Bustillo MA, Young WL, Mohr JP, Shah J,

Robinson JV. Reemergence of stroke deficits with midazolam challenge. Stroke. 2002;33(1):283–5.
49. Thal GD, Szabo MD, Lopez-Bresnahan M, Crosby G. Exacerbation or unmasking of focal neurologic deficits by sedatives. Anesthesiology. 1996;85(1):21–5.
50. Lunn JK, Stanley TH, Webster LR, et al. Arterial blood-pressure and pulse-rate responses to pulmonary and radial arterial catheterization prior to cardiac and major vascular operations. Anesthesiology. 1979;51(3):265–8.
51. Flexman AM, Wong H, Riggs KW, et al. Enzyme-inducing anticonvulsants increase plasma clearance of Dexmedetomidine: a pharmacokinetic and pharmacodynamic study. Anesthesiology. 2014;120(5):1118–25.
52. Perry J, Zinman L, Chambers A, et al. Neuro-oncology Disease Site Group. The use of prophylactic anticonvulsants in patients with brain tumours—a systematic review. Curr Oncol. 2006;13(6):222.
53. Paul F, Veauthier C, Fritz G, et al. Perioperative fluctuations of lamotrigine serum levels in patients undergoing epilepsy surgery. Seizure. 2007;16(6):479–84.
54. Yeh JS, Dhir JS, Green AL, Bodiwala D, Brydon HL. Changes in plasma phenytoin level following craniotomy. Br J Neurosurg. 2006;20(6):403–6.
55. Bruder NJ, Ravussin P, Schoettker P. Supratentorial masses: anesthetic considerations. In: Cottrell J, Patel P, editors. Neuroanesthesia. 6th ed. Amsterdam: Elsevier; 2016. p. 189–206.

Question 8

56. Kimura K, Iguchi Y, Inoue T, Shibazaki K, Matsumoto N, Kobayashi K, Yamashita S. Hyperglycemia independently increases the risk of early death in acute spontaneous intracerebral hemorrhage. J Neurol Sci. 2007;255(1–2):90–4.
57. McGirt MJ, Woodworth GF, Brooke BS, et al. Hyperglycemia independently increases the risk of perioperative stroke, myocardial infarction, and death after carotid endarterectomy. Neurosurgery. 2006;58:1066–73; discussion 1066–1073.
58. Graham DH. Monitoring neuromuscular block may be unreliable in patients with upper-motor-neuron lesions. Anesthesiology. 1980;52(1):74–5.
59. Magnus N, D'Asti E, Garnier D, Meehan B, Rak J. Brain neoplasms and coagulation. In: Seminars in thrombosis and hemostasis, vol. 39. New York: Thieme Medical; 2013. p. 881–95.
60. Goh KY, Tsoi WC, Feng CS, et al. Haemostatic changes during surgery for primary brain tumours. J Neurol Neurosurg Psychiatry. 1997;63:334–8.
61. Sawaya R, Glas-Greenwalt P. Post-operative venous thromboembolism and brain tumours. J Neurooncol. 1992;14:127–34.
62. Sawaya R, Donlon JA. Chronic disseminated intravascular coagulation and metastatic brain tumor: a case report and review of the literature. Neurosurgery. 1983;12(5):580–4.
63. Moppett IK, Mahajan RP. Transcranial Doppler ultrasonography in anaesthesia and intensive care. Br J Anaesth. 2004;93(5):710–29.

Question 9

64. Kandasamy R, Tharakan J, Idris Z, Abdullah JM. Intracranial bleeding following induction of anesthesia in a patient undergoing elective surgery for refractory epilepsy. Surg Neurol Int. 2013; 4:124.
65. Bruder NJ, Ravussin P, Schoettker P. Cottrell and Patel's neuroanesthesia. Supratentorial masses: anesthetic considerations. In: Cottrell J, Patel P, editors. Neuroanesthesia. 6th ed. Amsterdam: Elsevier; 2016. p. 189–208.
66. Kovarik WD, Mayberg TS, Lam AM, et al. Succinylcholine does not change intracranial pressure, cerebral blood flow velocity, or the electroencephalogram in patients with neurologic injury. Anesth Analg. 1994;78(3):469–73.

Question 10

67. Bayer-Berger MM, Ravussin P, Fankhauser H, Freeman J. Effect of three pretreatment techniques on hemodynamic and CSFP responses to skull-pin head-holder application during thiopentone/isoflurane or propofol anesthesia. J Neurosurg Anesthesiol. 1989;1(3):227–32.
68. Papangelou A, Radzik BR, Smith T, Gottschalk A. A review of scalp blockade for cranial surgery. J Clin Anesth. 2013;25(2):150–9.
69. Andrews RJ, Bringas JR. A review of brain retraction and recommendations for minimizing intraoperative brain injury. Neurosurgery. 1993;33(6): 1052–64.
70. Petersen KD, Landsfeldt U, Cold GE, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors, a randomized prospective study of patients subjected to craniotomy in Propofol-fentanyl, Isoflurane-fentanyl, or Sevoflurane-fentanyl anesthesia. Anesthesiology. 2003;98(2):329–36.
71. Chui J, Mariappan R, Mehta J, et al. Comparison of propofol and volatile agents for maintenance of anesthesia during elective craniotomy procedures: systematic review and meta-analysis. Can J Anesth. 2014;61(4):347–56.
72. Magni GM, Baisi F, La Rosa I, et al. No difference in emergence time and early cognitive function between sevoflurane-fentanyl and propofol-remifentanil in patients undergoing craniotomy for supratentorial intracranial surgery. J Neurosurg Anesthesiol. 2005;17(3):134–8.
73. Talke P, Caldwell JE, Brown R, et al. A comparison of three anesthetic techniques in patients undergoing craniotomy for supratentorial intracranial surgery. Anesth Analg. 2002;95(2):430–5.

74. Necib S, Tubach F, Peuch C, et al. PROMIFLUNIL trial group. Recovery from anesthesia after craniotomy for supratentorial tumors: comparison of propofol-remifentanil and sevoflurane-sufentanil (the PROMIFLUNIL trial). J Neurosurg Anesthesiol. 2014;26(1):37–44.
75. Matta BF, Heath KJ, Tipping K, Summors AC. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. Anesthesiology. 1999;91(3):677.
76. Kaisti KK, Långsjö JW, Aalto S, et al. Effects of sevoflurane, propofol, and adjunct nitrous oxide on regional cerebral blood flow, oxygen consumption, and blood volume in humans. Anesthesiology. 2003;99(3):603–13.
77. Cole CD, Gottfried ON, Gupta DK, Couldwell WT. Total intravenous anesthesia: advantages for intracranial surgery. Oper Neurosurg. 2007;61(suppl_5):ONSE369–78.
78. Soliman RN, Hassan AR, Rashwan AM, Omar AM. Prospective, randomized controlled study to assess the role of dexmedetomidine in patients with supratentorial tumors undergoing craniotomy under general anesthesia. Middle East J Anaesthesiol. 2011;21(1):23–33.
79. Tanskanen PE, Kyttä JV, Randell TT, Aantaa RE. Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumour surgery: a double-blind, randomized and placebo-controlled study. Br J Anaesth. 2006;97(5):658–65.
80. Maier C, Steinberg GK, Sun GH, Zhi GT, Maze M. Neuroprotection by the alpha 2-adrenoreceptor agonist dexmedetomidine in a focal model of cerebral ischemia. Anesthesiology. 1993;79(2):306–12.
81. Yildiz M, Tavlan A, Tuncer S, et al. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation. Drugs R D. 2006;7(1):43–52.
82. Uyar AS, Yagmurdur H, Fidan Y, et al. Dexmedetomidine attenuates the hemodynamic and neuroendocrinal responses to skull-pin headholder application during craniotomy. J Neurosurg Anesthesiol. 2008;20(3):174–9.
83. Del AG, Ciritella P, Perrotta F, et al. Remifentanil vs fentanyl with a target controlled propofol infusion in patients undergoing craniotomy for supratentorial lesions. Minerva Anestesiol. 2006;72(5):309–19.
84. Bhagat H, Dash HH, Bithal PK, et al. Planning for early emergence in neurosurgical patients: a randomized prospective trial of low-dose anesthetics. Anesth Analg. 2008;107(4):1348–55.
85. Bilotta F, Caramia R, Paoloni FP, et al. Early postoperative cognitive recovery after remifentanil–propofol or sufentanil–propofol anaesthesia for supratentorial craniotomy: a randomized trial. Eur J Anaesthesiol. 2007;24(2):122–7.
86. Gelb AW, Salevsky F, Chung F, et al. Remifentanil with morphine transitional analgesia shortens neurological recovery compared to fentanyl for supratentorial craniotomy. Can J Anesth. 2003;50(9):946–52.

Question 13

87. Futier E, Constantin JM, Paugam-Burtz C, Pascal J, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med. 2013;369(5):428–37.
88. Coles JP, Fryer TD, Coleman MR, et al. Hyperventilation following head injury: effect on ischemic burden and cerebral oxidative metabolism. Crit Care Med. 2007;35(2):568–78.
89. Sogame LC, Vidotto MC, Jardim JR, Faresin SM. Incidence and risk factors for postoperative pulmonary complications in elective intracranial surgery. J Neurosurg. 2008;109:222–7.

Question 14

90. Dostal P, Dostalova V, Schreiberova J, et al. A comparison of equivolume, equiosmolar solutions of hypertonic saline and mannitol for brain relaxation in patients undergoing elective intracranial tumor surgery: a randomized clinical trial. J Neurosurg Anesthesiol. 2015;27(1):51–6.
91. Hernández-Palazón J, Fuentes-García D, Doménech-Asensi P, et al. A comparison of equivolume, equiosmolar solutions of hypertonic saline and mannitol for brain relaxation during elective supratentorial craniotomy. Br J Neurosurg. 2016;30(1):70–5.
92. Rozet I, Tontisirin N, Muangman S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. Anesthesiology. 2007;107(5):697–704.
93. Rasmussen M, Bundgaard H, Cold GE. Craniotomy for supratentorial brain tumors: risk factors for brain swelling after opening the dura mater. J Neurosurg. 2004;101(4):621–6.
94. Burke AM, Quest DO, Chien S, Cerri C. The effects of mannitol on blood viscosity. J Neurosurg. 1981;55(4):550–3.
95. Hijiya N, Horiuchi K, Asakura T. Morphology of sickle cells produced in solutions of varying osmolarities. J Lab Clin Med. 1991;117(1):60–6.
96. Fang J, Yang Y, Wang W, Liu Y, An T, Zou M, Cheng G. Comparison of equiosmolar hypertonic saline and mannitol for brain relaxation during craniotomies: a meta-analysis of randomized controlled trials. Neurosurg Rev. 2018;41(4):945–56.
97. Tsaousi G, Stazi E, Cinicola M, Bilotta F. Cardiac output changes after osmotic therapy in neurosurgical and neurocritical care patients: a systematic review of the clinical literature. Br J Clin Pharmacol. 2018;84(4):636–48.
98. Stiff JL, Munch DF, Bromberger-Barnea B. Hypotension and respiratory distress caused by rapid infusion of mannitol or hypertonic saline. Anesth Analg. 1979;58(1):42–8.

99. McAlister V, Burns KE, Znajda T, Church B. Hypertonic saline for peri-operative fluid management. Cochrane Database Syst Rev. 2010;(1):CD005576.

Question 15

100. Atkins JH, Smith DS. A review of perioperative glucose control in the neurosurgical population. J Diabetes Sci Technol. 2009;3(6):1352–64.
101. Bilotta F, Rosa G. Glucose management in the neurosurgical patient: are we yet any closer? Curr Opin Anesthesiol. 2010;23(5):539–43.
102. Stephens RC, Mythen MG. Saline-based fluids can cause a significant acidosis that may be clinically relevant. Crit Care Med. 2000;28(9):3375–6.
103. Bunn F, Trivedi D, Ashraf S. Colloid solutions for fluid resuscitation. Cochrane Database Syst Rev. 2008;(1):CD001319.

Question 18

104. Fagan C, Frizelle HP, Laffey J, Hannon V, Carey M. The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. Anesth Analg. 2000;91(1):201–5.
105. Tanaka Y, Nakayama T, Nishimori M, Sato Y, Furuya H. Lidocaine for preventing postoperative sore throat. Cochrane Database Syst Rev. 2009;(3):CD004081.
106. Stone DJ, Gal TJ. Airway management. In: Miller RD, editor. Textbook of Anesthesia. 5th ed. Philadelphia: Churchill Livingstone; 2000. p. 1414–51.
107. Todd MM, Warner DS, Sokoll MD, Maktabi MA, Hindman BJ, Scamman FL, Kirschner J. A prospective, comparative trial of three anesthetics for elective supratentorial craniotomy. Propofol/fentanyl, isoflurane/nitrous oxide, and fentanyl/nitrous oxide. Anesthesiology. 1993;78(6):1005–20.
108. Muzzi DA, Black S, Losasso TJ, Cucchiara RF. Labetalol and esmolol in the control of hypertension after intracranial surgery. Anesth Analg. 1990;70(1):68–71.
109. Schubert A. Cerebral hyperemia, systemic hypertension, and perioperative intracranial morbidity: is there a smoking gun? Anesth Analg. 2002;94:485–7.
110. Seifman MA, Lewis PM, Rosenfeld JV, Hwang PY. Postoperative intracranial haemorrhage: a review. Neurosurg Rev. 2011;34(4):393–407.
111. Neelakanta G, Miller J. Minimum alveolar concentration of isoflurane for tracheal extubation in deeply anesthetized children. Anesthesiology. 1994;80(4):811–3.
112. Lee JH, Choi SH, Choi YS, Lee B, Yang SJ, Lee JR. Does the type of anesthetic agent affect remifentanil effect-site concentration for preventing endotracheal tube-induced cough during anesthetic emergence? Comparison of propofol, sevoflurane, and desflurane. J Clin Anesth. 2014;26(6):466–74.
113. Choi SH, Min KT, Lee JR, Choi KW, Han KH, Kim EH, Oh HJ, Lee JH. Determination of EC95 of remifentanil for smooth emergence from propofol anesthesia in patients undergoing transsphenoidal surgery. J Neurosurg Anesthesiol. 2015;27(2):160–6.
114. Nishina K, Mikawa K, Maekawa N, Obara H. Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta Anaesthesiol Scand. 1995;39(1):85–9.
115. Saghaei M, Reisinejad A, Soltani H. Prophylactic versus therapeutic administration of intravenous lidocaine for suppression of post-extubation cough following cataract surgery: a randomized double blind placebo controlled clinical trial. Acta Anaesthesiol Taiwan. 2005;43(4):205–9.
116. Turan G, Ozgultekin A, Turan C, Dincer E, Yuksel G. Advantageous effects of dexmedetomidine on haemodynamic and recovery responses during extubation for intracranial surgery. Eur J Anaesthesiol. 2008;25(10):816–20.
117. Luthra A, Prabhakar H, Rath GP. Alleviating stress response to tracheal extubation in neurosurgical patients: a comparative study of two infusion doses of dexmedetomidine. J Neurosci Rural Pract. 2017;8(Suppl 1):S49.
118. Grillo P, Bruder N, Auquier P, Pellissier D, Gouin F. Esmolol blunts the cerebral blood flow velocity increase during emergence from anesthesia in neurosurgical patients. Anesth Analg. 2003;96(4):1145–9.
119. Bebawy JF, Houston CC, Kosky JL, Badri AM, Hemmer LB, Moreland NC, Carabini LM, Koht A, Gupta DK. Nicardipine is superior to esmolol for the management of postcraniotomy emergence hypertension: a randomized open-label study. Anesth Analg. 2015;120(1):186–92.
120. Mahajan C, Rath GP, Sharma MS, Dube SK, Rajagopalan V, Bithal PK. Rate and reasons for elective ventilation in patients undergoing intracranial tumour surgery. J Neuroanaesthesiol Crit Care. 2014;1(2):125.
121. Misal US, Joshi SA, Shaikh MM. Delayed recovery from anesthesia: a postgraduate educational review. Anesth Essays Res. 2016;10(2):164.
122. Cottrell JE, Patel P. Cottrell and Patel's neuroanesthesia e-book. New York: Elsevier Health Sciences; 2016.
123. Bui JQ, Mendis RL, Van Gelder JM, Sheridan MM, Wright KM, Jaeger M. Is postoperative intensive care unit admission a prerequisite for elective craniotomy? Clinical article. J Neurosurg. 2011;115(6):1236–41.

Question 19

124. Gottschalk A, Berkow LC, Stevens RD, Mirski M, Thompson RE, White ED, Weingart JD, Long DM, Yaster M. Prospective evaluation of pain and analgesic use following major elective intracranial surgery. J Neurosurg. 2007;106(2):210–6.
125. Vacas S, Van de Wiele B. Designing a pain management protocol for craniotomy: a narrative review and consideration of promising practices. Surg Neurol Int. 2017;8:291.
126. Yu EH, Tran DH, Lam SW, Irwin MG. Remifentanil tolerance and hyperalgesia: short-term gain, long-term pain? Anaesthesia. 2016;71(11):1347–62.

Question 20

127. Latz B, Mordhorst C, Kerz T, Schmidt A, Schneider A, Wisser G, Werner C, Engelhard K. Postoperative nausea and vomiting in patients after craniotomy: incidence and risk factors. J Neurosurg. 2011;114(2):491–6.
128. Jain V, Mitra JK, Rath GP, Prabhakar H, Bithal PK, Dash HH. A randomized, double-blinded comparison of ondansetron, granisetron, and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. J Neurosurg Anesthesiol. 2009;21(3):226–3.

18 Management of Patient with Traumatic Brain Injury: Epidural Hematoma

Letha Mathews

Stem Case Terminology

An 18-year-old male was brought to the emergency department (ED) following a motor vehicle crash (MVC). The paramedics found him awake at the crash site but noted mild confusion and a history of brief loss of consciousness (LOC). He complained of pain on the (L) side of his head and chest. But he was hemodynamically stable en-route to the hospital. In the ED, the patient complained of worsening headache and was became more confused and combative. The anesthesia team was consulted for sedation prior to head CT (computerized tomography). When you arrived at the ED to assess the patient, he was somnolent and not following commands.

Vital Signs: BP 180/95 mmHg, HR 51 bpm, RR 18, SpO_2 94% on 2 L O_2 via nasal cannula. His cervical spine was immobilized with a C-collar. A 16 G IV was present on the left hand with lactated Ringer's infusing.

- What other information would you like before you transfer the patient to the CT scanner? How would you sedate this patient for the head CT? Would you intubate this patient? Discuss the various options for sedation and intubation of a head injured patient.

After the patient was intubated and ventilation established, patient was transferred to the CT scanner. Head CT showed a large "lens shaped mass" on the left frontoparietal area with 9 mm midline shift. He was emergently transferred to the operating room (OR) for evacuation of an epidural hematoma (EDH).

- What are the common causes of EDH? How do they usually present? How is the decision for operative intervention made? What are your concerns during transport to the OR? How would you monitor the patient?

The patient is in the OR now and his vital signs are as follows: BP 195/70 mmHg, HR 59 bpm, $SapO_2$ 96% on 40% FiO_2. Pt is placed on the ventilator and breath sounds are confirmed bilaterally. Temperature is 36.9° C.

- Would you lower his BP before surgery starts? Is an arterial line indicated for this case? Would you delay starting the case to place an a-line? What is the BP goal?

The surgeon requests 1 g/kg of mannitol to lower ICP (intracranial pressure).

L. Mathews (✉)
Division of Neuroanesthesiology, Vanderbilt University Medical Center, Nashville, TN, USA
e-mail: letha.mathews@vumc.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_18

- What is the mechanism of action of mannitol and what other options are available to decrease ICP?

The patient is turned over to the surgeons and his vital signs are stable and adequate ventilation is established.

- How would you maintain anesthesia? Is total intravenous anesthesia (TIVA) indicated? Does TIVA offer any advantage over inhalational anesthesia?

Anesthesia is maintained with TIVA with propofol infusion supplemented with fentanyl boluses and neuromuscular blockade with vecuronium bromide. The first arterial blood gas (ABG) shows pH 7.36, $PaCO_2$ 36 mmHg, PaO_2 140 mmHg, Base Excess −5.6, PCV-32, Na-134 mEq/L, K 3.9 mEq/L, and the remainder of the labs were within normal limits. As the cranial bone flap is removed, the dura appears to be tense. The surgeon asks for improved brain relaxation.

- What other options are available to decrease brain edema and provide brain relaxation?

The surgeon evacuated the hematoma and your efforts to reduce brain swelling have improved the operating conditions. You notice that the peak inspiratory pressure (PIP) has increased from 20 cm H_2O from 30 cm H_2O. BP 90–95 mmHg systolic, HR 101 bpm, SaO_2 89%. An ABG, and a complete blood count with platelets and coagulation panel were sent to the lab, with results currently pending.

- What is your differential diagnosis? How would you manage this situation?
- Discuss neuroprotection strategies based on brain trauma foundation (BTF) guidelines.

The patient is stabilized with your intervention and ventilation normalized. SaO_2 is 97%. What is your emergence plan? Would you extubate this patient?

ABG shows PaO_2 98 mmHg on FiO_2 0.5 and serum sodium 128 mEq/L. Hb 10.5 g/dL and coagulation labs still pending.

What are the causes of hyponatremia in the setting of head injury? Would you treat this?

After discussion with the surgical team it was decided to awaken the patient to do a neuro exam and if he remains stable to extubate. Patient was very slow to awake, purposeful with his (L) side, but not the right side. It was decided to leave the patient intubated and transport to the neuro-ICU.

- Would you sedate the patient for transport? Why or why not?
- What are the postoperative concerns for this patient? What neuromonitors would you consider in the postoperative period? Is seizure prophylaxis indicated in the postoperative period?

Discussion: This 18-year-old patient was involved in a MVC with history of brief LOC followed by worsening confusion and agitation in the ED. He has sustained injury to the left side of his head and chest and complains of tenderness in those areas. He becomes increasingly somnolent and unable to lie still for an emergent head CT. His vital signs showed hypertension and bradycardia which along with decreasing level of consciousness in this setting would suggest increased ICP as defined by Cushing's reflex. Cushing's reflex is named after Harvey Cushing and is characterized by increasing systolic BP and pulse pressure and bradycardia with respiratory irregularities eventually leading to brain herniation and fatal brain stem compression [1–4].

His neck is in a C-collar as per standard protocol following MVC.

18.1 Preoperative

Question 1:
What other information would you like before you transfer the patient to the CT scanner? How would you sedate this patient for the head CT? Would you intubate this patient? Discuss the

various options for sedation and intubation in a head injured patient.

Answer:
It would be ideal to obtain the usual preanesthetic information such as allergies, PMH, laboratory values, and the presence of other associated injuries before any anesthesia is administered. A rapid neurological assessment should be performed and the severity of traumatic brain injury (TBI) should be recorded using GCS. However, any delay in obtaining the CT scan should be avoided in a patient who is displaying signs of intracranial hypertension. Also, in a patient who was involved in a MVC, it would be prudent to assume that the C-spine is injured and should be immobilized. A quick airway exam should be done to prepare for appropriate airway management.

The goals of management for a patient with acute intracranial hypertension are:

1. Minimize further rise in ICP and prevent further brain injury and risk of brain herniation.
2. Facilitate early diagnosis and intervention as indicated.
3. Maintain adequate Cerebral Perfusion Pressure (CPP) defined as MAP − ICP.
4. Prevent secondary injuries resulting from hypotension, hypoxemia, hypercarbia or hypocarbia, hypo- or hyperglycemia, and hyperthermia.
5. Secure the airway while minimizing C-spine movement and establish ventilation and provide adequate amnesia and analgesia.

Secondary injuries resulting from hypotension, hypoxemia, hypercarbia or hypocarbia, hypo- or hyperglycemia, and intracranial hypertension can worsen outcome following TBI [5]. So, in this patient who is combative and somnolent it would be advisable to secure the airway with an endotracheal tube (ETT) to improve both oxygenation and ventilation and decrease the risk of pulmonary aspiration.

Induction and Intubation: Laryngoscopy and intubation can increase ICP acutely and should be avoided. The patient should be adequately anesthetized before laryngoscopy is attempted. Since this patient with acute traumatic injury is considered to have full stomach, rapid sequence induction (RSI) and intubation are recommended. There is no ideal induction agent. Propofol can cause hypotension, but addition of phenylephrine 50–100 μg with the propofol can help prevent or decrease the severity of hypotension. Etomidate [6]and ketamine are other options. The use of ketamine was contraindicated in the neurosurgical patients until recently due to its potential to increase ICP. But more recent studies have shown that ketamine has neuroprotective effects [7] even in stroke, neurotrauma, and subarachnoid hemorrhage. Ketamine could be used in a select group of patients, e.g., in the presence of hypotension. RSI can be achieved with an induction agent of choice, a neuromuscular blocking agent (NMBA) and narcotic such as fentanyl 1–2 μg/kg and lidocaine 1–1.5 mg/kg. The addition of narcotics such as fentanyl and lidocaine would help blunt the sympathetic response to laryngoscopy and intubation [8, 9].

The use of succinylcholine to facilitate intubation in the setting of intracranial hypertension is much debated because of its potential to increase ICP related to muscle fasciculations. However, studies have shown that the impact of succinylcholine-induced rise in ICP is minimal [10–12]. Additionally, the minimal increase in ICP from succinylcholine can be attenuated by pretreating with defasciculating doses of a non-depolarizing NMBA [13]. As such, vecuronium, rocuronium, or cisatracurium (0.3 mg, 2 mg, 1.5 mg IV, respectively) is commonly used although the evidence is poor to show that it impacts outcome in patients with head injury [14]. In an emergent situation when time is of the essence to secure an airway, succinylcholine can be used unless it is contraindicated for other reasons. Delay in intubation and oxygenation and ventilation carries greater risk in the setting of increased ICP than the potential for a succinylcholine-induced rise in ICP. If succinylcholine cannot be used, RSI can achieved with rocuronium 1.2 mg/kg.

Airway Management in the ED can be challenging in a multitrauma patient. In a patient in whom the neck is not cleared, it is best to assume there is a potential for C-spine injury and all pre-

cautions should be taken to minimize C-spine movement. It is imperative that experienced personnel familiar with airway management as well as advanced airway equipment are available. The commonly employed methods for endotracheal intubation include direct laryngoscopy or video laryngoscopy with manual in line stabilization (MILS). MILS has shown to decrease glottic visualization and prolongs time to intubation and increases the rate of failed intubation [15]. The application of cricoid pressure or gum elastic bougie can improve glottic view and facilitate intubation [16], but cricoid pressure should be used with caution if unstable C-spine fracture is suspected. Fiberoptic or flexible scope intubation may be indicated if extreme difficulty with airway is suspected. But there is no evidence to show that any one approach improves outcome. The recommendation is that the anesthesia provider should use the equipment that they are most familiar with to secure the airway rapidly to avoid hypoxia and hypercarbia. It is common practice to remove the front of the C-collar while maintaining the neck in a neutral position with MILS to facilitate intubation if difficulty with intubation is encountered.

Once the patient's airway is secured and ventilation and hemodynamic stability is established, patient can be sedated with propofol infusion for the CT scan.

The CT scan revealed a large EDH with midline shift, and a decision for operative intervention for evacuation was made.

Question 2:
What are the common causes of EDH? How do they usually present? How is the decision for operative intervention made? What are your concerns during transport to the OR? How would you monitor the patient?

Answer:
An EDH occurs in 2% of all head injuries and up to 10–15% of all fatal head injuries [17]. The most common causes of EDH are motor vehicle accidents, falls, or assaults. The incidence is higher among males, adolescents, and young adults. The mean age of a patient with EDH is 20–30 [17] years and it is less common in adults over 50–60 years. Most EDHs result from arterial bleeding resulting from injury to the middle meningeal artery. About 10% of EDHs are due to venous bleeding following the laceration of a dural venous sinus. In adults, up to 75% of EDHs occur in the temporal region. However, in children, they occur with similar frequency in the temporal, occipital, frontal, and posterior fossa regions. Often EDH present with a history of brief LOC followed by a lucid interval.

EDH with GCS < 9 is a surgical emergency and should be evacuated as soon as possible. The decision to operate is based on the size of the EDH and GCS score and symptoms. Any EDH > 30 cm^3 should be evacuated irrespective of patient's GCS. If the EDH is <30cm^3 with less than 5 mm midline shift and GCS > 8 and no focal deficit, it can be managed nonoperatively, but with close neurological monitoring and serial CT scans [17].

Based on the CT imaging and symptomatology, a decision has been made to do operative intervention. Craniotomy and evacuation of the hematoma are the standards of surgical treatment of symptomatic EDH. The major concerns during emergent transport to the OR are to maintain hemodynamic stability by avoiding hypertension or hypotension and avoiding any triggers that would increase ICP such as coughing and straining on the ETT and agitation. Patient's vital signs and oxygenation and ventilation should be closely monitored, and he should be adequately sedated. The usual monitoring during such a case would include EKG, noninvasive BP (NIBP), and Spo_2. The patient should be ventilated via ETT to prevent hypercarbia or hypoxia.

18.2 Intraoperative

Question 3:
Would you lower his BP (190/70 mmHg) before surgery starts? Is an arterial line indicated for this case? Would you delay starting the case to place an a-line? What is the BP goal?

Answer:
The patient is hypertensive and bradycardic (HR 59) which are signs of intracranial hypertension in the presence of EDH. The elevation in BP is a compensatory mechanism to maintain CPP. A

reduction in MAP can exacerbate cerebral ischemia. Cerebral autoregulation is impaired following TBI [18, 19] and a sudden rise in BP can lead to hemorrhage, edema, and further elevation of ICP. On the other hand, hypotension can worsen outcome in the presence of intracranial hypertension. The BTF guidelines recommend SBP > 110 mmHg or above for patients in the 15–49 years age group [20].

The minimum CPP required for survival and improved outcomes is unclear, but the recommendation of the BTF guidelines is between 60 and 70 mmHg [20]. In the presence of severe intracranial hypertension, higher MAP must be maintained to maintain CPP. Therefore, lowering of SBP must be done with extreme caution during anesthesia. But other measures to lower ICP such as elevation of the head of the bed to 30°, hyperventilation for a limited period, and osmotic diuretics such as mannitol can all be used. The choice of anesthetic agents will be discussed in the following section.

Monitors: Standard ASA monitors and arterial line for close monitoring of BP are recommended. ABG monitoring would allow assessment of arterial PaO_2 and $PaCO_2$. But undue delay in placing the arterial line and holding up surgery must be avoided. The evacuation of EDH must be completed as quickly as possible to improve outcome. An arterial line can be placed simultaneously as the surgical team prepares the head for incision. A central venous line (CVL) is usually not needed provided large bore peripheral IV access can be obtained. In patients with other associated injuries and significant blood loss and acute hypovolemia, a CVL may be indicated for resuscitation and administration of vasopressors such as norepinephrine and for hypertonic saline (HS) administration. A CVL can also help with postoperative management, but that can be done after evacuation of hematoma in the OR if deemed necessary.

Question 4:
What is the mechanism of action of mannitol and what other options are available to decrease ICP?

Answer:
Mannitol produces osmotic diuresis by increasing the osmotic pressure of glomerular filtrate, which inhibits tubular reabsorption of water and electrolytes and increases urinary output. Mannitol expands plasma volume and decreases blood viscosity and increases cerebral blood flow (CBF). It also decreases ICP by causing vasoconstriction [21, 22]. The standard dose of mannitol for effective control of ICP is 0.25–1 g/kg bodyweight. The BTF guidelines recommend restricting mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurologic deterioration [20].

Furosemide inhibits production of cerebrospinal fluid (CSF) and can potentiate the effects of mannitol and cause more sustained decrease in ICP. But the diuresis and volume depletion caused by these diuretics can cause hypotension which should be prevented.

HS which comes in 3%, 7.5%, and 23.4% concentration is an alternative to mannitol when mannitol is contraindicated, or maximum allowable dosage has been used. Three percent HS is the most commonly used concentration and usually given as an infusion titrated to serum sodium of 145–155 mEq/L. HS has a lower risk of rebound intracranial hypertension and renal failure. Studies have shown that 7.5% HS is very effective in improving CPP and reducing ICP when other measures have failed [23, 24]. HS should be used with caution and patients should be monitored for adverse effects such as hypernatremia and central pontine myelinolysis, seizures, congestive heart failure, and coagulopathy. HS is usually administered via a CVL because of the risk of thrombophlebitis and extravasation injury. However, in an emergency it can be administered through a large bore PIV.

Other options available to decrease ICP are CSF drainage via ventriculostomy, decompressive craniectomy, and barbiturate-induced burst suppression.

Ventriculostomy via external ventricular drain (EVD) is a very effective way to control ICP in patients with head injury. However, when the brain edema is severe leading to ventricular collapse the utility of EVD becomes limited.

Maintenance of Anesthesia

Question 5:
How would you maintain anesthesia? Is TIVA (total intravenous anesthesia) indicated?

Does TIVA offer any advantage over inhalational anesthesia?

Answer:
Anesthesia can be maintained with inhalational anesthetic agents with a combination of low dose propofol with narcotics or TIVA. The choice of anesthetic agents depends on the condition of the patient. The effects of anesthetic agents on CBF, $CMRO_2$, ICP, and cerebral vascular resistance vary. TIVA vs. inhalational anesthesia has been much debated and there is no clear evidence to support the use of one technique over the other. Chui et al. [25] have published a review and meta-analysis comparing the effects of propofol and volatile agents during elective craniotomy. They concluded that the brain relaxation score was similar in both groups, but mean ICP values were lower and CPP values were higher in the propofol maintained group. All inhalational agents cause dose-dependent cerebral vasodilation. They reduce CMR and can blunt cerebral autoregulation by uncoupling CBF and metabolism [26, 27]. The increase in CBF produced by volatile agents can be decreased by hyperventilation, but it is important to avoid hyperventilation below PCO_2 < 30 mmHg except as a temporizing measure in brain herniation. The standard combination of drugs used for maintenance of anesthesia are fentanyl 1–2 μg/kg boluses, or remifentanil 0.05–0.2 μg/kg/min with isoflurane or sevoflurane <1 MAC end tidal concentration or propofol 50–150 μg/kg/min. High dose propofol can cause hypotension and can worsen outcome [20].

Question 6:
Brain herniation into the surgical field—What other options are available to decrease brain edema and provide brain relaxation?

Answer:
This has been discussed above—elevation of the head of the bed, osmotic diuresis, CSF drainage, hyperventilation, etc.

Associated Injury/Complication: Hypoxia, Increased PIP, Hypotension

Question 7:
What is your differential diagnosis (D/D)? How would you manage this situation?

Answer:
In a patient with history of MVA, the D/D would include but is not limited to: pneumothorax, hemothorax, pulmonary embolus, occlusion of the ETT with blood or mucus, mainstem bronchus intubation, anaphylaxis to drugs or blood products, cardiac events such as MI, pulmonary edema or cardiac tamponade.

This patient had sustained injury to his head and his left chest with rib fractures. The triad of symptoms of hypotension, increased PIP, and hypoxia would place pneumothorax or hemothorax high on the list of differential diagnosis. A chest X-ray that was done in the ER reported a (L) apical pneumothorax. Increased intrathoracic pressure would decrease venous return from the brain and worsen ICP. Increased ICP along with hypotension and hypoxia in TBI would worsen outcome and should be treated immediately. Administer 100% oxygen, treat hypotension with vasopressors. Once other causes are ruled out and pneumothorax is confirmed, if conservative measures do not temporize the situation, a chest tube should be placed, and air evacuated. ABG and CBC, BMP and coagulation panels should be checked to rule out bleeding from other injuries.

Question 8:
Discuss neuroprotection strategies for TBI based on the BTF guidelines during the perioperative period.

Answer:
Much of the neuroprotection strategies have been discussed already. The primary goal during the perioperative period in a patient with TBI is to prevent secondary brain injury resulting from hypotension, hypertension, increased ICP, hypoxemia, hypo/hypercarbia, hypo/hyperglycemia, and fever.

The complete guidelines can be found at:
https://braintrauma.org/guidelines/guidelines-for-the-management-of-severe-tbi-4th-ed

A few of the topics that have not been discussed already will be briefly discussed here.

ICP Thresholds: ICP >22 mmHg should be treated as levels above this are associated with increased mortality.

The DECRA (Decompressive Craniectomy in diffuse TBI) trial [28] compared those who underwent craniectomy to the standard nonsurgical treatment group. Although the patients in the craniectomy group had less time in ICPs above treatment thresholds, they had worse outcome as measured by the extended Glasgow Outcome Scale and was at greater risk of an unfavorable outcome.

The RESCUE-ICP trial [29] included patients with TBI with refractory elevated ICP who underwent craniotomy vs. standard therapy, which showed lower mortality, higher rates of vegetative states, and lower severe disability. The rates of moderate disability and good recovery were similar in the two groups.

So, the decision for surgical intervention should be based on ICP values, serial neurologic exams, and CT scans.

Glycemic Control: Perioperative hypo/hyperglycemia can worsen neuronal injury. Hyperglycemia is common after TBI and has been shown to worsen outcome [30]. However, intensive insulin therapy has shown no benefits, but rather only increased risk of hypoglycemia [31, 32]. So, blood glucose (BG) should be monitored frequently and treated if warranted. Many practices would treat BG >160 g/dL.

Ventilation and Oxygenation: Prolonged hyperventilation with $PaCO_2$ of <25 mmHg is not recommended. Hyperventilation is recommended only as a temporizing measure to decrease ICP [33]. Studies have shown deleterious effects and brain ischemia with $PaCO_2$ at 25–30 mmHg [34].

Intraoperatively, unless absolutely indicated due to brain edema and risk of herniation, we maintain $PaCO_2$ in the 35 mmHg range. Hypercarbia increases CBF and can lead to edema which should be avoided.

Oxygenation: PaO_2 should be maintained >60 mmHg [35].

Temperature Management: Normothermia is the goal during the intraoperative period. Therapeutic hypothermia has not shown benefit and is not recommended. Induced hypothermia has not shown benefit in improving long-term outcomes [35].

Fever can worsen outcome [36] and should be aggressively treated with antipyretic medications or surface cooling devices.

Steroids: There is Level I evidence to show that the use of methylprednisolone was associated with increased mortality and the use of steroids is not recommended [20].

Barbiturates: High dose barbiturate therapy is recommended to control elevated ICP refractory to standard medical and surgical treatment. But high dose barbiturates can cause hypotension which is detrimental in the TBI patients. Hemodynamic stability must be established before this therapy is instituted. Propofol for burst suppression has shown benefits anecdotally, but lacks robust evidence.

Hyponatremia in TBI: Serum sodium 128 mEq/L. What are the causes of hyponatremia in the setting of head injury? Would you treat this?

Hyponatremia is defined as serum sodium <135 mEq/L. It is the most common electrolyte abnormality following TBI [37] and a predictor of poor neurologic outcome. The common causes of hyponatremia in the setting of TBI are cerebral salt-wasting syndrome (CSWS), syndrome of inappropriate ADH secretion (SIADH), hypopituitarism, and inadequate salt consumption [37].

The exact incidence, pathophysiology, and clinical differentiation between CSW and SIADH remain unclear [38]. In the acute intraoperative setting, mannitol-induced hypervolemia that occurs due to fluid shift from the intracellular space to the intravascular space which can cause dilutional hyponatremia is the most likely the cause. But impaired hypothalamic-pituitary adrenal axis in

TBI is also common. This should be monitored closely and if the hyponatremia does not improve, serum osmolality and urinary specific gravity and urinary sodium should be checked and treated if necessary. Treatment would include HS, fludrocortisone, or DDAVP.

18.3 Postoperative

Emergence and ICU Transport: The patient was very slow to awake, purposeful with his left side, but not the right side. It was decided to leave the patient intubated and to transport to the neuro-ICU.

- Would you sedate the patient for transport? Why or why not?
- What are the postoperative concerns for this patient? Is seizure prophylaxis indicated in the postoperative period?

Since the patient had significant brain edema and intracranial hypertension, it would be better to sedate the patient during transport to prevent any agitation and coughing on the ETT.

He also had hemodynamic instability resulting from a pneumothorax and has a chest tube in place. Transport to ICU is not in a very controlled environment and untoward events can happen during this time. So, our practice is to sedate the patient during transport while monitoring vital signs. As mentioned earlier, hypotension and hypoxemia should be avoided.

Following TBI, release of local mediators of inflammation (excitotoxins), alteration of CBF, and impairment of autoregulation occur. The resulting inflammation and excitotoxicity cause edema and further rise in ICP and decrease in cerebral perfusion. The reparative mechanisms of the injured brain can take time and during this period patient should be closely monitored. During this time, brain tissue oxygenation ($PbtO_2$) and ICP monitors can help with management.

Seizure prophylaxis is recommended [35] to decrease the incidence of early (within 7 days) posttraumatic seizures, but not for preventing late seizures. Phenytoin/fosphenytoin is the drug recommended and there is not enough evidence to recommend levetiracetam although many institutions use it routinely.

To summarize, TBI is a major cause of death and disability across the world. The medical community cannot limit the extent of the primary injury. But we play a major role in preventing secondary injuries to improve outcomes. The BTF guidelines are helpful in guiding the treatment although evidence-based guidelines are still lacking on certain topics.

Multiple Choice Questions

1. All of the following are true of EDH except:
   (a) EDH is present in 1–4% cases of TBI.
   (b) Skull fracture is present in 75–95% of EDH.
   (c) Highest incidence of EDH is in adolescents and young adults.
   (d) EDH in adults is most commonly due to venous injury.

   Answer: d

   EDH is most commonly due to arterial injury. The major cause of arterial bleed is trauma to the skull base associated with tearing of the middle meningeal artery.
2. The factors that have been associated with poor outcome following EDH are:
   (a) Older age.
   (b) Low GCS score on admission.
   (c) Presence of pupillary abnormalities.
   (d) All of the above.
   (e) None of the above.

   Answer: d

   All of the answers are true.
3. EDH is a neurologic emergency. The following are the indications for surgical evacuation except:
   (a) EDH volume < 30 cm^3 and less than 5 mm midline shift.
   (b) EDH with GCS < 9.
   (c) Patients who are comatose on admission and have early signs of brain herniation.
   (d) Acute EDH with a hematoma volume > 30 cm^3 regardless of the GCS score.

   Answer: d

EDH volume < 30 cm3 and less than 5 mm midline shift can be managed conservatively with close observation with frequent neurologic exams.

4. The following statements regarding monitoring in TBI based on the BTF guidelines are true except:
   (a) ICP should be monitored in all salvageable patients with severe TBI (GCS 3–8) with an abnormal CT scan.
   (b) ICP monitoring is indicated for patients with TBI with a normal CT scan if 2 or more of the following features are noted on at admission: Age > 40 years, SBP <90 mmHg or motor posturing.
   (c) ICP monitor can be used as the sole monitor for making management decisions.
   (d) Avoid aggressive attempts to maintain CPP > 70 mmHg with fluids and pressors because of the risk of respiratory failure.

   Answer: c

   ICP monitor can be used as the sole monitor for making management decisions is incorrect. ICP monitoring by itself is insufficient to make sound clinical decisions as the cascade of pathophysiology following TBI is very complex. A combination of ICP values and clinical and brain CT findings must be used to manage patients with TBI.

References

1. Menon DK, Schwab K, Wright DW, Maas AI, Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health. Position statement: definition of traumatic brain injury. Arch Phys Med Rehabil. 2010;91(11):1637–40.
2. Centers for Disease Control and Prevention, N. C. f. I. P. a. C., Division of Unintentional Injury Prevention Rates of TBI-related Emergency Department Visits, Hospitalizations, and Deaths—United States, 2001–2010. https://www.cdc.gov/traumaticbraininjury/data/rates.html.
3. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2(7872):81–4.
4. Fodstad H, Kelly PJ, Buchfelder M. History of the Cushing reflex. Neurosurgery. 2006;59(5):1132–7. discussion 1137
5. Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM, Jane JA, Marmarou A, Foulkes MA. The role of secondary brain injury in determining outcome from severe head injury. J Trauma. 1993;34(2):216–22.
6. Benson M, Junger A, Fuchs C, Quinzio L, Bottger S, Hempelmann G. Use of an anesthesia information management system (AIMS) to evaluate the physiologic effects of hypnotic agents used to induce anesthesia. J Clin Monit Comput. 2000;16(3):183–90.
7. Bell JD. In vogue: ketamine for neuroprotection in acute neurologic injury. Anesth Analg. 2017;124(4):1237–43.
8. Thippeswamy RR, Shetty SR. Intravenous low dose fentanyl versus lignocaine in attenuating the hemodynamic responses during endotracheal intubation: a randomized double-blind study. Anesth Essays Res. 2018;12(4):778–85.
9. Kumar A, Seth A, Prakash S, Deganwa M, Gogia AR. Attenuation of the hemodynamic response to laryngoscopy and tracheal intubation with fentanyl, lignocaine nebulization, and a combination of both: a randomized controlled trial. Anesth Essays Res. 2016;10(3):661–6.
10. Kramer N, Lebowitz D, Walsh M, Ganti L. Rapid sequence intubation in traumatic brain-injured adults. Cureus. 2018;10(4):e2530.
11. Kovarik WD, Mayberg TS, Lam AM, Mathisen TL, Winn HR. Succinylcholine does not change intracranial pressure, cerebral blood flow velocity, or the electroencephalogram in patients with neurologic injury. Anesth Analg. 1994;78(3):469–73.
12. Brown MM, Parr MJ, Manara AR. The effect of suxamethonium on intracranial pressure and cerebral perfusion pressure in patients with severe head injuries following blunt trauma. Eur J Anaesthesiol. 1996;13(5):474–7.
13. Stirt JA, Grosslight KR, Bedford RF, Vollmer D. "Defasciculation" with metocurine prevents succinylcholine-induced increases in intracranial pressure. Anesthesiology. 1987;67(1):50–3.
14. Clancy M, Halford S, Walls R, Murphy M. In patients with head injuries who undergo rapid sequence intubation using succinylcholine, does pretreatment with a competitive neuromuscular blocking agent improve outcome? A literature review. Emerg Med J. 2001;18(5):373–5.
15. Thiboutot F, Nicole PC, Trepanier CA, Turgeon AF, Lessard MR. Effect of manual in-line stabilization of the cervical spine in adults on the rate of difficult orotracheal intubation by direct laryngoscopy: a randomized controlled trial. Can J Anaesth. 2009;56(6):412–8.
16. Nolan JP, Wilson ME. Orotracheal intubation in patients with potential cervical spine injuries. An indication for the gum elastic bougie. Anaesthesia. 1993;48(7):630–3.
17. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, Servadei F, Walters BC, Wilberger JE, Surgical Management of Traumatic Brain Injury

Author Group. Surgical management of acute epidural hematomas. Neurosurgery. 2006;58(3 Suppl):S7–15; discussion Si-iv.
18. Hlatky R, Furuya Y, Valadka AB, Gonzalez J, Chacko A, Mizutani Y, Contant CF, Robertson CS. Dynamic autoregulatory response after severe head injury. J Neurosurg. 2002;97(5):1054–61.
19. Junger EC, Newell DW, Grant GA, Avellino AM, Ghatan S, Douville CM, Lam AM, Aaslid R, Winn HR. Cerebral autoregulation following minor head injury. J Neurosurg. 1997;86(3):425–32.
20. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GWJ, Bell MJ, Bratton SL, Chesnut R, Harris OA, Kissoon N, Rubiano AM, Shutter L, Tasker RC, Vavilala MS, Wilberger J, Wright DW, Ghajar J. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017;80(1):6–15.
21. Muizelaar JP, Wei EP, Kontos HA, Becker DP. Mannitol causes compensatory cerebral vasoconstriction and vasodilation in response to blood viscosity changes. J Neurosurg. 1983;59(5):822–8.
22. Mendelow AD, Teasdale GM, Russell T, Flood J, Patterson J, Murray GD. Effect of mannitol on cerebral blood flow and cerebral perfusion pressure in human head injury. J Neurosurg. 1985;63(1):43–8.
23. Hartl R, Medary MB, Ruge M, Arfors KE, Ghahremani F, Ghajar J. Hypertonic/hyperoncotic saline attenuates microcirculatory disturbances after traumatic brain injury. J Trauma. 1997;42(5 Suppl):S41–7.
24. Horn P, Munch E, Vajkoczy P, Herrmann P, Quintel M, Schilling L, Schmiedek P, Schurer L. Hypertonic saline solution for control of elevated intracranial pressure in patients with exhausted response to mannitol and barbiturates. Neurol Res. 1999;21(8):758–64.
25. Chui J, Mariappan R, Mehta J, Manninen P, Venkatraghavan L. Comparison of propofol and volatile agents for maintenance of anesthesia during elective craniotomy procedures: systematic review and meta-analysis. Can J Anaesth. 2014;61(4):347–56.
26. Lutz LJ, Milde JH, Milde LN. The cerebral functional, metabolic, and hemodynamic effects of desflurane in dogs. Anesthesiology. 1990;73(1):125–31.
27. Todd MM, Drummond JC. A comparison of the cerebrovascular and metabolic effects of halothane and isoflurane in the cat. Anesthesiology. 1984;60(4):276–82.
28. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, Kossmann T, Ponsford J, Seppelt I, Reilly P, Wolfe R. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med. 2011;364(16):1493–502.
29. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J, Anderson I, Bulters DO, Belli A, Eynon CA, Wadley J, Mendelow AD, Mitchell PM, Wilson MH, Critchley G, Sahuquillo J, Unterberg A, Servadei F, Teasdale GM, Pickard JD, Menon DK, Murray GD, Kirkpatrick PJ. Trial of decompressive craniectomy for traumatic intracranial hypertension. N Engl J Med. 2016;375(12):1119–30.
30. Jeremitsky E, Omert LA, Dunham CM, Wilberger J, Rodriguez A. The impact of hyperglycemia on patients with severe brain injury. J Trauma. 2005;58(1):47–50.
31. Finfer S, Chittock DR, Su SY, Blair D, Foster D, Dhingra V, Bellomo R, Cook D, Dodek P, Henderson WR, Hebert PC, Heritier S, Heyland DK, McArthur C, McDonald E, Mitchell I, Myburgh JA, Norton R, Potter J, Robinson BG, Ronco JJ. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283–97.
32. Bilotta F, Caramia R, Cernak I, Paoloni FP, Doronzio A, Cuzzone V, Santoro A, Rosa G. Intensive insulin therapy after severe traumatic brain injury: a randomized clinical trial. Neurocrit Care. 2008;9(2):159–66.
33. https://braintrauma.org/guidelines/guidelines-for-the-management-of-severe-tbi-4th-ed#/:guideline/5-ventilation-therapies.
34. Coles JP, Fryer TD, Coleman MR, Smielewski P, Gupta AK, Minhas PS, Aigbirhio F, Chatfield DA, Williams GB, Boniface S, Carpenter TA, Clark JC, Pickard JD, Menon DK. Hyperventilation following head injury: effect on ischemic burden and cerebral oxidative metabolism. Crit Care Med. 2007;35(2):568–78.
35. https://braintrauma.org/guidelines/guidelines-for-the-management-of-severe-tbi-4th-ed.
36. Madden LK, DeVon HA. A systematic review of the effects of body temperature on outcome after adult traumatic brain injury. J Neurosci Nurs. 2015;47(4):190–203.
37. Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342(21):1581–9.
38. Lohani S, Devkota UP. Hyponatremia in patients with traumatic brain injury: etiology, incidence, and severity correlation. World Neurosurg. 2011;76(3–4):355–60.

Suggested Reading

https://braintrauma.org/guidelines/guidelines-for-the-management-of-severe-tbi-4th-ed#/
https://www.uptodate.com/contents/anesthesia-for-patients-with-acute-traumatic-brain-injury?search=anesthesia%20for%20patients%20with%20traumatic%20brain%20injury-%
https://www.uptodate.com/contents/intracranial-epidural-hematoma-in-adults?search=Epidural%20hematoma%20-Brain&source=search_result&selectedTitle=1~150&usage_type
Phan RD, Bendo AA. Perioperative management of adult patients with severe head injury. Cottrell and Patel's neuroanesthesia, 6th ed. Elsevier; 2017. Chapter 19. p. 326–36.

19 Management of Patient with Traumatic Brain Injury: SDH

Dhritiman Chakrabarti and Deepti B. Srinivas

Traumatic brain injury (TBI) is one of the major causes of mortality and long-term morbidity in today's society. The incidence of TBI in India has not been published till date although individual state data is published from time to time [1].

Stem Case Terminology

A 52-year-old man was received in the emergency department (ED) after a road traffic accident involving a two-wheeler collision with a four wheeler. The patient was the motorcycle rider and was not wearing a helmet. The accident had happened 1 h earlier and patient was brought to the ED by an ambulance which was called to the scene by bystanders. The patient was delirious and agitated with face and scalp lacerations. The patient was evaluated in the ED for other injuries and vitals obtained. There was no evidence of limb injuries. Blood pressure was found to be lower than normal (100/60 mmHg) and heart rate was 125/min. Neurological examination revealed a Glasgow coma score (GCS) of 10 (E2, V_3, M5), no apparent motor deficits and pupils 3 mm bilaterally and equally reactive. After examination, an urgent non-enhanced computed tomography (NCCT) scan of the head was acquired, which revealed a large right-sided fronto-temporo-parietal acute subdural haematoma, with mass effect on the ipsilateral lateral ventricle and midline shift of 6 mm. The patient was planned for emergency right decompressive hemicraniectomy. Blood investigations including haemogram and serum biochemistries were obtained. During his stay in the ED, the patient was infused with 0.9% normal saline and supplemental oxygen using facemask was administered. He was kept under constant monitoring of physiological parameters. He was wheeled into the operation theatre within 1 h of arrival to the ED. The anaesthesiologist induced anaesthesia using 250 mg of IV thiopentone, 150 μg IV fentanyl, and 8 mg IV vecuronium, and endotracheal intubation was performed. The anaesthesiologist performed a bilateral scalp block to reduce intraoperative opioid requirements. Anaesthesia was maintained using 0.8 MAC sevoflurane and vasopressor (noradrenaline) was required to maintain systolic blood pressure (SBP) >100 mmHg. Apart from standard monitors, external ventricular drain (EVD) was placed by the surgeon intraoperatively and connected to a pressure transducer for intracranial pressure (ICP) monitoring. The surgeon evacuated the haematoma, performed a lax duroplasty, and bone flap was not replaced. During the surgery, the anaesthesiologist administered 250 mL of 3% hypertonic saline. Blood product replacement was not required. Intraoperative blood glucose levels were found to be 140 and

D. Chakrabarti (✉)
Department of Neuroanesthesiology and Neurocritical Care, NIMHANS, Bangalore, India

D. B. Srinivas
Division of Neuroanaesthesia and Neurocritical Care, Apollo Hospitals, Bangalore, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_19

160 mg/dL at the beginning and end of surgery, respectively. The patient was not extubated after the surgery and was shifted to intensive care unit for further management. Postoperative GCS was recorded to be E2, V_T, M5. The patient was mechanically ventilated for 1 day and reassessed. No sedation was administered during this period apart from IV morphine (6 mg, QID). The patient improved to E3, V_T, M6 after one more day and was weaned off ventilator within 24 h and extubated. There were no other complications and patient was discharged with GCS of 15/15.

Question 1:
What are the pertinent points of history in a suspected case of TBI?

Answer:
There are multiple points in the history of a TBI case which may be important for the clinician in terms of diagnosis, immediate treatment required for resuscitation, definitive treatment for the injury per se, and prognostication. Demographic details (age and sex) are important in relation of epidemiology of the pathology and long-term prognosis. Higher age group is a known risk factor for poorer neurological outcome and higher mortality within surgically treated and conservatively managed subgroups [2, 3]. Elderly age group is also associated with the "talk-and-deteriorate" phenomenon, wherein the patient is apparently clinically normal during early examination and later deteriorates within 6 h. This phenomenon is caused due to the presence of atrophic brain in the elderly which allows for haematoma expansion before leading to any observable signs [4]. Males are more commonly afflicted compared to females although this does not translate to any prognostic or therapeutic importance.

Mode of injury has not been found to be a significant predictor of mortality in cases of SDH or TBI as a whole [5, 6]. Time duration from injury to surgery has been found to be increased in patients with favourable outcomes. Although unintuitive, this can be explained by the fact that preoperative resuscitation and haemodynamic stabilization often lead to delayed surgical intervention and may be a more important contributor to outcomes than surgery itself [7]. Mode of transport to trauma centre also does not contribute to outcomes after head injury [8].

19.1 Preoperative

Question 2:
What are the components of physical examination in a patient of TBI?

Answer:
Physical examination of a patient of suspected TBI reveals the need for various investigative imaging studies, therapeutic interventions, and information related to prognostication. The first concern for any trauma patient is haemodynamic resuscitation and airway management. Recommendations for GCS estimation include conducting neurological examination only after haemodynamic and pulmonary resuscitation [9, 10]. One of the first prospective studies proving and quantifying the link between hypotension (SBP <90 mmHg) and mortality in severe TBI was conducted by Manley et al., wherein one hypotensive episode led to a twofold increase in the chances of death and two episodes led to an eightfold increase [11]. However, they did not find any association between number of episodes of hypoxia and mortality or neurological morbidity. The deleterious effect of hypoxia on neurological outcome has been shown to be present by Chestnut in a retrospective study and by McHugh in their IMPACT study. The combination of hypoxic and hypotensive episodes was associated with poorer outcome than either alone [12, 13].

Taking into view the physiological plausibility of causation, the Brain Trauma Foundation (BTF) suggests aggressive resuscitation and prevention of hypotension, whose thresholds are mapped out in terms of SBP and cerebral perfusion pressure (CPP). The third edition of the guidelines suggested an SBP >90 mmHg (level 2 recommendation) and a CPP of 50–70 mmHg [14, 15]. Latest recommendation states age wise blood pressure thresholds with SBP at ≥100 mmHg for 50–69 years or ≥110 mmHg for patients 15–49 or over 70 years of age [16].

Glasgow coma scale has been the go to scale for assessing overall neurological status of head-injured patients since its inception by Jennett and Teasdale in 1974 [17]. Although the entire 15-point scale has been validated, the motor component of the scale (6 levels) has higher sensitivity for predicting mortality and encapsulates the entire prognostic power of this scale [18]. The GCS is also used for grading the severity of head injury, with the stratification having prognostic significance for mortality. GCS range of 13–15 is termed mild (mortality 0.1%), 9–12 is termed moderate (mortality 10%), and <9 is severe (40%) [19]. Patients with GCS $\leq$ 8 should undergo endotracheal intubation for airway protection.

Pupillary examination provides information about status of transtentorial herniation and should be obtained after the patient has been haemodynamically stabilized. Pupillary asymmetry is defined as >1 mm difference in diameter and "fixed" pupil is defined by <1 mm change in diameter after stimulus of bright light [10].

Examination of cervical spine is an important step which reveals the need for obtaining a lateral cervical spine radiograph to document the presence of any injury. If present, it would necessitate the use of stabilization techniques (hard collar) until definitive treatment. This step is guided by either of two sets of criteria—the Canadian C-spine rule (Fig. 19.1) and the NEXUS criteria

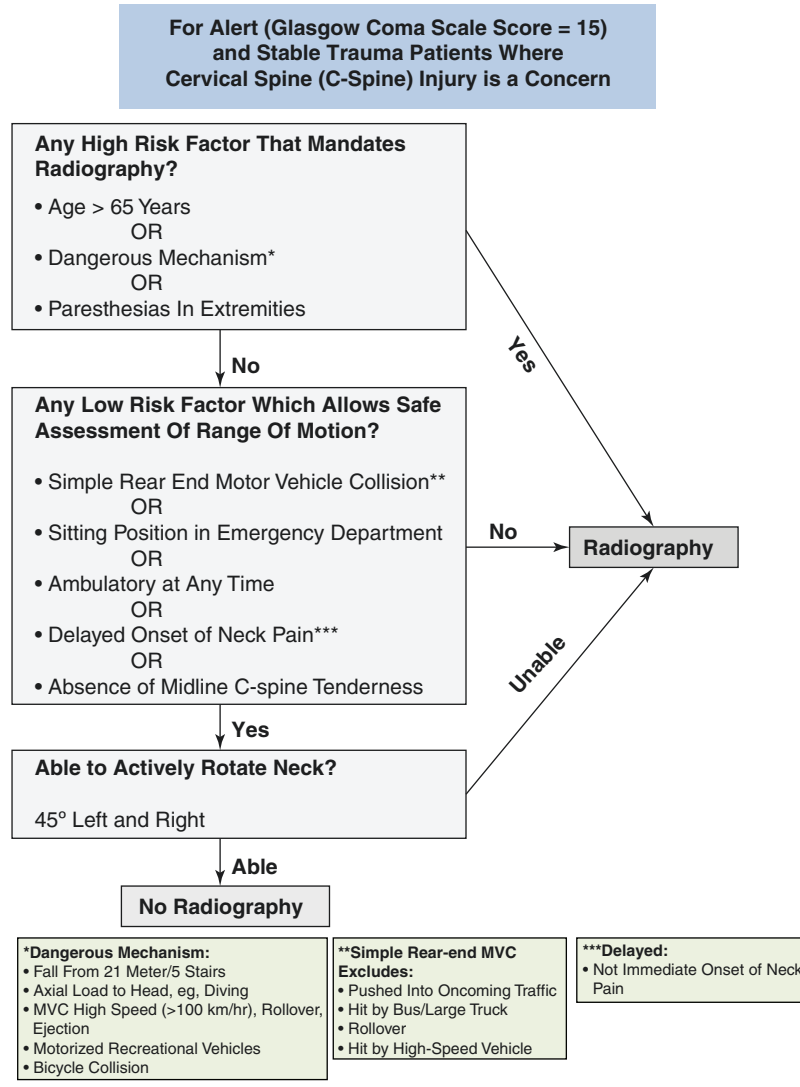


Fig. 19.1 The Canadian C-Spine rule algorithm [21]

[20, 21]. Canadian C-spine rule has been found to be superior to NEXUS criteria [22].

Question 3:
What information can be obtained from an NCCT scan of the brain in a head injury patient?

Answer:
National Institute for Health and Care Excellence (NICE) has provided criteria for obtaining brain CT scan of head-injured patients as part of early management. If the patient has GCS ≤13 at any point, <15 after 2 h of injury, any sign of depressed fracture or skull base fracture, focal neurological deficit or seizure, or more than one episode of vomiting, an NCCT should be obtained [23]. NCCT is the imaging modality of choice for early management due to its ubiquity, low cost, and rapid acquisition times.

A subdural haematoma on an NCCT appears as a hyperdense layer of clotted blood, spread in a concavo-convex fashion over the surface of the brain. It can be readily distinguished from an extradural haematoma (EDH) due to its shape (EDH is lens shaped) and because it is not limited by skull suture lines (EDH stays within suture lines due to attachment of dura). An NCCT also gives information regarding skull fracture, underlying contusions, mass effect of haematoma and ischaemia of surrounding brain structures, volume of the haematoma, state of basal cisterns/transtentorial herniation, and midline shift. The state of basal cisterns, midline shift (MLS), and the presence of subarachnoid haemorrhage in basal cisterns are predictive of outcome [24].

Important notes:
1. **Method of calculating midline shift (MLS)**: MLS should be determined at the level of the foramen of Monro. First a line is drawn across the septum pellucidum from ipsilateral skull to contralateral (*M*). Then, the distance from the bone of the contralateral side to the septum pellucidum is measured (*S*). The MLS is measured by calculating (*M*/2) − *S* [24] (Fig. 19.2).
2. **Determining status of basal cisterns**: Basal cisterns comprise of pockets of cerebrospinal fluid (CSF) surrounding the midbrain. For prognostication purpose using CT scan, they may be viewed as three limbs (one posterior—*C* and two lateral—*A*, *B*) (Fig. 19.3). They are classified as open (all cisterns patent), partially closed (one or two are obliterated) and closed (all cisterns obliterated). The obliteration happens as a consequence of increased ICP which results in squeezing of the CSF out of cranial cavity. Status of cisterns is correlated with outcome [24].
3. **Calculation of volume of SDH**: This may be accomplished automatically using volumetric

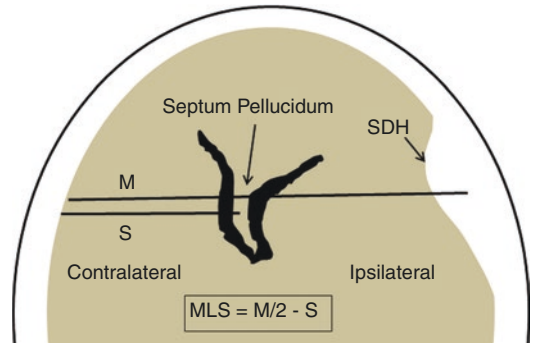


Fig. 19.2 Representative diagram showing calculation of midline shift (MLS)

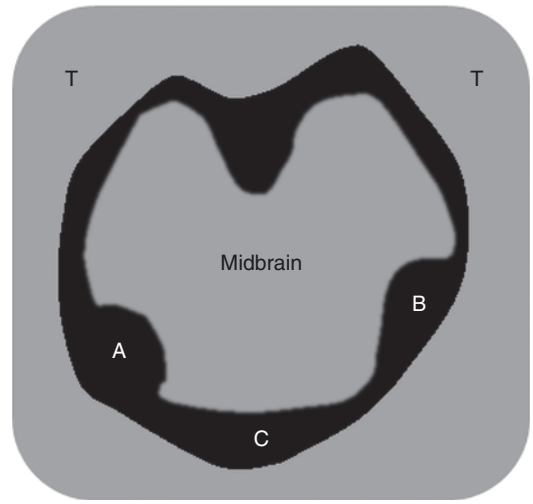


Fig. 19.3 Representative diagram showing basal cisterns around the midbrain. *T*—temporal lobe, *A*, *B*, *C*—cisterns

measurement in the imaging software, or manually using the ellipsoid method. The ellipsoid method entails measurement of three representative diameters of the SDH (*A*, *B,* and *C*) along the Cartesian coordinates and applying them to the formula—**Volume = 4/3π(*A*/2)(*B*/2)(*C*/2).**

First, find the CT scan slice with the largest area of the SDH (Slice L). "*A*" represents the largest diameter of the SDH on this slice. "*B*" is the diameter of the SDH 90° to "*A*". The trauma CT scan usually has 10 mm spacing between slices. For "*C*", count the number of slices which have the SDH in them. If the volume of SDH is >75% relative to slice *L*, count it as 1. If volume of SDH is 25–75% of slice *L*, count it as 0.5. If <25%, do not count the slice. Add up the slice counts to get "*C*".

The same method can be applied to EDH volume measurements also, where volume is more relevant.

For SDH, thickness >10 mm on any slice or MLS >5 mm determines the need for surgical evacuation regardless of the patient's GCS [24].

Question 4:
What are options of surgical treatment of SDH?

Answer:
Before discussing treatment options, we discuss the pathophysiology of SDH and its correlation with prognosis and treatment strategies. SDH is caused when the primary traumatic impact on the skull causes rupture of bridging veins between the dura and the capillaries on the surface of brain parenchyma. Other sources of bleeding in SDH are due to damage to cortical vessels and bleeding from the underlying parenchyma.

However, unlike an isolated EDH, the morbidity of SDH is not only due to its volume but also a mass effect on the brain parenchyma. Often SDH is only the epiphenomenon, with the prognosis being dictated by other factors such as coexisting parenchymal haematomas and diffuse oedema [4]. SDH is sometimes associated with transmission of the impact force across the brain, such that the brain experiences a shearing force. Usually, this shearing force is perpendicular to the axis of the brainstem, which along with white matter tracts act as an anchor for the grey matter. This shearing force has the potential to cause disruption of grey-white matter junctions, which leads to micro-haemorrhages at these interfaces and portends a poor outcome. This sort of brain injury is known as diffuse axonal injury and may occur as an accompaniment to SDH with poor GCS [25, 26].

Coup and contrecoup lesions: SDH present at the site of trauma is known as a "coup" lesion, while a lesion on the opposite site of impact is known as "contrecoup" injury. The presence of an isolated contrecoup injury or both coup and contrecoup injuries portend a poorer outcome in terms of mortality and neurological morbidity. This may be due to the underlying pathophysiology. Contrecoup injury is caused by continuance of the primary shockwave of the trauma across the brain parenchyma, leading to more damage across the parenchyma and at the contralateral surface [27].

Indications for surgery: Treatment options of acute SDH are either surgical or non-surgical. Surgical treatment of SDH is recommended when [24]:

1. CT scan imaging shows maximum thickness of SDH >10 mm on any slice or MLS >5 mm, irrespective of patient's neurological status.
2. If patient has GCS <9 and CT criteria are not met but:
   (a) Deterioration of GCS between times of injury to hospital admission by >2 points.
   (b) Pupils asymmetric or fixed and dilated.
   (c) ICP >20 mmHg.

Timing of surgery: The BTF surgical guidelines suggest that surgery should be conducted as soon as possible [24]. However, most studies have failed to show a correlation between time duration between injury and surgery, and outcome. As noted above, this may be due to better resuscitation in cases operated late, or it may be due to an inherent bias of poorer grade patients being operated earlier than better grade patients [4].

Surgical procedure: Type of surgical procedure had not been rigorously studied till recently. The BTF guidelines suggest that the procedure should include craniotomy with or without bone flap removal and lax duroplasty [24]. Decompressive craniectomy versus medical management has been studied in the context of severe head injury in two recent trials. The DECRA trial randomized diffuse injury patients to undergo either bifrontal decompressive craniectomy or standard care and found greater risk of unfavourable outcome in craniectomy group with an odds ratio of 2.21 (95% CL 1.14–4.26) [28]. This study has been heavily criticized for its restricted patient population (diffuse injury), choice of poorly effective craniectomy technique, and larger number of poorer grade patients (bilaterally non-reactive pupils) in the craniectomy group [29]. The second trial (RESCUEicp) addressed many of these limitations with the inclusion of a broad group of TBI patients with refractory elevated ICP (>25 mmHg) and subjecting them to either unilateral hemicraniectomy/bifrontal craniectomy, or medical management for ICP control. The surgical group had lower incidence of mortality but higher incidence of vegetative states and neurological morbidity [30].

Overall, the choice of surgery depends on hospital policy, surgeon's expertise, radiological and clinical findings, availability of operation theatre, and degree of intraoperative brain swelling [4].

Rationale behind surgical treatment: Any therapy for acute SDH follows an ICP reduction policy. High ICP has potential of causing transtentorial herniation and also cerebral ischaemia. Thus, ICP measurement has a crucial role in planning treatment. The third edition of BTF guidelines had given succinct instructions regarding when to place an EVD for ICP measurement. They recommended ICP monitoring for any salvageable patient of severe TBI with abnormal CT scan findings. If CT scan was normal, monitoring was recommended in patients with age >40 years, unilateral or bilateral motor posturing, or SBP <90 mmHg [31]. The current edition of guidelines dilutes it down to a general recommendation favouring the use of ICP monitoring for mortality reduction and revised the threshold of ICP for treatment to >22 mmHg [16].

Question 5:
What are the concerns during haemodynamic management in a patient of SDH?

Answer:
The medical management of any TBI patient may be viewed as an ongoing campaign to limit the impact of any secondary injuries to the brain. The campaign starts during transport, continues in the ED, perioperatively, and into the postoperative period. The role anaesthesiologist usually begins from the time of resuscitation and continues until discharge from the hospital. Most of the topics discussed in this section are not specific to SDH, but to TBI as a whole. Wherever any SDH-specific aspect is present, it shall be described separately.

The BTF guidelines cover topics of crucial decisions that need to be taken during the course of treatment, but only provide a broad overview of specific aspects. The care of the individual patient is based on the patient's clinical profile, hospital resources available, and the clinician's expertise.

Haemodynamic resuscitation: The thresholds for treatment of haemodynamic alterations have already been discussed above. The treatment may be divided into fluid-based resuscitation and the use of vasopressors/inotropes, with the final aim of provision of adequate circulatory volume for sufficient delivery of oxygen to vital organs.

Fluid resuscitation: Aims of fluid administration include normal volume maintenance, recuperating lost volume in the form of blood loss and apparent third space loss. Compared to a non-head-injured patient, fluid management in these cases requires extra care to maintain serum osmolarity to prevent exacerbating cerebral oedema. The amount of fluid infused for maintenance should stay in the empiric zone between forced hypovolaemia and volume overload.

Crystalloids are the mainstay of fluid resuscitation in the perioperative period. Hypotonic fluids such as 0.45% NS or 5% dextrose solutions are avoided. Some clinicians recommend avoidance of Ringer's lactate which is mildly hypotonic relative to human plasma [32]. Iso-osmolar solutions such as 0.9% NS or balanced salt solutions are preferred. Hypertonic crystalloids such as 20% mannitol or 3% hypertonic saline (HS) are used primarily as hyperosmolar agents for reduction of cerebral oedema although they produce transient (mannitol) or prolonged (HS) volume expansion.

Colloids are used primarily as volume expanders when crystalloids prove ineffective. In scenarios of reduced blood oncotic pressure (haemorrhage with crystalloid only replacement), crystalloids fail to stay within the intravascular space and "leak out" into the interstitium. The ideal therapy in such scenarios would be blood replacement. If, due to logistical problems blood products are not available readily, colloids may be used as a bridge therapy. Colloids are not used as standard volume replacement due to their propensity to impair coagulation and precipitate kidney injury [33]. Credibility of safety of colloidal starch solutions diminished considerably when long-term research fraud was detected within the subtopic of crystalloid versus colloid safety [34]. Albumin has also been shown to have adverse effect on survival in TBI patients compared to crystalloids [35].

Vasopressors/Inotropes: There is paucity of credible research which can guide the choice of vasopressors in haemodynamic resuscitation of TBI patients. Observational studies have shown worse outcomes with their use, but are prone to high selection bias [36]. Phenylephrine, noradrenaline, and dopamine are all used commonly in this context. Based on expected pharmacodynamic effects, phenylephrine is associated with lower heart rates compared to the others [37]. The effects of vasoactive agents on an injured brain need to be further studied to provide conclusive evidence of relative efficacy and safety of these drugs.

Question 6:
What are the concerns during airway management in a patient of SDH?

Answer:
Pulmonary resuscitation in TBI cases is both necessary and potentially dangerous. The usual guideline is to perform endotracheal intubation in a patient if GCS is scored less than 9 [10]. It is assumed that these patients do not have control over their airway, and there is risk of pulmonary aspiration of gastric contents if the patient vomits due to raised ICP. The risk in intubation lies in iatrogenic damage to the cervical spine if the patient sustains an unobserved cervical spine injury, and potential systemic and cerebral haemodynamic changes due to the procedure itself or the drugs administered during the procedure.

Rapid sequence intubation (RSI): RSI is recommended with concomitant administration of drugs to reduce ICP surges [38]. The BTF prehospital guidelines do not recommend routine use of paralytic agents for endotracheal intubation during transport [10]. In the ED, the clinician needs to make empirical decisions regarding choice of drugs to facilitate intubation. Using only muscle relaxants as adjuncts to intubation is discouraged as the laryngoscopy produces an independent haemodynamic response leading to spiking of ICP [39]. Commonly used drugs include lignocaine (weak evidence), fentanyl/remifentanyl, etomidate, propofol, and esmolol. Ketamine is a controversial drug in this aspect due to its ICP increasing properties. However, recent evidence shows no difference in ICP changes, or outcomes when compared with etomidate [40, 41]. Thus, ketamine may be preferred for sedation in RSI if the patients are haemodynamically unstable.

Cervical spine concerns: Importance of cervical spine screening has already been discussed in the setting of the ED. However, prehospital resuscitation may require laryngoscopy before an X-ray can be obtained. Manual inline stabilization of the spine is recommended in such cases

[42]. While pre-intubation airway management techniques of chin lift, jaw thrust, and mask ventilation have been shown to increase cervical instability and cause narrowing of cord space, cricoid pressure during RSI has been found to be a safe manoeuvre [43, 44].

19.2 Intraoperative

Question 7:
Which anaesthetic technique would you prefer while conducting a case of SDH?

Answer:
Most aspects of medical management of TBI patients are covered in the BTF guidelines, and the principles stay the same during all parts of management, whether in the ED, operation theatre or the intensive care unit. However, in the intraoperative period an added intervention is the use of anaesthetic agents which have significant pharmacodynamic influences on neurophysiology.

Based on pharmacodynamics, the use of inhalational agents leads to reduced cerebral metabolic rate (CMR) with concomitant decoupling of metabolism and blood flow (CBF) due to direct cerebral vasodilation. At >1 MAC concentrations, vasodilation supersedes CBF reduction due to CMR drop and overall CBF increases. Intravenous agents are associated with a steady drop in CBF as the CMR decreases. In addition, in the background of cerebral metabolic suppression (as in early stages of TBI), the CMR reduction of inhalational agents is less prominent and CBF augmentation much more [45]. Theoretically, intravenous agents should be preferred in cases of reduced cerebral compliance; however, studies have failed to show difference in outcomes between the two classes of agents [46, 47]. The BTF guidelines do not provide any recommendations on this subtopic, and there are few studies in this context. Thus, the initial choice of agents is empirical-based on anaesthesiologist's judgement or hospital policy. If brain is seen to be bulging or ICP is high intraoperatively with inhalational agents, it is prudent to shift to intravenous anaesthetic agents (propofol) for maintenance.

Nitrous oxide (N_2O) is known to increase CMR, CBF, cerebral blood volume, and ICP mildly although the effects are offset with concomitant hypocapnia [48]. There are no formal studies evaluating the effect of N_2O on outcome in TBI patients. It is safer to err on the side of caution and avoid it as an adjunct anaesthetic in TBI.

Question 8:
What are blood transfusion targets in a patient of SDH?

Answer:
Going with the tenet of reducing secondary injury to the brain in TBI patients, oxygen delivery to the brain is an important consideration. Traditionally, neurosurgical patients have been transfused with target haemoglobin (Hb) level of 10 g/dL. Recently, restrictive transfusion practices (target Hb >7 g/dL) have become the norm due to the realization that liberal transfusion strategies are unnecessary and concern regarding adverse effects of blood transfusion. The Hb threshold for transfusion in trauma varies between countries and different consensus guidelines although all are between 7 and 9 g/dL. There is no specific threshold described for TBI. The BTF guidelines do not hold a recommendation for this subtopic [49].

Although it is reasonable to presume higher metabolic activity and oxygen requirement in an injured brain, there are currently no studies powerful enough to demonstrate that effect. The presumed association between anaemia and poor outcomes has not been demonstrated consistently. Moreover, blood transfusion has also not been consistently tied to poor outcomes [49].

Meta-analysis has revealed no difference in mortality between patients transfused and those that were not [50]. A multicenter cohort study from Canadian trauma centres showed higher mortality among those who were transfused [51]. The pertinent question is whether the transfusion is cause of higher mortality or effect of the pathology which caused the mortality. Due to high heterogeneity in patient population, such questions can only be answered by well-designed and controlled studies.

Question 9:
How would you plan mechanical ventilation in patients with SDH in an intensive care unit?

Answer:
TBI patients have multiple pathophysiologic processes which are exquisitely sensitive to ventilation strategies. Hypoxia, hypocapnia, and hypercapnia can have deleterious effects on outcome in these patients.

Hypocapnia: Hypocapnia is a known cerebral vasoconstrictor and may lead to cerebral ischaemia, especially in the first 24 h period following TBI. It has been shown that the ICP reducing effect of hyperventilation may be limited, and aiming for higher levels of hypocapnia may reduce cerebral blood flow with no change in ICP. In one study, hypocapnia led to reduction of cerebral blood volume by only 7%, while the cerebral blood flow reduced by 30% [52]. Overall, the recommendation is to avoid hyperventilation in the said time period in the third edition of BTF guidelines [53]. The fourth edition carries another recommendation which is to avoid prolonged prophylactic hyperventilation with $PaCO_2 \leq 25$ mmHg [16].

Hypercapnia: Hypercapnia is known to cause cerebral vasodilation, increased cerebral blood flow and increase in ICP. In TBI, hypercapnia is usually observed in the pre-hospital setting due to airway obstruction or respiratory failure, wherein hyperventilation may be instituted carefully under arterial blood gas monitoring to avoid hypocapnia.

Hyperoxia: Normobaric hyperoxia is one of the relatively new therapies aimed at improving outcomes in patients of TBI. Earlier studies focussed on *hyperbaric oxygen therapy*, which was found to be effective in modulating ICP and improving neuroinflammation, reducing cortical spreading depression and improving aerobic metabolism in the injured brain, when administered early (at least <48 h after head injury) and for prolonged periods (at least 6 h) [54]. However, the procedure is technically cumbersome and unlikely to be included in clinical practice.

Normobaric hyperoxia entails increasing fraction of inspired oxygen concentration (FiO_2 40–100%) at atmospheric pressure. It provides similar promising results when tested using microdialysis techniques. Brain tissue oxygen concentrations are increased and lactate-based indices reduced with prolonged hyperoxia [54]. Concerns regarding lung injury may be mitigated with the use of lower concentrations (FiO_2 60%) [55]. This technique requires more comprehensive studies to prove improvement in long-term outcomes before it can be included in clinical practice. There is no comment on this technique in the current BTF guidelines [16].

Ventilatory parameters: The use of lung protective strategies has been proven to be beneficial for outcomes in general ICU population and patients with acute respiratory distress syndrome (ARDS). These strategies include application of low tidal volume (V_t 6–8 mL/kg) and high positive end expiratory pressures (PEEP 6–8 cm H_2O). Concerns of hypercapnia with low tidal volume ventilation and consequent increase of ICP can be easily ameliorated with frequent $PaCO_2$ monitoring using arterial blood gas analysis and ventilatory adjustment. PEEP has been shown to have statistically significant but clinically insignificant effect on ICP (1 cm H_2O increase causing 0.31 mmHg increase) and CPP (0.85 mmHg decrease), and thus can be safely used [56].

Retrospective and prospective cohort studies have shown improvement in ventilator-free days and mortality in TBI patients with the use of lung protective ventilation strategies [57, 58].

19.3 Postoperative

Extubation strategies: Extubation of mechanically ventilated patients in the ICU is a contentious issue which is usually driven based on empirical clinical judgement of the treating physician. Relying on improvement of neurological outcome often delays extubation and is not necessarily associated with successful extubation and may lead to increased incidence of nosocomial pneumonia and length of ICU/hospital stay [59]. Multiple authors have described factors significantly associated with successful extubation in TBI patients [60–63]:

(a) Age <40 years old/younger age
(b) Visual pursuit
(c) Attempts to swallow
(d) GCS >10 on the day of extubation
(e) Preserved upper airway reflexes
(f) Negative fluid balance
(g) Presence of cough
(h) Secretion volume
(i) Duration of mechanical ventilation

Tracheostomy: Few comatose patients of severe head injury need to undergo tracheostomy for prolonged mechanical ventilation. The controversial aspect surfaces with decision of early tracheostomy (≤8 days) in patients who may or may not recover quickly. One large retrospective study found no change in mortality but reduction in mechanical ventilation duration, length of hospital stay, incidence of pneumonia, and deep venous thrombosis [64]. The guideline in the latest BTF statement was developed from two randomized controlled trials and stated that early tracheostomy was recommended when overall risk was perceived to be less than the benefit [16]. Eventually, it is an open-ended decision in favour of clinicians who favour an early tracheostomy.

Question 10:
What are broad treatment philosophies in TBI?—Discuss Rosner's and Lund's concept.

Answer:
ICP control is the corner stone of TBI management philosophy. Treatment philosophies in TBI patients may be broadly classified into ICP based, CPP based and cerebral volume based.

Rosner's protocol: CPP-based therapy was proposed by Rosner and included systemic volume expansion and the use of vasopressors to improve arterial blood pressures, and CSF drainage and mannitol for reduction of ICP. Overall, the goal was to maintain CPP above 70 mmHg [65]. Although encouraging results were published from single centres, this philosophy of therapy has come under fire due to 5 times increased risk of ARDS with induced hypertension [66]. Physiologically, the lack of optimal autoregulation in TBI patients may lead to exacerbation of cerebral oedema if high CPP is maintained. Based on these concerns, the third edition of BTF guidelines recommended avoidance of aggressive attempts to elevate CPP >70 mmHg and maintenance of CPP between a range of 50 and 70 mmHg [15]. Current BTF recommends maintenance of CPP within range of 60–70 mmHg, and also cautions that the optimal CPP may depend on the patient's autoregulatory status [16].

Optimal CPP concept: The issue of individualized optimal CPP target for a patient has come up due to the varied levels of autoregulatory impairments in patients of TBI. This concept has been facilitated by derivation of novel indices from the ICP waveform by correlating 30 s long sequences of the 10 s averaged ICP and MAP. This index is called pressure reactivity index or PRx. PRx is an index of autoregulation and ranges from −1 to 1. Patients with impaired autoregulation have positive values of PRx and those with preserved autoregulation have zero or less [67] (Fig. 19.4). Plotting the PRx and the CPP over time provides a picture of change in autoregulation with different levels of CPP and usually forms a U-shaped plot. This plot depicts high PRx at either ends of the CPP spectrum, with low CPP causing loss of pressure head leading to tandem reduction of AMP and MAP, and high CPP causing pressure-induced dilation of arterioles and tandem increase in AMP with MAP. The trough of the plot with lowest values of PRx represents the optimal CPP for that patient [68] (Fig. 19.5).

Lund's protocol: The Lund concept originated in Lund University, Sweden, as a relatively strict and holistic protocol for management of head-injured patients. The concept targeted a cerebral "volume"-based approach, with the baseline assumptions that the blood–brain barrier is disrupted and autoregulation impaired after TBI. The foundation of this concept was prevention of brain oedema by reduction of transcapillary hydrostatic and osmotic gradients which could potentially

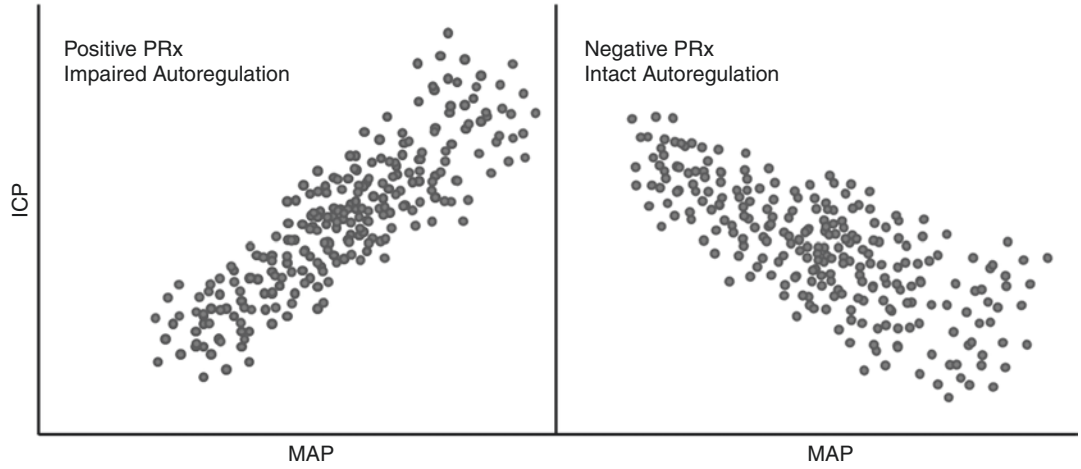


Fig. 19.4 Representative image showing PRx changes with autoregulation

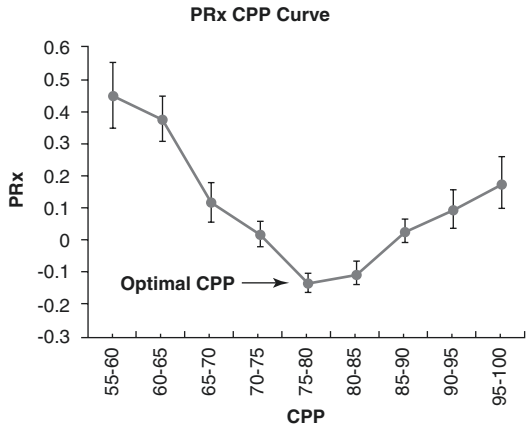


Fig. 19.5 Representative image showing plot of PRx and CPP. Trough of the plot corresponds to optimal CPP

increase oedema. The protocol targets the systemic circulation by using metoprolol and clonidine for reduction of hydrostatic pressure, thiopentone, and analgesics for reduction of stress response and catecholamine levels, dihydroergotamine for reducing cerebral venous volume, and albumin and red blood cell transfusion for increasing colloidal oncotic pressure of blood and improving oxygenation. The protocol avoids using osmotherapy (mannitol and HS) and vasopressors. The protocol allows for CPP levels up to 50 mmHg in adults and 40 mmHg in children [69].

This approach has been criticized at multiple levels (its assumptions, choice of agents, liberal use of blood transfusion, acceptance of low CPP) and has not been used or studied outside Sweden [70].

Question 11:
What steps can be taken for ICP control in patients of SDH?

Answer:
The question of whether and how to monitor ICP, and the thresholds for instituting treatment for it have been detailed in Answer 4. EVD are the gold standard for ICP monitoring due to their therapeutic potential. If ICP is observed to be high, CSF drainage can be done. Some centres prefer to place intraparenchymal probes for ICP measurement which are based on strain gauge microtransducer (Codman™) at the tip, fiberoptic microtransducer (Camino™), or pneumatic type (Spiegelberg™). However, these transducers suffer from the phenomenon of zero drift to varying degrees and thus ICP measurement becomes unreliable after 2–3 days [71]. EVD-based modality can be zeroed at level of foramen of Monro whenever required and thus is more reliable.

Is ICP monitoring useful? Utility of ICP monitoring has been questioned from time to time, and to date there is only one randomized controlled trial which addresses this concern. The trial

revealed no added benefit of ICP monitoring in improving outcomes in TBI patients [72]. The problem with such research questions is that while a monitoring modality may be useful in gathering information about the ICP status of the patient, it is the treatment the clinician institutes based on the information that leads to improved outcomes. There is also an ethical concern with observing values of high ICP in a patient and keeping the treating physician blinded to it (which an RCT would entail). Due to this, it is unlikely that such an RCT would ever be performed in the future, and the general consensus of utility of ICP monitoring is in its favour, as outlined in the BTF guidelines [16].

Three-tier therapy for ICP control: The American College of Surgeons Trauma Quality Improvement Program (ACS TQIP) guidelines for TBI management provide a good overview of a three-tier approach for treatment of raised ICP, based on the ICP level and response to the treatment provided [73] (Table 19.1).

The ***tier 1 therapies*** include improvement of position-induced cerebral venous drainage, reduction of systemic sympathetic stress response via sedatives and analgesics, and intermittent CSF drainage via EVD. 30° head-up position is a standard position of patients in ICU, and the importance of this is the need to zero the ICP transducer at the level of foramen of Monro (landmark—tragus). The topic of sedatives and analgesics is covered in BTF guidelines but only in the context of tier 3 therapy of high dose barbiturates for control of refractory ICP. Propofol has also been recommended with the added caution that high dose can contribute to morbidity (propofol infusion syndrome). Prophylactic high dose barbiturates are not recommended (to be used only at tier 3 stage) [16]. In the context of CSF drainage, the BTF recommends the use of continuous CSF drainage to reduce ICP more effectively than intermittent drainage [16]. The problem with this approach is that ICP monitoring with continuous drainage produces erroneous ICP values if done via the same EVD, and thus requires a separate dedicated catheter or microtransducer device to be inserted.

Table 19.1 Three-tier approach for treatment of high ICP in TBI patients—based on ACS TQIP guidelines [80]

Tier 1
Head of bed elevation (30°)
Sedation and analgesia (propofol, fentanyl, midazolam)
Intermittent ventricular drainage
Repeat CT imaging and neurological examination
Tier 2
Intermittent hyperosmolar therapy (Mannitol 0.25–1 g/kg; 3% HS 250 mL over 30 min)
Cerebral autoregulation testing to determine optimal CPP
$PaCO_2$ goal of 30–35 mmHg
Repeat CT imaging and neurological examination
Neuromuscular paralysis may be tested and continued if ICP improves
Tier 3
Decompressive craniectomy
Neuromuscular paralysis continued if ICP improves with test dose
Barbiturate or propofol infusion if patient responds to test dose—maintain blood pressure, EEG may be monitored
Hypothermia only as rescue or "salvage" therapy (not recommended by current guidelines)

Tier 2 therapies are concentrated on hyperosmolar agents, ventilation therapy, and neuromuscular paralysis. Hyperosmolar therapy is a standard ICP reduction technique which has stood the test of time. The standard drugs used for this purpose are mannitol (as bolus of 0.25–1 g/kg) and hypertonic saline (HS—as bolus of 250 mL of 3% saline; or equivalent volume of varying concentrations). There are many differences between the two agents, with HS having certain advantages (higher reflection coefficient, better maintenance of intravascular volume, no sequestration in brain tissue). Meta-analyses of studies comparing the two agents show HS to have an advantage of better control of ICP and improved brain relaxation, but no statement could be made about long-term outcomes [74–76]. The BTF makes a generic statement of probable benefit of hyperosmolar therapy in reducing ICP but does not specify the preferred agent [16]. Ventilation therapy and $PaCO_2$ goals in TBI have already been discussed in Answer 9.

Neuromuscular blocking agents either as bolus or continuous infusion are used infrequently for control of ICP in TBI patients. Advantages

include reduction in febrile shivering, reduced movement, and ICP surges during tracheal suctioning and reduced metabolic requirements (energy expenditure). Disadvantages are related to long-term or continuous infusions and include masking of seizure activity, polyneuropathy, and delayed weaning/rehabilitation [77]. There is no consensus on their usage, and it is left to the clinician's empirical judgement. The BTF does not include this subtopic in their list of recommendations.

Tier 3 therapies include salvage therapies which are used only if ICP is not controlled by tier 1 and 2 methods. Of these, decompressive craniectomy has already been dealt with in Answer 4. Barbiturate or propofol-induced coma has been recommended by BTF for controlling refractory ICP, but this therapy comes with caveats. Haemodynamic suppression needs to be controlled with adequate volume resuscitation and vasopressors therapy. There is also high incidence of hypothermia due to global vasodilation which needs to be corrected. The therapy is associated with full or partial control of ICP in approximately 30–50% of patients across studies, but is not associated with improvement in long-term outcomes. Patients who respond to barbiturate therapy have better outcomes compared to non-responders [78, 79].

Question 12:
Is prophylactic hypothermia useful as a neuroprotective strategy in a patient of SDH?

Answer:
Hypothermia as a neuroprotectant was a controversial therapeutic modality until recently. Theoretically, it helps to reduce the basal metabolic rate, oxygen and energy consumption in the brain as well as reduce concentrations of excitatory neurotransmitters. This view was supported by studies finding improved neurological outcome with hypothermia therapy following resuscitation from cardiac arrest [81]. It had also been shown to be useful in reducing ICP in small studies [82].

Thereafter, multiple large-scale studies have tried to provide credence to theoretical neuroprotective effect of hypothermia in TBI, but results have been noncommittal at best. Majority of work on hypothermia in TBI has been published by Clifton (NABIS-H trials), with progressive fine tuning of the study methodology in each iteration.

The first study used surface cooling which was initiated within 6 h of injury and target temperature of 33 °C reached after an average 8 h, followed by maintenance till 48 h and then slow rewarming was initiated. The study did not find any difference in neurological outcomes with higher in-hospital complications [83].

This led to the second study wherein faster cooling methods (IV administration of chilled crystalloids) were used with the aim of achieving target temperature of 35 or 33 °C (based on pre-defined patient characteristics) by 4 h after injury. Again, no difference in outcomes was seen in comparison with normothermia group, and the trial was terminated due to futility [84]. In 2012, Clifton published a post hoc analysis of the previous two trials and found that reaching target temperature of 35 °C within 1.5 h in patients of evacuated intracranial haematomas improved outcomes significantly [85]. The current BTF guidelines provides a recommendation contraindicating prophylactic hypothermia as a therapy for improving outcomes in patients with diffuse axonal injury (severe grade TBI patients without intracranial haematoma) [16]. This however leaves a loophole for patients with intracranial haematomas—whether to accept Clifton's results or not.

Since then two trials have been published—Eurotherm 3235 and POLAR RCT. The Eurotherm trial allowed inclusion of patient up to 10 days after the initial head injury, while POLAR RCT initiated hypothermia very early (median 1.8 h), with target temperature of 32–35 °C for at least 48 h in Eurotherm and 33–35 °C for at least 72 h in POLAR RCT. Both the trials reported no improvement in neurological outcome for the hypothermia arm [86, 87]. With good grade evidence accumulating, it would be fair to surmise that prophylactic hypothermia is to be avoided as a therapeutic strategy for improvement of outcomes in TBI.

Question 13:
What is the role of steroids in treatment of a patient with SDH?

Answer:
Steroids are proven to be beneficial in reduction of vasogenic oedema in cases of intracranial tumours. This had led to exploration of steroids in the domain of TBI also. However, most of the modest sized trials either did not show any benefit of steroid therapy (dexamethasone, triamcinolone, and methylprednisolone) or the benefit was not convincing due to poor study design. The controversy was put to rest by two prominent trials—GUDHIS (German Ultrahigh Dexamethasone Head Injury Study) and CRASH (Corticosteroid Randomization After Significant Head Injury), which included 300 and 10,008 samples, respectively. The former reported no difference in outcome with or without the use of dexamethasone in moderate to severe head injury patients [88]. The latter study was stopped midway after an interim analysis revealed higher 2-week and 6-month mortality in the methylprednisolone arm [89]. This study prompted the third edition of BTF guidelines to issue a level 1 recommendation contraindicating the use of corticosteroids for improving outcome or reducing ICP [90]. The fourth edition carries forward the guideline with no changes [16].

This however should not be taken as a blanket rule regarding steroids in TBI. Adrenal insufficiency (AI) is a known adverse effect of TBI with an incidence of approximately 25%. Clinically, it can be determined by the triad of hypotension, hyponatraemia, and hypoglycaemia. Hypotension due to AI often requires vasoactive agents for maintenance of haemodynamics [91]. This is one situation where empirical administration of stress dose steroids may be useful until a definitive assessment of hypothalamic-pituitary-adrenal axis is conducted [92].

Question 14:
What are the options for brain monitoring in a patient of SDH?

Answer:
Neuromonitoring has advanced rapidly over the past few decades to cover almost all aspects of brain functioning. Functional, metabolic, oxygenation, blood flow, and pressure, all have been covered by some modality. This has led to a major shift in the philosophy of treatment—from the average to the individual. The plethora of monitoring modalities has enabled the treating physician to tailor therapy according to the patient's individual requirements. ICP monitoring has already been discussed in Answer 10 and 11.

1. **Electrical monitoring**: Electroencephalography (EEG) is a method of monitoring real-time electrical signals generated by summation of post-synaptic potentials in the dendrites of pyramidal cells of the cerebral cortex. In the context of TBI, EEG is used for monitoring of seizure activity and also for depth of functional suppression when a patient is administered barbiturate coma. Depth of suppression is measured using a time domain parameter called "burst suppression ratio", which is the percentage of time duration during which the brain is in isoelectric state (no electrical activity). BSR of approximately 50% is usually targeted. Seizure activity may need to be monitored if the patient has experienced seizures during the hospital stay or if the patient is paralyzed for reducing ICP.

   Another context in which EEG may be used is as a confirmatory tool for diagnosis of brain death in a patient with refractory intracranial hypertension. It is diagnosed by observation of isoelectric waves for 30 min, in a widely spaced (at least 8 cm) montage with amplifier sensitivity set at 2 μV/division [93]. Evoked potentials, specifically, somatosensory evoked potentials (SSEP) have also been used in this regard.
2. **Metabolic monitoring**: This involves monitoring biochemical parameter concentrations in the injured brain. Microdialysis has been in vogue in the research field since the 1970s, for characterization of molecular milieu in extracellular fluid in animals. It has slowly progressed into the realm of clinical neuromonitoring in 1990s and is usually used in combination with ICP monitoring and brain tissue oxygen monitoring. The

modality consists of a coaxial catheter with semipermeable membrane at the tip. Dialysate is passed through the catheter at a slow rate (0.3 μL/min), which equilibrates with extracellular fluid at the tip and is then either collected for analysis or analysed in real time. For clinical purposes, it is used to measure glucose, lactate, pyruvate, glycerol, and glutamate.

Glucose, lactate, pyruvate, and lactate-to-pyruvate ratio (LPR) are used as markers for reduced energy substrate supply and mitochondrial dysfunction. Glutamate is a marker of excitotoxicity, which usually occurs as a consequence of cerebral ischaemia. Glycerol is a marker of cellular breakdown and is also associated with ischaemia/infarct [94].

A consensus statement regarding the use of microdialysis as a clinical and research tool was published in 2015. In context of SDH, recommendation was to place the catheter in radiographically normal part of the ipsilateral brain. Threshold levels of metabolites for diagnosing "at risk" status of brain are:

(a) Glucose- <0.2–0.8 mmol/L
(b) Lactate ->0.4 mmol/L
(c) LPR >25 and >40

More research needs to be conducted before definitive utility of this modality can be elucidated [95].

3. **Oxygenation monitoring**: Oxygenation of the brain is the primary goal in any therapy in TBI. Monitoring of oxygenation can be done at global level and focal level. Global oxygenation is monitored by jugular venous oximetry. Focal modalities include brain tissue oxygen monitoring (invasive) and near-infrared spectroscopy (NIRS)-based cerebral oximetry (non-invasive). A thorough discussion of all these modalities is beyond the scope of this chapter, but a brief overview is provided.

(a) **Brain tissue oxygen monitoring**: Includes a catheter with Clark's electrode at the tip for real-time monitoring of oxygen tension in a 1 cm diameter sphere around the probe. The interpretations of the brain tissue oxygen tension ($PbtO_2$) need to be made based on location of the probe (usually perilesional in case of haematoma). Threshold values of <15–20 mmHg herald the need for rescue intervention [94]. It was included in the third edition of BTF guidelines as an advanced neuromonitoring modality with threshold value of <15 mmHg for intervention [96]. In the fourth edition, it was excluded due to poor quality of evidence [16].

(b) **Jugular venous oximetry**: This is done using a catheter introduced into the dominant internal jugular vein which is ascended cranially up to the jugular bulb. The catheter used may be a single channel central venous catheter through which blood can be drawn slowly (<2 mL/min) for blood gas analysis, or it can be a fiber-optic equipped catheter which analyses blood oxygenation at the tip in real time. The rationale behind this modality is that the dominant jugular usually carries 70% blood from the ipsilateral lobe and 30% from the contralateral lobe and provides a global estimate of oxygenation. Values <50 to 55% herald a demand versus supply oxygen deficit. Interpretation of the value should be based on clinical scenario and always correlated in a demand versus supply manner [97].

This modality has been recommended in both third and fourth edition of BTF guidelines with threshold for intervention set at <50% [16, 96].

(c) **NIRS-based cerebral oximetry**: This modality is based on reflectance spectroscopy with light-emitting diodes placed on forehead and sensing optodes placed at 4 cm distance. Near-infrared spectrum light (700–1000 nm wavelength) is emitted and goes through skin, subcutaneous tissue, bone and takes a curved path through the superficial frontal lobe to reach the sensing optodes. It provides information about oxygen saturation in the blood within the frontal lobe

(maximum depth 2 cm). The blood is a mixture of arterial, capillary, and venous blood and hence the saturation ranges from 60 to 80%. Threshold for ischaemia is set at <50%; however, this level is arbitrary. It is more useful to focus on trends of change relative to baseline, rather than absolute values.

Although research has been conducted in the context of TBI, clinical utility is limited and the BTF does not endorse this monitoring modality [98].

4. **Blood flow monitoring**: Cerebral blood flow (CBF) monitoring is a cumbersome process and not suitable for regular clinical use. In this regard, cerebral blood flow velocities in the major intracranial vessels (FV) may be used as a proxy for CBF measurements. Transcranial Doppler (TCD) provides a non-invasive and point-of-care modality for measurement of FV in real time.

In context of TBI, TCD along with Xe^{133} clearance-based CBF estimation has been used to chart out pattern of CBF changes after TBI [99]:

(a) In the initial 24 h following the injury, there is a reduction in CBF with maintenance of flow velocities—hypoperfusion phase.
(b) 1–2 days post injury, there occurs a hyperaemic phase with an increase in both CBF and FV.
(c) After day 4, there is the vasospastic phase, with reduction in CBF and continued increases in FV until 2 weeks post injury.

Other uses of TCD in head injury are [100]:

1. Non-invasive estimation of ICP based on changes in pulsatility index.
2. Detection of low CBF states (low mean FV and high pulsatility).
3. Assessment of autoregulation and carbon dioxide reactivity.

BTF guidelines do not include any recommendation regarding TCD in either third or fourth editions.

Question 15:
How do you deal with seizures in a case of SDH?

Answer:
Post-traumatic seizures (PTS) can be classified as immediate (within minutes after head injury), early (within ≤1 week), and late (>1 week) [101]. Incidence of PTS varies widely with the demographic characteristics of the patients as well as type of head injury (4–53%) [102]. Immediate PTS are evident immediately and need to be dealt with as per hospital protocol for any seizure episode. The uncertainty arises when prophylactic measures need to be taken for prevention of early or late PTS.

Early PTS occurs more commonly in patients of younger age group, intracranial haematoma (especially SDH), high injury severity, and chronic alcoholism. Late PTS are more likely to happen in patients who experience early PTS, older age group (>65 years), high injury severity, and the presence of intracranial haematoma (SDH) and contusions [102].

In patients with severe TBI, the rate of clinical seizures is approximately 12%. The call for prophylaxis is due to high occurrence rate of seizure after severe TBI. However, phenytoin prophylaxis also leads to impairment in neuropsychological tests at 1 month although the effect is not apparent at 12 months.

PTS prophylaxis using phenytoin or valproate led to significant reduction in incidence of early PTS, while no difference was found for late PTS. This led to the BTF recommendation of using either phenytoin or valproate for prophylaxis against early PTS but not late PTS. The choice of agent was kept equivocal, but one study showed a trend towards higher mortality in patients using valproate [16, 103, 104].

Levetiracetam is an upcoming drug for this purpose, but good quality studies are not available for providing any guidelines.

Conclusion: TBI is a vast multifaceted topic which holds many unanswered questions for the practising neurophysician. A lot has been done, and a lot more needs to be done. Covering the entirety of subject is impossible in a single chapter, and the interested reader is referred to niche reviews which cover each of the subtopics in detail.

Acknowledgement This manuscript would not have been possible without the support of Arpitha A. J. who also helped in reviewing the manuscript.

Multiple Choice Questions

1. Which of the following brain oxygenation monitoring modalities is recommended in the fourth edition of BTF guidelines?
   (a) Brain tissue oxygen monitoring.
   (b) NIRS-based cerebral oximetry.
   (c) Jugular venous oximetry.
   (d) Microdialysis.
   Answer: c
2. Is prophylactic hypothermia useful for improving outcomes in severe head injury?
   (a) If initiated early (<2.5 h), it improves outcomes.
   (b) If target temperature (<32 °C) is achieved, it improves outcomes.
   (c) If target temperature is maintained for 48 h, it improves outcomes.
   (d) It is not useful.
   Answer: d
3. Which of the following statements is correct?
   (a) Methylprednisolone administration does not improve outcomes in patients with SDH.
   (b) Steroids may be used in management of TBI patients if central adrenal insufficiency is suspected.
   (c) None of the above.
   (d) Both 1 and 2.
   Answer: d
4. Which of the following statements is correct?
   (a) Phenytoin reduces incidence of early post-traumatic seizures.
   (b) Phenytoin reduces incidence of late post-traumatic seizures.
   (c) Phenytoin is better than valproate in reducing incidence of early post-traumatic seizures.
   (d) Phenytoin is not recommended for reducing incidence of any post-traumatic seizures.
   Answer: a
5. Pressure reactivity index (PRx) is useful quantifying:
   (a) Cerebral compliance.
   (b) Intracranial pressure.
   (c) Autoregulation.
   (d) Cerebral blood flow.
   Answer: c

References

1. Agrawal A, Munivenkatappa A, Shukla DP, Menon GR, Alogolu R, Galwankar S, et al. Traumatic brain injury related research in India: an overview of published literature. Int J Crit Illn Inj Sci. 2016;6:65–9.
2. Hanif S, Abodunde O, Ali Z, Pidgeon C. Age related outcome in acute subdural haematoma following traumatic head injury. Ir Med J. 2009;102:255–7.
3. Vollmer DG, Torner JC, Jane JA, Sadovnic B, Charlebois D, Eisenberg HM, et al. Age and outcome following traumatic coma: why do older patients fare worse? J Neurosurg. 1991;75:S37–49.
4. Karibe H, Hayashi T, Hirano T, Kameyama M, Nakagawa A, Tominaga T. Surgical management of traumatic acute subdural hematoma in adults: a review. Neurol Med Chir (Tokyo). 2014;54:887–94.
5. Leitgeb J, Mauritz W, Brazinova A, Janciak I, Majdan M, Wilbacher I, et al. Outcome after severe brain trauma due to acute subdural hematoma. J Neurosurg. 2012;117:324–33.
6. Fountain DM, Kolias AG, Lecky FE, Bouamra O, Lawrence T, Adams H, et al. Survival trends after surgery for acute subdural hematoma in adults over a 20-year period. Ann Surg. 2017;265:590–6.
7. Walcott BP, Khanna A, Kwon C-S, Phillips HW, Nahed BV, Coumans J-V. Time interval to surgery and outcomes following the surgical treatment of acute traumatic subdural hematoma. J Clin Neurosci. 2014;21:2107–11.
8. Bulger EM, Guffey D, Guyette FX, MacDonald RD, Brasel K, Kerby JD, et al. Impact of prehospital mode of transport after severe injury: a multicenter evaluation from the Resuscitation Outcomes Consortium. J Trauma Acute Care Surg. 2012;72:567–73; discussion 573–5; quiz 803.
9. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Glasgow coma scale score. J Neurotrauma. 2000;17:563–71.
10. Badjatia N, Carney N, Crocco TJ, Fallat ME, Hennes HMA, Jagoda AS, et al. Guidelines for prehospital management of traumatic brain injury 2nd edition. Prehosp Emerg Care. 2008;12:S1–52.
11. Manley G, Knudson MM, Morabito D, Damron S, Erickson V, Pitts L. Hypotension, hypoxia, and head injury: frequency, duration, and consequences. Arch Surg. 2001;136:1118–23.
12. Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM, et al. The role of secondary brain injury in determining outcome from severe head injury. J Trauma. 1993;34:216–22.

13. McHugh GS, Engel DC, Butcher I, Steyerberg EW, Lu J, Mushkudiani N, et al. Prognostic value of secondary insults in traumatic brain injury: results from the IMPACT study. J Neurotrauma. 2007;24:287–93.
14. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. I. Blood pressure and oxygenation. J Neurotrauma. 2007;24:S-7–S-13.
15. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. IX. Cerebral perfusion thresholds. J Neurotrauma. 2007;24:S-59–64.
16. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GWJ, Bell MJ, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2016;80:1.
17. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2:81–4.
18. Healey C, Osler TM, Rogers FB, Healey MA, Glance LG, Kilgo PD, et al. Improving the Glasgow Coma Scale Score: motor score alone is a better predictor. J Trauma. 2003;54:671–80.
19. Clark A, Mesfin FB. Trauma neurological exam. Treasure Island: StatPearls Publishing; 2018.
20. Hoffman JR, Wolfson AB, Todd K, Mower WR. Selective cervical spine radiography in blunt trauma: methodology of the National emergency X-Radiography Utilization Study (NEXUS). Ann Emerg Med. 1998;32:461–9.
21. Stiell IG, Wells GA, Vandemheen KL, Clement CM, Lesiuk H, De Maio VJ, et al. The Canadian C-Spine Rule for radiography in alert and stable trauma patients. JAMA. 2001;286:1841.
22. Stiell IG, Clement CM, McKnight RD, Brison R, Schull MJ, Rowe BH, et al. The Canadian C-Spine Rule versus the NEXUS low-risk criteria in patients with trauma. N Engl J Med. 2003;349:2510–8.
23. Hodgkinson S, Pollit V, Sharpin C, Lecky F, National Institute for Health and Care Excellence (NICE) Guideline Development Group. Early management of head injury: summary of updated NICE guidance. BMJ. 2014;348:g104.
24. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, et al. Guidelines for the surgical management of traumatic brain injury author group. Neurosurgery. 2006;58:S2–vi.
25. Sahuquillo-Barris J, Lamarca-Ciuro J, Vilalta-Castan J, Rubio-Garcia E, Rodriguez-Pazos M. Acute subdural hematoma and diffuse axonal injury after severe head trauma. J Neurosurg. 1988;68:894–900.
26. Gusmão SNS, Pittella JEH. Acute subdural hematoma and diffuse axonal injury in fatal road traffic accident victims: a clinico-pathological study of 15 patients. Arq Neuropsiquiatr. 2003;61:746–50.
27. Bhateja A, Shukla D, Devi BI, Sastry Kolluri V. Coup and contrecoup head injuries: predictors of outcome. Indian J Neurotrauma. 2009;6:115–8.
28. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, et al. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med. 2011;364:1493–502.
29. Torres R. DECRA…where do we go from here? Surg Neurol Int. 2012;3:54.
30. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J, et al. Trial of decompressive craniectomy for traumatic intracranial hypertension. N Engl J Med. 2016;375:1119–30.
31. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. VIII. Intracranial pressure thresholds. J Neurotrauma. 2007;24:S-55–8.
32. Tommasino C, Picozzi V. Volume and electrolyte management. Best Pract Res Clin Anaesthesiol. 2007;21:497–516.
33. Hahn RG. Adverse effects of crystalloid and colloid fluids. Anestezjol Intens Ter. 2014;49:303–8.
34. Wise J. Boldt: the great pretender. BMJ. 2013;346:f1738.
35. The SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the Intensive Care Unit. N Engl J Med. 2004;350:2247–56.
36. Hylands M, Toma A, Beaudoin N, Frenette AJ, D'Aragon F, Belley-Côté É, et al. Early vasopressor use following traumatic injury: a systematic review. BMJ Open. 2017;7:e017559.
37. Sookplung P, Siriussawakul A, Malakouti A, Sharma D, Wang J, Souter MJ, et al. Vasopressor use and effect on blood pressure after severe adult traumatic brain injury. Neurocrit Care. 2011;15:46–54.
38. Li J, Murphy-Lavoie H, Bugas C, Martinez J, Preston C. Complications of emergency intubation with and without paralysis. Am J Emerg Med. 1999;17:141–3.
39. Rudy EB, Turner BS, Baun M, Stone KS, Brucia J. Endotracheal suctioning in adults with head injury. Heart Lung. 1991;20:667–74.
40. Bar-Joseph G, Guilburd Y, Tamir A, Guilburd JN. Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension. J Neurosurg Pediatr. 2009;4:40–6.
41. Upchurch CP, Grijalva CG, Russ S, Collins SP, Semler MW, Rice TW, et al. Comparison of etomidate and ketamine for induction during rapid sequence intubation of adult trauma patients. Ann Emerg Med. 2017;69:24–33.e2.
42. Pimentel L, Diegelmann L. Evaluation and management of acute cervical spine trauma. Emerg Med Clin North Am. 2010;28:719–38.
43. Hauswald M, Sklar DP, Tandberg D, Garcia JF. Cervical spine movement during airway management: cinefluoroscopic appraisal in human cadavers. Am J Emerg Med. 1991;9:535–8.
44. Donaldson WF, Heil BV, Donaldson VP, Silvaggio VJ. The effect of airway maneuvers on the unstable C1-C2 segment. A cadaver study. Spine (Phila Pa 1976). 1997;22:1215–8.

45. Drummond JC. Baseline cerebral metabolic rate is a critical determinant of the cerebral vasodilating potency of volatile anesthetic agents. Anesthesiology. 2018;129:187–9.
46. Hassan WMNW, Nasir YM, Zaini RHM, Shukeri WFWM. Target-controlled infusion propofol versus sevoflurane anaesthesia for emergency traumatic brain surgery: comparison of the outcomes. Malays J Med Sci. 2017;24:73–82.
47. Grathwohl KW, Black IH, Spinella PC, Sweeney J, Robalino J, Helminiak J, et al. Total intravenous anesthesia including ketamine versus volatile gas anesthesia for combat-related operative traumatic brain injury. Anesthesiology. 2008;109:44–53.
48. Hancock SM, Nathanson MH. Nitrous oxide or remifentanil for the "at risk" brain. Anaesthesia. 2004;59:313–5.
49. East JM, Viau-Lapointe J, McCredie VA. Transfusion practices in traumatic brain injury. Curr Opin Anaesthesiol. 2018;31:219–26.
50. Boutin A, Chassé M, Shemilt M, Lauzier F, Moore L, Zarychanski R, et al. Red blood cell transfusion in patients with traumatic brain injury: a systematic review and meta-analysis. Transfus Med Rev. 2016;30:15–24.
51. Boutin A, Moore L, Lauzier F, Chassé M, English S, Zarychanski R, et al. Transfusion of red blood cells in patients with traumatic brain injuries admitted to Canadian trauma health centres: a multicentre cohort study. BMJ Open. 2017;7:e014472.
52. Curley G, Kavanagh BP, Laffey JG. Hypocapnia and the injured brain: more harm than benefit. Crit Care Med. 2010;38:1348–59.
53. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. XIV. Hyperventilation. J Neurotrauma. 2007;24:S-87–90.
54. Kumaria A, Tolias CM. Normobaric hyperoxia therapy for traumatic brain injury and stroke: a review. Br J Neurosurg. 2009;23:576–84.
55. Bullock MR. Hyperoxia. J Neurosurg. 2008;109:421–3.
56. Boone MD, Jinadasa SP, Mueller A, Shaefi S, Kasper EM, Hanafy KA, et al. The effect of positive end-expiratory pressure on intracranial pressure and cerebral hemodynamics. Neurocrit Care. 2017;26:174–81.
57. Roquilly A, Cinotti R, Jaber S, Vourc'h M, Pengam F, Mahe PJ, et al. Implementation of an evidence-based extubation readiness bundle in 499 brain-injured patients. A before–after evaluation of a quality improvement project. Am J Respir Crit Care Med. 2013;188:958–66.
58. Asehnoune K, Mrozek S, Perrigault PF, Seguin P, Dahyot-Fizelier C, Lasocki S, et al. A multi-faceted strategy to reduce ventilation-associated mortality in brain-injured patients. The BI-VILI project: a nationwide quality improvement project. Intensive Care Med. 2017;43:957–70.
59. Coplin WM, Pierson DJ, Cooley KD, Newell DW, Rubenfeld GD. Implications of extubation delay in brain-injured patients meeting standard weaning criteria. Am J Respir Crit Care Med. 2000;161:1530–6.
60. McCredie VA, Ferguson ND, Pinto RL, Adhikari NKJ, Fowler RA, Chapman MG, et al. Airway management strategies for brain-injured patients meeting standard criteria to consider extubation. A prospective cohort study. Ann Am Thorac Soc. 2017;14:85–93.
61. Asehnoune K, Seguin P, Lasocki S, Roquilly A, Delater A, Gros A, et al. Extubation success prediction in a multicentric cohort of patients with severe brain injury. Anesthesiology. 2017;127:338–46.
62. Godet T, Chabanne R, Marin J, Kauffmann S, Futier E, Pereira B, et al. Extubation failure in brain-injured patients. Anesthesiology. 2017;126:104–14.
63. dos Reis HFC, Gomes-Neto M, Almeida MLO, da Silva MF, Guedes LBA, Martinez BP, et al. Development of a risk score to predict extubation failure in patients with traumatic brain injury. J Crit Care. 2017;42:218–22.
64. Alali AS, Scales DC, Fowler RA, Mainprize TG, Ray JG, Kiss A, et al. Tracheostomy timing in traumatic brain injury. J Trauma Acute Care Surg. 2014;76:70–8.
65. Rosner MJ, Rosner SD, Johnson AH. Cerebral perfusion pressure: management protocol and clinical results. J Neurosurg. 1995;83:949–62.
66. Contant CF, Valadka AB, Gopinath SP, Hannay HJ, Robertson CS. Adult respiratory distress syndrome: a complication of induced hypertension after severe head injury. J Neurosurg. 2001;95:560–8.
67. Czosnyka M, Smielewski P, Kirkpatrick P, Laing RJ, Menon D, Pickard JD. Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery. 1997;41:11–7; discussion 17–9.
68. Steiner LA, Czosnyka M, Piechnik SK, Smielewski P, Chatfield D, Menon DK, et al. Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury. Crit Care Med. 2002;30:733–8.
69. Grände P-O. The "Lund Concept" for the treatment of severe head trauma—physiological principles and clinical application. Intensive Care Med. 2006;32:1475–84.
70. Sharma D, Vavilala MS. Lund concept for the management of traumatic brain injury. J Neurosurg Anesthesiol. 2011;23:363–7.
71. Raboel PH, Bartek J, Andresen M, Bellander BM, Romner B. Intracranial pressure monitoring: invasive versus non-invasive methods—a review. Crit Care Res Pract. 2012;2012:1–14.
72. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, et al. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med. 2012;367:2471–81.
73. American College of Surgeons. ACS TQIP best practices in the management of traumatic brain injury. [Internet]. 2015 [cited 2019 Feb 26]. https://www.east.org/content/documents/45_podcast_acstqip_tbi_guidelines_2.pdf.

74. Prabhakar HKM. Mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy (review). Cochrane Database Syst Rev. 2017.
75. Mortazavi MM, Romeo AK, Deep A, Griessenauer CJ, Shoja MM, Tubbs RS, et al. Hypertonic saline for treating raised intracranial pressure: literature review with meta-analysis. J Neurosurg. 2012;116:210–21.
76. Kamel H, Navi BB, Nakagawa K, Hemphill JC, Ko NU. Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: a meta-analysis of randomized clinical trials. Crit Care Med. 2011;39:554–9.
77. Sanfilippo F, Santonocito C, Veenith T, Astuto M, Maybauer MO. The role of neuromuscular blockade in patients with traumatic brain injury: a systematic review. Neurocrit Care. 2015;22:325–34.
78. Majdan M, Mauritz W, Wilbacher I, Brazinova A, Rusnak M, Leitgeb J. Barbiturates use and its effects in patients with severe traumatic brain injury in five European countries. J Neurotrauma. 2013;30: 23–9.
79. Roberts I, Sydenham E. Barbiturates for acute traumatic brain injury. Cochrane Database Syst Rev. 2012;12:CD000033.
80. American College of Surgeons. ACS TQIP best practices in the management of traumatic brain injury; 2015.
81. Arrich J, Holzer M, Havel C, Müllner M, Herkner H. Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation. In: Arrich J, editor. Cochrane database of systematic reviews. Chichester: Wiley; 2012. p. CD004128.
82. Rim HT, Ahn JH, Kim JH, Oh JK, Song JH, Chang IB. Therapeutic hypothermia for increased intracranial pressure after decompressive craniectomy: a single center experience. Korean J Neurotrauma. 2016;12:55–60.
83. Clifton GL, Miller ER, Choi SC, Levin HS, McCauley S, Smith KR, et al. Lack of effect of induction of hypothermia after acute brain injury. N Engl J Med. 2001;344:556–63.
84. Clifton GL, Valadka A, Zygun D, Coffey CS, Drever P, Fourwinds S, et al. Very early hypothermia induction in patients with severe brain injury (the national acute brain injury study: hypothermia II): a randomised trial. Lancet Neurol. 2011;10:131–9.
85. Clifton GL, Coffey CS, Fourwinds S, Zygun D, Valadka A, Smith KR, et al. Early induction of hypothermia for evacuated intracranial hematomas: a post hoc analysis of two clinical trials. J Neurosurg. 2012;117:714–20.
86. Andrews PJD, Sinclair HL, Rodriguez A, Harris BA, Battison CG, Rhodes JKJ, et al. Hypothermia for intracranial hypertension after traumatic brain injury. N Engl J Med. 2015;373:2403–12.
87. Cooper DJ, Nichol AD, Bailey M, Bernard S, Cameron PA, Pili-Floury S, et al. Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury. JAMA. 2018;320:2211.
88. Gaab MR, Trost HA, Alcantara A, Karimi-Nejad A, Moskopp D, Schultheiss R, et al. Ultrahigh dexamethasone in acute brain injury. Results from a prospective randomized double-blind multicenter trial (GUDHIS). German Ultrahigh Dexamethasone Head Injury Study Group. Zentralbl Neurochir. 1994;55:135–43.
89. Roberts I, Yates D, Sandercock P, Farrell B, Wasserberg J, Lomas G, et al. Effect of intravenous corticosteroids on death within 14 days in 10 008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial. Lancet. 2004;364:1321–8.
90. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. XV. Steroids. J Neurotrauma. 2007;24:S-91–5.
91. Powner DJ, Boccalandro C. Adrenal insufficiency following traumatic brain injury in adults. Curr Opin Crit Care. 2008;14:163–6.
92. Fan E, Skippen PW, Sargent MA, Cochrane DD, Chanoine J-P. Central adrenal insufficiency following traumatic brain injury: a missed diagnosis in the critically injured. Childs Nerv Syst. 2017;33: 2205–7.
93. Szurhaj W, Lamblin M-D, Kaminska A, Sediri H, Société de Neurophysiologie Clinique de Langue Française. EEG guidelines in the diagnosis of brain death. Neurophysiol Clin. 2015;45:97–104.
94. Smith M. Multimodality neuromonitoring in adult traumatic brain injury. Anesthesiology. 2018;128:401–15.
95. Hutchinson PJ, Jalloh I, Helmy A, Carpenter KLH, Rostami E, Bellander B-M, et al. Consensus statement from the 2014 International Microdialysis Forum. Intensive Care Med. 2015;41:1517–28.
96. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. X. Brain oxygen monitoring and thresholds. J Neurotrauma. 2007;24:S-65–70.
97. Bhardwaj A, Bhagat H, Grover V. Jugular venous oximetry. J Neuroanaesth Crit Care. 2015;2: 225–31.
98. Davies DJ, Su Z, Clancy MT, Lucas SJE, Dehghani H, Logan A, et al. Near-infrared spectroscopy in the monitoring of adult traumatic brain injury: a review. J Neurotrauma. 2015;32:933–41.
99. Martin NA, Patwardhan RV, Alexander MJ, Africk CZ, Lee JH, Shalmon E, et al. Characterization of cerebral hemodynamic phases following severe head trauma: hypoperfusion, hyperemia, and vasospasm. J Neurosurg. 1997;87:9–19.
100. Bouzat P, Oddo M, Payen J-F. Transcranial Doppler after traumatic brain injury. Curr Opin Crit Care. 2014;20:153–60.

101. Najafi MR, Tabesh H, Hosseini H, Akbari M, Najafi MA. Early and late posttraumatic seizures following traumatic brain injury: a five-year follow-up survival study. Adv Biomed Res. 2015;4:82.
102. Frey LC. Epidemiology of posttraumatic epilepsy: a critical review. Epilepsia. 2003;44:11–7.
103. Temkin NR, Dikmen SS, Anderson GD, Wilensky AJ, Holmes MD, Cohen W, et al. Valproate therapy for prevention of posttraumatic seizures: a randomized trial. J Neurosurg. 1999;91:593–600.
104. Temkin NR, Dikmen SS, Wilensky AJ, Keihm J, Chabal S, Winn HR. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. N Engl J Med. 1990;323:497–502.

20 Management of Patient with Motor Strip Gliomas (Awake Craniotomy)

L. Jane Easdown

Stem Case Terminology

A 50-year-old woman with new onset neurological symptoms is seen in the preoperative clinic 1 week prior to left temporal craniotomy for resection of tumor. Over the last month she has noticed left sided weakness and a difficulty with finding words. She is right handed. Prior medical history is significant for well-controlled hypertension, gastroesophageal reflux disease (GERD), and some mild obstructive sleep apnea (OSA) which does not require her to use a sleep device. Her past surgical history includes a hysterectomy under general anesthesia. Her medications include Lisinopril and omeprazole, and she was prescribed dexamethasone 2 weeks ago by the surgical team. In preparation for the surgery she had a functional MRI (fMRI) that showed that her speech center was significantly close to the tumor site. For this reason, the surgeon is intending to resect the tumor with the patient awake and able to participate in language and motor testing.

The patient is apprehensive but willing to learn more about awake craniotomy (AC).

Question 1:
What additional information will you need to obtain in the preoperative period?

Answer:
Preoperative preparation for the surgery is key to success. Not only do the medical issues of the patient require review but also there is an excellent opportunity to develop a trusting relationship with the patient [1]. As in any preoperative case you will need to review the patient's past medical and surgical history, anesthesia history, other medical conditions, medications, allergies, and family history. In addition to the usual physical examination of airway, respiratory and cardiac status, a detailed neurological exam should be performed documenting mental status, speech, and focal deficits. Preoperative testing for a patient with a tumor may include any of the following: electrolytes, CBC, coagulation studies, and type and screen for blood products. The anesthesia provider should review all neurological scans for tumor position, size, proximity to surrounding structures, degree of shift, or other evidence of raised intracranial pressure.

Selection for AC is determined by the ability of the patient to fully participate in the testing. There is no absolute contraindication to AC except patient refusal or the inability of the patient to participate. Many medical issues make this surgery challenging. This procedure has been performed with many high-risk patients

L. J. Easdown (✉)
Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, TN, USA
e-mail: jane.easdown@vumc.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_20

including those with significant obesity, OSA, pregnancy, hearing or language barrier but they have reached a successful conclusion [2–5]. Children as young as 11 years old have participated in AC [6].

This patient has a mild degree of OSA—this is a risk for airway obstruction and hypoventilation with sedation as well as increased sensitivity to sedation. It is important to obtain more history on sleep testing and perform a careful airway exam. During the procedure it will be important to monitor oxygenation and ventilation. She might need a nasal airway or other device support [7–9]. The use of continuous positive airway pressure (CPAP) devices has been reported during AC [10].

The patient is curious about the use of AC and language mapping—why is this approach better for her?

Question 2:
What factors support this approach for awake surgery?

Answer:
With her tumor so close to the language and motor centers, ensuring a complete resection and protecting her neurological function will be better accomplished with her ability to provide feedback on function. There is good evidence for this approach:

Dr. Wilder Penfield brought craniotomy with an awake patient to international attention through his work on epilepsy in the 1950s [11]. Through surgical and anesthesia advancements, AC is considered a safe and efficacious plan for lesions found in the eloquent areas of the brain compared with craniotomy under general anesthesia [12–17]. This patient has a glioma in the temporal lobe but AC has been the procedure of choice for other lesions including resection of epilepsy foci, angioma, metastatic lesions, aneurysm clipping, and AVM resection [18–22]. The determination to resect the tumor with the patient awake instead of using general anesthesia is made by determining the proximity of the tumor to the eloquent centers. The eloquent centers, including Wernicke and Broca's areas, are located predominantly on the left side of the brain in both right-handed and left-handed patients [23]. A complex of connections between these areas and the frontal lobe controls language. Repeat AC with language mapping has shown that these pathways demonstrate plasticity [24, 25]. A recent review article describes the research into this fascinating and complex topic [26].

To determine the proximity to the speech center and margins of the tumor, CT and MRI scans will be performed. The fMRI is a scan which determines active neural tissue with the patient performing certain tasks such as reading or speaking [27, 28]. There is evidence that this scan can assist in predicting surgical outcomes of speech [28]. With an AC, the patient is able to participate in speech, motor or sensory testing before and during resection of the tumor.

There has been very successful research concerning outcomes with AC versus craniotomy under general anesthesia, both retrospective and prospective. The desired outcome is better function in the postoperative period in regard to neurological function. Other outcomes include size of resection, patient satisfaction, and long-term survival. Compared with surgery with general anesthesia, several series have reported that patients have better outcomes generally [12, 29]. This includes greater resection of the tumor, especially important with glioma or other tumors [30–32]. A benefit to testing is that a greater amount of tumor may be resected in the awake patient protecting speech and motor centers and as a result have longer survival [32]. They demonstrate fewer neurological defects after surgery [17]. Some centers report using intraoperative MRI during AC [33, 34]. This is done to ensure best neurological outcome with the resection. Patient survival with AC compared with GA is difficult to determine because of tumor type, grade, and other patient co-morbidities [35].

There are also reports that patients with AC will have decreased length of hospital stay and decreased cost with AC, even some performed as outpatient surgery [29, 36, 37]. It is possible that AC might be a safe method to manage patients in low resource settings as well [38].

Our patient is eager to hear more and interested in how you might manage the anesthesia.

Question 3:
What anesthesia options are available to you to provide awake surgery?

Answer:
Centers performing this type of surgery report two techniques: monitored anesthesia care (MAC) or asleep-awake-asleep technique (AAA). There has been a lively debate concerning the efficacy of the two techniques with pros and cons [30, 39, 40]. These studies are limited in comparing the two because of the nature of the surgery, small numbers of patients, and institutional experience in one technique over the other. However, both are considered safe and have good patient acceptance [41].

The MAC approach has the patient sedated throughout the procedure without general anesthesia or airway assistance at any time. The AAA technique begins with general anesthesia and definitive airway management-oral or nasal endotracheal (ET) tube or LMA. When the surgeon is ready for the patient to assist in testing, the anesthesia will be reduced until consciousness is obtained. After testing and/or resection, anesthesia can be induced with return to the airway device or nasal prongs. Thus the patient is asleep, then awake and then asleep.

The advantage of the MAC technique is the avoidance of general anesthesia and airway management. A number of sedative medications have been used in this technique. The most common anesthesia agents are those that provide variable depth of sedation. Agents such as propofol and remifentanil infusions are used commonly. The use of dexmedetomidine for AC has been very successful for the MAC technique [42–44]. Incisional pain can be managed with infiltration along the path of the incision and the pin sites by the surgical team. Many centers use scalp blocks to more definitely block pain including the greater and lesser occipital nerves, great auricular, auriculotemporal, zygomaticotemporal, supratrochlear and supraorbital nerves [45, 46]. During resection, the surgeons can infiltrate the areas close to inflections of the dura and major arteries, as these are sensitive to pain. The brain tissue is insensitive except for these areas.

The AAA technique is also well accepted. Benefits include performing the craniotomy without a conscious patient eliminating pain or anxiety. The airway can be controlled and hyperventilation initiated. Anesthesia agents such as inhaled agents or total intravenous anesthesia (TIVA) method with propofol can be used [14]. With arousal however, there is a risk of emergence delirium until the patient has resumed a cooperative stage. At this stage it is possible to move in pins, lacerating the scalp. Patients may not make the transition to full cooperation and the procedure must be converted to general anesthesia missing the opportunity to test. The MAC technique avoids this possibility but patients with MAC may also fail and risk be converted to GA.

Generally each center develops a technique for surgery and anesthesia based on experience [39, 40].

The patient appears cooperative and keen to proceed understanding the benefits and risks. She would like to know the plans for the operative day.

Question 4:
Discuss your plan for anesthesia including risks and benefits.

Answer:
Developing a supportive relationship with the patient prior to surgery is key to the success of the process [1, 47]. This conversation should occur prior to the day of surgery with opportunity for open discussion and questions. The patient must feel confident in the success of the procedure. The expertise of the anesthesia and surgical teams should be emphasized. It is also important to be honest about the process and what will occur. Because the patient is awake, there needs to be a more detailed discussion of the events before and during the surgery. In the preoperative conversation, the following points should be made: perioperative medications, use of monitors, process of placing scalp blocks or wound infiltration and airway management. Airway devices might include nasal airways, ET tubes, or LMAs. The

position of the patient and padding should be explained. Klimek mentions the use of slides and short movies to orient the patient to the process [48]. Some centers use a horseshoe for head position and some pin with the Mayfield apparatus [49]. The patient should be aware of the testing that will occur and be shown the materials that might be used-pictures of items, etc. It should be emphasized that the anesthesia team will always be in attendance. Many centers have a neuropsychologist meet with the patients if that person is going to do the testing [50].

This is an excellent time to speak of potential complications. Minor complaints involve thirst or positioning discomfort. Significant risks such as seizures or the need to convert to GA for anxiety or pain can occur. The patient can be advised that these complications are rare and can be addressed immediately.

On the day of surgery you see the patient in the holding area. She and her husband are quite anxious but still committed to going ahead.

20.1 Preoperative

Question 5:
What should be the preoperative instructions to the patient? What can you use for preoperative medications?

Answer:
The patient should be NPO according to institutional guidelines. Prior to surgery this patient will be counseled to take her dexamethasone and her lisinopril on the day of surgery. If the patient has been prescribed epilepsy medications by the surgeon, they should be continued. The use of ACE and ARBS prior to surgery is controversial [51–53]. Eseoni et al. found MAC patients in their series of 81 patients had more hypertension than the AAA group [30]. For awake procedures, since there is more risk of hypertension, there is a case for continuing with daily antihypertensive medications. Perioperative pain is a concern and a multimodal approach is often used. A review of perioperative anesthesia medications used in AC shows the following meds: midazolam, ondansetron, clonidine, acetaminophen, metoclopramide, diclofenac, atenolol, scopolamine, and haloperidol [40]. In this publication, there is a comprehensive table of all sedatives and local anesthetics used in AC. https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0156448.t002 (this is an open access publication and they are ok with publishing if given the citation).

Nausea is not a common complaint but preemptive treatment can be used based on patient's co-morbidities and age. Benzodiazepines may be used for intractable anxiety. The addition of these medications should be balanced against the potential for sedation and risk for failure to arouse for testing. There is always a risk and benefit with sedation for neurological procedures—risk of oversedation and change of mental status, and hypoventilation leading to raised ICP. Sedation should be added judiciously and might be delayed until full monitoring can be applied in the operating room. In our center we begin the loading infusion of dexmedetomidine on entry to the room. Some centers report using no sedation at all [54].

Intraoperative sedation can be maintained with low dose propofol (20–50 μ/kg/min) with remifentanil (0.01–0.05 μ/kg/min) or dexmedetomidine (0.3–0.5 μ/kg/h).

The surgeons might order antiepilepsy medications in the perioperative period although this is controversial in patients without demonstrated seizure activity [13]. The most common one prescribed is levetiracetam. Seizures during cortical electrical stimulation are a risk to the patient and might terminate the testing. In Nossek's study of failed AC, 2% were due to seizures [55]. The surgical team might also order dexamethasone and mannitol if these are being used.

The patient is calm and cooperative as you apply monitors.

20.2 Intraoperative

Question 6:
In addition to standard ASA monitors, what will you use to monitor this patient?

Answer:
Most centers place an arterial line for blood pressure management and blood testing. All IVs and

arterial lines will be placed with local anesthesia and should be placed on the contralateral side from the brain lesion, if possible, so as not to interfere with motor testing. The urinary catheter should be placed in a private location prior to entering the operating room. An additional intravenous catheter should be placed for dedicated infusions especially if remifentanil is to be used. An inadvertent bolus of remifentanil can lead to apnea and hypercapnia in the awake patient. When using specially designed nasal prongs it is possible to measure respiratory rate. The ETco2 will not be accurate but the provider can obtain an end-tidal carbon dioxide trend.

The patient is properly sedated and all monitors applied. You are ready to perform scalp blocks.

Question 7:
Describe the procedure for placing scalp blocks. What local anesthesia will you use? Is Exparel acceptable?

Answer:
Scalp blocks for AC have been well described [45]. There are 6 nerves that require blocking: the greater and lesser occipital nerves, great auricular, auriculotemporal, zygomaticotemporal, supratrochlear and supraorbital nerves (Fig. 20.1 from Osborn). The largest nerve, the greater occipital, should be blocked first to allow time for effect. In our practice, the attending physician performs the blocks on the surgical side and the trainee on the other. It has been recommended to block selectively if the craniotomy is anterior or posterior (Table 20.1) but in our practice, we block all nerves in anticipation of pinning.

Local anesthesia medications should be chosen for fast onset and duration of action. The total amount of local anesthesia should not reach the toxic level for the patient. This usually requires mixing the medications. Bupivacaine 0.25 and 0.5%, ropivacaine and lidocaine have been noted with or without the addition of epinephrine [40]. Each nerve is blocked with 2–5 ccs of the local anesthesia. Onset is rapid. Pin sites and incision site can also be infiltrated as long as the total amount of local anesthetic agent does not reach the toxic level. The long-acting liposomal bupivacaine (Exparel) is not released for scalp blocks at this time.

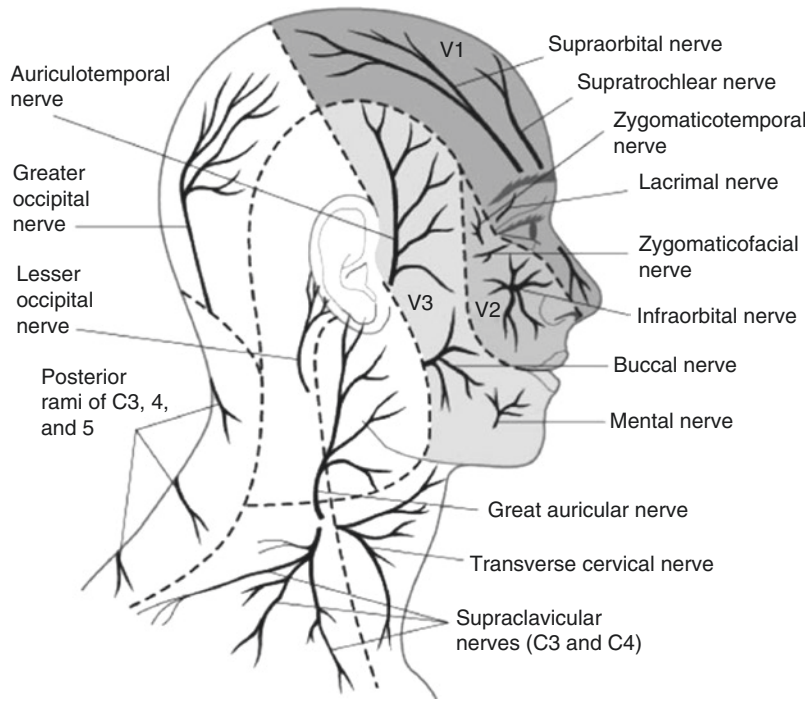


Fig. 20.1 Innervation of the scalp and face. (Source: Lalwani AK: Current Diagnosis &Treatment in Otolaryngology_Head and Neck Surgery, 2nd edition: http://www.accessmedicine.com. Authorization obtained from McGraw-Hill companies to use this copyrighted material)

Table 20.1 Nerves to be blocked for craniotomy

Nerves to be blocked	Branch	Anterior craniotomy	Posterior craniotomy
Supraorbital	Ophthalmic branch of TG n	Yes	No
Supratrochlear	Ophthalmic branch of TG n	Yes	No
Auriculotemporal	Mandibular branch of TG n	Yes	No
Zygomaticotemporal	Maxillary branch of TG n	Yes	Yes
Greater occipital	Posterior ramus of C2	No	Yes
Lesser occipital	Ventral rami of C2, C3	No	Yes

The table displays the six nerves blocked for craniotomy, their origins, and whether they should be blocked for anterior or posterior craniotomies
C indicates cervical nerve, *n* nerve, *TG* trigeminal

The patient is turned onto her right side on a well-padded OR bed and she tolerates placement of cranial pins indicating successful nerve blocks. The surgeons start the craniotomy. The patient find the pressure is hurting her.

Question 8:
What can you do to improve her pain control at this time?

Answer:
The comfort of the patient is crucial to proceeding. In a study of nine French hospital centers, over 50% of patients admit to some pain during AC usually characterized by a 1–2/10 pain rating. But 25% admitted to moderate amounts of pain [56]. Firstly the patient should be questioned concerning the pain quality. Dull aching or headache might be due to pressure on intracranial sensitive structures. The surgeons should infiltrate areas known to be sensitive—especially the dura mater of the skull base, the falx cerebri, and the leptomeninges of the lateral fissure and neighboring sulci. Sedation should be increased. Infusions of remifentanil can be increased as tolerated by respiratory rate. Infusions of propofol or dexmedetomidine can be increased. It is also useful to distract the patient from unnecessary noise or other activities in the room that might increase anxiety. Choosing her favorite music can be very helpful and has been used successfully to decrease anxiety in AC [57]. Two studies note the use of hypnosis during AC with some success in averting anxiety [58, 59]. In most cases, all of the above will improve conditions. In the cases investigated by Nossek, no failure was attributed to inability to control pain [55].

Nausea is also not a common complaint. Manninen found that patients with AC had less nausea within the first 4 h after surgery compared with GA craniotomy patients [60]. Nausea is not only a significant factor for patient satisfaction but it is also a concern for safety. Emesis might lead to aspiration with the patient unable to move in pins. At this time it is reasonable to increase the levels of medications already given and add to them additional agents such as promethazine with the understanding that this will have a sedative effect.

The surgeon indicates that it is time in 30 min to map out the parameter for resection and ask the patient to speak.

Question 9:
Describe the procedure to examine the patient for fluent speech. How will you convey information convey information to the surgeon?

Answer:
This is a critical time in the procedure. The patient must be aroused from sedation or GA and respond.

At this time for cases progressing with MAC technique, the level of sedation is lowered or removed. Some recommend infusions of low amounts of remifentanil (0.01–0.05 μ/kg/min) or dexmedetomidine (0.3–0.5 μ/kg/min) to continue. There was a concern that adequate cortical stimulation could not occur with ongoing sedation but studies have shown it can be used during the testing [43]. With the sedation decreasing, the

patient should be oriented to the task and reassured. With the patient able to hear and speak, the neurocognitive testing can begin.

For patients with the AAA method, arousal is more complex. The patient is emerging from general anesthesia with the potential for a stormy transition to full awareness. The process can be prolonged. The hyperactive emergence delirium can lead to combative behavior with risk of injury such as scalp lacerations. Hypoactive delirium can reduce the opportunity to do the awake testing. If an LMA or oral ET tube has been used, it will be removed with the risk of airway obstruction or laryngospasm. The nasal ET tube can be moved back to the pharynx and readvanced at the termination of testing. All have been described for the AAA technique.

Once the patient is fully alert and able to converse, the testing will begin. The surgeon will stimulate the cortex close to the lesion to delineate the margins of the tumor. Electrical stimulation mapping (ESM) is the gold standard [61, 62], ESM is done with an Ojemann stimulator and 2.4–6 mV stimuli are used on the cortex. The small amount of current is used to avoid risk of seizure. Both involve stimulation of the surrounding cortex while the patient is active in language tasks. The mapping is done to determine the cortical and also the subcortical tracts that constitute the speech centers [63].

A neuropsychologist or neurologist might carry out the testing. In many centers, the anesthesia provider carries out this task. Many studies concerning AC do not provide details about how the language testing is carried out. There is no standardization to the process. Most centers mention the patient reciting numbers or the alphabet. The patient might name objects or read out loud. Some require the patient to hold a conversation during testing and resection. Abnormalities would be aphasia or anomia, the inability to name an object, or arrest of speech. De Witte advocates for standardized language testing before and after the surgery and using a standardized approach to testing during the surgery. His team has developed a standardized Dutch linguistic test battery (measuring phonology, semantics, syntax) to reliably identify the critical language centers [64, 65]. This testing is used pre/post and during the surgery.

The patient initially presented with left sided weakness. How are the motor centers tested?

Question 10:
How is the motor testing carried out?

Answer:
If the tumor is located near the primary motor strip (M1), there are methods to test during AC. The direct cortical stimulation is also done to determine the extent of the motor cortex involved in the tumor. It is possible to use the same direct cortical stimulation on the motor areas. Shinoura and colleagues describe the process using a modified Ojemann stimulator using 3–5 mA, 60 Hz biphasic 1 ms/phase for 4 s [66]. During the stimulation, they ask the patient to move the face and tongue, clench hands and demonstrate flexion of elbows and knees on the contralateral side. The low current is used to avoid seizure activity [66–68]. The motor functions can also be tested with the patient having craniotomy with GA. The same stimulation can be applied using motor evoked potentials and SSEPS with phase reversal.

The testing is going well and the patient is cooperating with the object naming but notices that her toes are twitching. You suspect she may be experiencing some seizure activity.

Question 11:
How do you manage an intraoperative seizure?

Answer:
Seizures can be focal or generalized. The patient might be aware of an oncoming seizure or it might be observed by the anesthesia provider or by EEG monitoring if it is being used. With a generalized seizure, there is risk to the patient with loss of consciousness, uncontrolled movements, scalp lacerations, neck injury, and potential loss of airway. In the postictal state, the patient might not be able to continue with testing. In the recent review of AC by Kulikov, the efficacy of antiepileptic medications for prevention of seizures is not com-

plete but the agent most prescribed is levetiracetam [14]. When intraoperative seizures occur, the first step in management is to alert the surgeon and halt stimulation. The surgeon will pour cold saline over the cortex to stop electrical spread. If this does not correct the problem, then the seizure must be treated with additional levetiracetam and benzodiazepines or small doses of propofol. In a large retrospective series by Hervey-Jumper of over 600 cases of AC, the incidence of seizures was 3% and depended on the site of the tumor and the preexisting incidence of epilepsy. The seizures responded to cold saline but three patients were unable to complete testing [4]. A meta-analysis of 25 studies of AC looked at seizure in the perioperative course of AC. The incidence is in the range of 8–10% [69]. Retrospective series have identified seizures as a significant problem to be anticipated in AC requiring quick work by the surgical and anesthesia team. Nossek found patients with seizures during AC were more likely to be young, have frontal tumors and have an existing seizure history [70]. Spena surveyed a group of 20 European centers preforming ACs to question to use of antiepileptic medications. The incidence of seizures was quite wide—2.5–54%. It should be noted that over 50% used EEG or electrocortography (ECoG) as a monitor. The authors noted that seizures might be linked to the mastery of mapping technique. In this series, the risk of seizures increased with preexisting epilepsy. Seizure occurrence was similar in patients with or without perioperative drugs [13]. ECOG is a common monitor used during surgery for epileptic foci. It can be used in AC for tumor but the use might be not useful [61].

The surgeon has completed mapping and is requesting the patient sleep for resection. The brain is a bit tight.

Question 12:
What can be done to improve the conditions for the surgical team?

Answer:
In the awake patient, it is not possible to control respiration and hyperventilate. There are a few maneuvers that can improve conditions—elevating the head, decreasing sedation to improve respiration and use of mannitol. If the surgeon has no additional need for the patient's assistance, GA could be induced with replacement of ET tube (nasal intubation) or LMA and then hyperventilation could be initiated.

The surgeon informs you that there might be some blood loss in the next few minutes.

Question 13:
What would you do if a major vessel was incised and the surgeons alert you to bleeding?

Answer:
The potential for active bleeding in AC is very low because the structures involved are superficial. Nevertheless, in the preoperative stage the patients should be consented for transfusion of blood or blood products and type and screen should be sent. Management of active bleeding in an awake patient requires maintaining verbal contact with the patient, calling for help, assessing vital signs, sending appropriate blood tests, and all doing so in a calm and efficient manner. It is the judgment of the anesthesia provider to determine if the airway should be secured and GA induced until hemostasis is achieved.

The surgeons have completed the resection. They are ready to close the incision.

Question 14:
What plans will you make for the post resection management of this patient?

Answer:
At this time further testing of the patient will not be necessary. In the MAC cases, the sedation can be reapplied. Very little sedation is needed as the patient is likely to be exhausted from the experience. Sedation might include dexmedetomidine, remifentanil or propofol and sedatives such as benzodiazepines are now acceptable. The patency of the airway will require attention. Nasal airways or other airway adjuncts might need to be reinstated if it was removed. In patients with the AAA technique, GA will be induced and the airway reinstalled. Use of LMA is common at this time instead of ET tube placement.

Most centers will recover the patient in the ICU to perform neurological vital signs for a

certain number of hours. The usual stay for AC might be decreased compared with GA patients. One center in Canada has reported success with same day surgery for craniotomy with a protocol for patient selection and a team for standardized care [71–73]. Clearly the requirement for 24-h vital signs is not a rule and must be guided by patient safety.

You see the patient the next morning and she is stable but complaining of nausea and headache. She is delighted that the surgery is completed and was so successful.

20.3 Postoperative

Question 15:
What factors effect the satisfaction of patients and AC? What could you do to improve her postoperative course?

Answer:
The postoperative visit and follow-up is especially important for AC. The ultimate goal of AC is to protect the language/motor and/or sensory function of the patient while performing the best possible resection. The surgeon has spoken to the patient about the surgical outcomes and any further testing, scans or oncology follow up treatments. It is the job of the anesthesia provider to provide feedback about the procedures and elicit patient reflection and feedback. In the postop visit, you will need to emphasize the importance of the procedure they have participated in. The patient should be commended on their efforts and success. It is truly an amazing task they have accomplished. There have been several studies of surveys or questionnaires given to patients following AC. Klimek followed up 61 patients and inquired about memories of the procedure. All the patients had had the MAC technique so they had received varying amounts of sedation. The memories were mainly neutral or positive. The discomfort that they recalled was related to placement of the Mayfield pins, the discomfort from lying still for the case and the discomfort from the urinary catheter. Overall the patients demonstrated high satisfaction [74]. Another postoperative survey of 15 patients with the AAA technique demonstrated that most recollected various aspects of the procedure although awake for 45 min or less. Three patients (20%) had little memory of actually being awake during the surgery. A minority reported more than minor discomfort (20%), fear (15%), or anxiety (29%). Reports of discomfort mentioned the pain from the cranial pin holding device, operative position (hard uncomfortable bed), pain in the wound with infiltration and the urinary catheter [47]. Milian reviewed 12 studies of AC (396 patients) performed with both AAA and MAC techniques between 1998 and 2013. Patients responded to postoperative interviews or questionnaires. Overall, the patients felt well prepared and satisfaction was high. Thirty percent reported a memory of considerable pain and 10–14% recalled anxiety. In all patients noted there were no cases of posttraumatic stress disorder [75]. In a similar review of AC patients from five European centers, 105 patients were surveyed. The patient questionnaire revealed that the majority of patients feel comfortable with the procedure. Pain levels on a 10-cm visual analogue scale were 1.3 cm at the beginning, 1.9 cm the middle, and 2.1 cm at the end of awake phase. Levels of anxiety were positive yet low. The highest mean anxiety levels were noted in women and patients less than 60 years of age. Discomfort resulted from head fixation or positioning [76].

From these studies it is clear that patient who elect to have surgery for brain lesions under AC has a good experience generally. However, a fair proportion still experience pain and anxiety. Environmental conditions can be improved—padding of the OR bed, elimination of cranial pins, local anesthesia gel for urinary catheter placement, or use of condom catheters in male patients.

Multiple Choice Questions

1. Which of the following neurological problems is most likely to require AC?
   (a) Dysphagia
   (b) Tremor
   (c) Dysesthesia over left upper extremity
   (d) Ataxia
   (e) Anomia
   Answer: e

All of the above are neurological symptoms. The most common reason to perform AC is a defect found in the language center so the best answer from this list is anomia—the inability to name items. Awake procedures are performed for deep brain stimulation for tremors but this is not a craniotomy procedure.

2. What patient described below would not be acceptable as a candidate for an AC?
   (a) Patient with hearing disability who uses sign language
   (b) 8-year-old child
   (c) Pregnant woman at 20 weeks gestation
   (d) Patient with BMI 50
   (e) All are acceptable

   Answer: e

   All of these patients have been described in case reports.
3. Which nerves require blocking?
   (a) Supratrochlear, greater auricular, lesser occipital
   (b) Supraorbital, zygomaticofacial, greater auricular
   (c) Greater occipital, temporal, supraorbital
   (d) Facial, supratrochlear, lesser orbital
   (e) Supraorbital, subtrochlear, lesser occipital

   Answer: a

   Just memory really!
4. After calling for help, what is the first step to initiate if the patient experiences a generalized seizure?
   (a) Notify the surgeon
   (b) Application of cold saline to cortex
   (c) Begin infusion of keppra
   (d) Administer 2 mg of midazolam
   (e) Place LMA

   Answer: a

   The surgeon must initiate the cold saline so alerting them is the first step in treatment.
5. What would be a valid indication to abandon the procedure?
   (a) Pain > 2
   (b) Focal Seizure
   (c) Anxiety
   (d) Patient refusal to participate
   (e) Tumor invasion of deep structures

   Answer: d

Patient cooperation and consent is best reason on this list.

References

1. Meng L, McDonagh DL, Berger MS, Gelb AW. Anesthesia for awake craniotomy: a how-to guide for the occasional practitioner. Can J Anaesth. 2017;64(5):517–29.
2. Dreier JD, Williams B, Mangar D, Camporesi EM. Patients selection for awake neurosurgery. HSR Proc Intensive Care Cardiovasc Anesth. 2009;1(4):19–27.
3. Garavaglia MM, Das S, Cusimano MD, Crescini C, Mazer CD, Hare GM, et al. Anesthetic approach to high-risk patients and prolonged awake craniotomy using dexmedetomidine and scalp block. J Neurosurg Anesthesiol. 2014;26(3):226–33.
4. Hervey-Jumper SL, Li J, Lau D, Molinaro AM, Perry DW, Meng L, et al. Awake craniotomy to maximize glioma resection: methods and technical nuances over a 27-year period. J Neurosurg. 2015;123(2): 325–39.
5. Meng L, Han SJ, Rollins MD, Gelb AW, Chang EF. Awake brain tumor resection during pregnancy: decision making and technical nuances. J Clin Neurosci. 2016;24:160–2.
6. Sheshadri V, Chandramouli BA. Pediatric awake craniotomy for seizure focus resection with dexmedetomidine sedation-a case report. J Clin Anesth. 2016;32:199–202.
7. Skucas AP, Artru AA. Anesthetic complications of awake craniotomies for epilepsy surgery. Anesth Analg. 2006;102(3):882–7.
8. Sivasankar C, Schlichter RA, Baranov D, Kofke WA. Awake craniotomy: a new airway approach. Anesth Analg. 2016;122(2):509–11.
9. Gross JB, Bachenberg KL, Benumof JL, Caplan RA, Connis RT, Cote CJ, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology. 2006;104(5):1081–93; quiz 117–8.
10. Huncke T, Chan J, Doyle W, Kim J, Bekker A. The use of continuous positive airway pressure during an awake craniotomy in a patient with obstructive sleep apnea. J Clin Anesth. 2008;20(4):297–9.
11. Ladino LD, Rizvi S, Tellez-Zenteno JF. The montreal procedure: the legacy of the great wilder penfield. Epilepsy Behav. 2018;83:151–61.
12. Gerritsen JKW, Vietor CL, Rizopoulos D, Schouten JW, Klimek M, Dirven CMF, et al. Awake craniotomy versus craniotomy under general anesthesia without surgery adjuncts for supratentorial glioblastoma in eloquent areas: a retrospective matched case-control study. Acta Neurochir. 2019;161(2):307-315.

13. Spena G, Schucht P, Seidel K, Rutten GJ, Freyschlag CF, D'Agata F, et al. Brain tumors in eloquent areas: a European multicenter survey of intraoperative mapping techniques, intraoperative seizures occurrence, and antiepileptic drug prophylaxis. Neurosurg Rev. 2017;40(2):287–98.
14. Kulikov A, Lubnin A. Anesthesia for awake craniotomy. Curr Opin Anaesthesiol. 2018;31(5):506–10.
15. Sacko O, Lauwers-Cances V, Brauge D, Sesay M, Brenner A, Roux FE. Awake craniotomy vs surgery under general anesthesia for resection of supratentorial lesions. Neurosurgery. 2011;68(5):1192–8. discussion 8-9.
16. Rajan S, Cata JP, Nada E, Weil R, Pal R, Avitsian R. Asleep-awake-asleep craniotomy: a comparison with general anesthesia for resection of supratentorial tumors. J Clin Neurosci. 2013;20(8):1068–73.
17. Eseonu CI, Rincon-Torroella J, ReFaey K, Lee YM, Nangiana J, Vivas-Buitrago T, et al. Awake craniotomy vs craniotomy under general anesthesia for perirolandic gliomas: evaluating perioperative complications and extent of resection. Neurosurgery. 2017;81(3):481–9.
18. Gamble AJ, Schaffer SG, Nardi DJ, Chalif DJ, Katz J, Dehdashti AR. Awake craniotomy in arteriovenous malformation surgery: the usefulness of cortical and subcortical mapping of language function in selected patients. World Neurosurg. 2015;84(5):1394–401.
19. Zanello M, Wager M, Corns R, Capelle L, Mandonnet E, Fontaine D, et al. Resection of cavernous angioma located in eloquent areas using functional cortical and subcortical mapping under awake conditions. Outcomes in a 50-case multicentre series. Neurochirurgie. 2017;63(3):219–26.
20. Passacantilli E, Anichini G, Cannizzaro D, Fusco F, Pedace F, Lenzi J, et al. Awake craniotomy for trapping a giant fusiform aneurysm of the middle cerebral artery. Surg Neurol Int. 2013;4:39.
21. Erickson KM, Cole DJ. Anesthetic considerations for awake craniotomy for epilepsy. Anesthesiol Clin. 2007;25(3):535–55. ix
22. Chua TH, See AAQ, Ang BT, King NKK. Awake craniotomy for resection of brain metastases: a systematic review. World Neurosurg. 2018;120:e1128–e35.
23. Tzourio N, Crivello F, Mellet E, Nkanga-Ngila B, Mazoyer B. Functional anatomy of dominance for speech comprehension in left handers vs right handers. NeuroImage. 1998;8(1):1–16.
24. Southwell DG, Hervey-Jumper SL, Perry DW, Berger MS. Intraoperative mapping during repeat awake craniotomy reveals the functional plasticity of adult cortex. J Neurosurg. 2016;124(5):1460–9.
25. Chang WH, Pei YC, Wei KC, Chao YP, Chen MH, Yeh HA, et al. Intraoperative linguistic performance during awake brain surgery predicts postoperative linguistic deficits. J Neuro-Oncol. 2018;139(1):215–23.
26. Lim LH, Idris Z, Reza F, Wan Hassan WMN, Mukmin LA, Abdullah JM. Language mapping in awake surgery: report of two cases with review of language networks. Asian J Neurosurg. 2018;13(2):507–13.
27. Kim, Nadkarni TN, Andreoli MJ, Nair VA, Yin P, Young BM, et al. Usage of fMRI for pre-surgical planning in brain tumor and vascular lesion patients: task and statistical threshold effects on language lateralization. NeuroImage Clin. 2015;7:415–23.
28. Kundu B, Penwarden A, Wood JM, Gallagher TA, Andreoli MJ, Voss J, et al. Association of functional magnetic resonance imaging indices with postoperative language outcomes in patients with primary brain tumors. Neurosurg Focus. 2013;34(4):E6.
29. Brown T, Shah AH, Bregy A, Shah NH, Thambuswamy M, Barbarite E, et al. Awake craniotomy for brain tumor resection: the rule rather than the exception? J Neurosurg Anesthesiol. 2013;25(3):240–7.
30. Eseonu CI, ReFaey K, Garcia O, John A, Quinones-Hinojosa A, Tripathi P. Awake craniotomy anesthesia: a comparison of the monitored anesthesia care and asleep-awake-asleep techniques. World Neurosurg. 2017;104:679–86.
31. Kim SS, McCutcheon IE, Suki D, Weinberg JS, Sawaya R, Lang FF, et al. Awake craniotomy for brain tumors near eloquent cortex: correlation of intraoperative cortical mapping with neurological outcomes in 309 consecutive patients. Neurosurgery. 2009;64(5):836–45; discussion 345–6.
32. Yordanova YN, Moritz-Gasser S, Duffau H. Awake surgery for WHO grade II gliomas within "noneloquent" areas in the left dominant hemisphere: toward a "supratotal" resection. Clinical article. J Neurosurg. 2011;115(2):232–9.
33. Whiting BB, Lee BS, Mahadev V, Borghei-Razavi H, Ahuja S, Jia X, et al. Combined use of minimal access craniotomy, intraoperative magnetic resonance imaging, and awake functional mapping for the resection of gliomas in 61 patients. J Neurosurg 2019:1–9.
34. Maldaun MV, Khawja SN, Levine NB, Rao G, Lang FF, Weinberg JS, et al. Awake craniotomy for gliomas in a high-field intraoperative magnetic resonance imaging suite: analysis of 42 cases. J Neurosurg. 2014;121(4):810–7.
35. Hervey-Jumper SL, Berger MS. Technical nuances of awake brain tumor surgery and the role of maximum safe resection. J Neurosurg Sci. 2015;59(4):351–60.
36. Eseonu CI, Rincon-Torroella J, ReFaey K, Quinones-Hinojosa A. The cost of brain surgery: awake vs asleep craniotomy for perirolandic region tumors. Neurosurgery. 2017;81(2):307–14.
37. Nassiri F, Li L, Badhiwala JH, Yeoh TY, Hachem LD, Moga R, et al. Hospital costs associated with inpatient versus outpatient awake craniotomy for resection of brain tumors. J Clin Neurosci. 2019;59:162–6.
38. Howe KL, Zhou G, July J, Totimeh T, Dakurah T, Malomo AO, et al. Teaching and sustainably implementing awake craniotomy in resource-poor settings. World Neurosurg. 2013;80(6):e171–4.
39. Suero Molina E, Schipmann S, Mueller I, Wolfer J, Ewelt C, Maas M, et al. Conscious sedation with dexmedetomidine compared with asleep-awake-asleep craniotomies in glioma surgery: an analysis of 180 patients. J Neurosurg. 2018;129(5):1223–30.

40. Stevanovic A, Rossaint R, Veldeman M, Bilotta F, Coburn M. Anaesthesia management for awake craniotomy: systematic review and meta-analysis. PLoS One. 2016;11(5):e0156448.
41. Meng L, Berger MS, Gelb AW. The potential benefits of awake craniotomy for brain tumor resection: an anesthesiologist's perspective. J Neurosurg Anesthesiol. 2015;27(4):310–7.
42. Mack PF, Perrine K, Kobylarz E, Schwartz TH, Lien CA. Dexmedetomidine and neurocognitive testing in awake craniotomy. J Neurosurg Anesthesiol. 2004;16(1):20–5.
43. Souter MJ, Rozet I, Ojemann JG, Souter KJ, Holmes MD, Lee L, et al. Dexmedetomidine sedation during awake craniotomy for seizure resection: effects on electrocorticography. J Neurosurg Anesthesiol. 2007;19(1):38–44.
44. Bekker AY, Kaufman B, Samir H, Doyle W. The use of dexmedetomidine infusion for awake craniotomy. Anesth Analg. 2001;92(5):1251–3.
45. Osborn I, Sebeo J. "Scalp block" during craniotomy: a classic technique revisited. J Neurosurg Anesthesiol. 2010;22(3):187–94.
46. McAuliffe N, Nicholson S, Rigamonti A, Hare GMT, Cusimano M, Garavaglia M, et al. Awake craniotomy using dexmedetomidine and scalp blocks: a retrospective cohort study. Can J Anaesth. 2018;65(10):1129–37.
47. Whittle IR, Midgley S, Georges H, Pringle AM, Taylor R. Patient perceptions of "awake" brain tumour surgery. Acta Neurochir. 2005;147(3):275–7; discussion 277.
48. Klimek M, van der Horst PH, Hoeks SE, Stolker RJ. Quality and quantity of memories in patients who undergo awake brain tumor resection. World Neurosurg. 2018;109:e258–e64.
49. Suess O, Picht T, Kuehn B, Mularski S, Brock M, Kombos T. Neuronavigation without rigid pin fixation of the head in left frontotemporal tumor surgery with intraoperative speech mapping. Neurosurgery. 2007;60(4 Suppl 2):330–8. discussion 8.
50. Pinsker MO, Nabavi A, Mehdorn HM. Neuronavigation and resection of lesions located in eloquent brain areas under local anesthesia and neuropsychological-neurophysiological monitoring. Minim Invasive Neurosurg. 2007;50(5):281–4.
51. Nathan N. Take it or leave it: a meta-analysis of perioperative ACE inhibitors and ARBs. Anesth Analg. 2018;127(3):589.
52. Bradic N, Povsic-Cevra Z. Surgery and discontinuation of angiotensin converting enzyme inhibitors: current perspectives. Curr Opin Anaesthesiol. 2018;31(1):50–4.
53. Walker SLM, Abbott TEF, Brown K, Pearse RM, Ackland GL. Perioperative management of angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers: a survey of perioperative medicine practitioners. PeerJ. 2018;6:e5061.
54. Sitnikov AR, Grigoryan YA, Mishnyakova LP. Awake craniotomy without sedation in treatment of patients with lesional epilepsy. Surg Neurol Int. 2018;9:177.
55. Nossek E, Matot I, Shahar T, Barzilai O, Rapoport Y, Gonen T, et al. Failed awake craniotomy: a retrospective analysis in 424 patients undergoing craniotomy for brain tumor. J Neurosurg. 2013;118(2):243–9.
56. Fontaine D, Almairac F. Pain during awake craniotomy for brain tumor resection. Incidence, causes, consequences and management. Neurochirurgie. 2017;63(3):204–7.
57. Wu PY, Huang ML, Lee WP, Wang C, Shih WM. Effects of music listening on anxiety and physiological responses in patients undergoing awake craniotomy. Complement Ther Med. 2017;32:56–60.
58. Frati A, Pesce A, Palmieri M, Iasanzaniro M, Familiari P, Angelini A, et al. Hypnosis-aided awake surgery for the management of intrinsic brain tumors versus standard awake-asleep-awake protocol: a preliminary, promising experience. World Neurosurg. 2019;121:e882–e91.
59. Zemmoura I, Fournier E, El-Hage W, Jolly V, Destrieux C, Velut S. Hypnosis for awake surgery of low-grade gliomas: description of the method and psychological assessment. Neurosurgery. 2016;78(1):53–61.
60. Manninen PH, Tan TK. Postoperative nausea and vomiting after craniotomy for tumor surgery: a comparison between awake craniotomy and general anesthesia. J Clin Anesth. 2002;14(4):279–83.
61. Bauer PR, Vansteensel MJ, Bleichner MG, Hermes D, Ferrier CH, Aarnoutse EJ, et al. Mismatch between electrocortical stimulation and electrocorticography frequency mapping of language. Brain Stimul. 2013;6(4):524–31.
62. So EL, Alwaki A. A guide for cortical electrical stimulation mapping. J Clin Neurophysiol. 2018;35(2):98–105.
63. Duffau H, Capelle L, Denvil D, Sichez N, Gatignol P, Taillandier L, et al. Usefulness of intraoperative electrical subcortical mapping during surgery for low-grade gliomas located within eloquent brain regions: functional results in a consecutive series of 103 patients. J Neurosurg. 2003;98(4):764–78.
64. De Witte E, Satoer D, Robert E, Colle H, Verheyen S, Visch-Brink E, et al. The Dutch linguistic intraoperative protocol: a valid linguistic approach to awake brain surgery. Brain Lang. 2015;140:35–48.
65. De Witte E, Marien P. The neurolinguistic approach to awake surgery reviewed. Clin Neurol Neurosurg. 2013;115(2):127–45.
66. Shinoura N, Yoshida M, Yamada R, Tabei Y, Saito K, Suzuki Y, et al. Awake surgery with continuous motor testing for resection of brain tumors in the primary motor area. J Clin Neurosci. 2009;16(2):188–94.
67. Shinoura N, Yamada R, Tabei Y, Saito K, Suzuki Y, Yagi K. Advantages and disadvantages of awake surgery for brain tumours in the primary motor cortex: institutional experience and review of literature. Br J Neurosurg. 2011;25(2):218–24.

68. Shinoura N, Midorikawa A, Yamada R, Hana T, Saito A, Hiromitsu K, et al. Awake craniotomy for brain lesions within and near the primary motor area: a retrospective analysis of factors associated with worsened paresis in 102 consecutive patients. Surg Neurol Int. 2013;4:149.
69. Yuan Y, Peizhi Z, Xiang W, Yanhui L, Ruofei L, Shu J, et al. Intraoperative seizures and seizures outcome in patients underwent awake craniotomy. J Neurosurg Sci. 2019;63(3):301–7.
70. Nossek E, Matot I, Shahar T, Barzilai O, Rapoport Y, Gonen T, et al. Intraoperative seizures during awake craniotomy: incidence and consequences: analysis of 477 patients. Neurosurgery. 2013;73(1):135–40; discussion 140.
71. Bernstein M. Outpatient craniotomy for brain tumor: a pilot feasibility study in 46 patients. J Can Sci Neurol. 2001;28(2):120–4.
72. Carrabba G, Venkatraghavan L, Bernstein M. Day surgery awake craniotomy for removing brain tumours: technical note describing a simple protocol. Minim Invasive Neurosurg. 2008;51(4):208–10.
73. Venkatraghavan L, Bharadwaj S, Au K, Bernstein M, Manninen P. Same-day discharge after craniotomy for supratentorial tumour surgery: a retrospective observational single-centre study. Can J Anaesth. 2016;63(11):1245–57.
74. van Ark TJ, Klimek M, de Smalen P, Vincent A, Stolker RJ. Anxiety, memories and coping in patients undergoing intracranial tumor surgery. Clin Neurol Neurosurg. 2018;170:132–9.
75. Milian M, Tatagiba M, Feigl GC. Patient response to awake craniotomy—a summary overview. Acta Neurochir. 2014;156(6):1063–70.
76. Beez T, Boge K, Wager M, Whittle I, Fontaine D, Spena G, et al. Tolerance of awake surgery for glioma: a prospective European low grade glioma network multicenter study. Acta Neurochir. 2013;155(7):1301–8.

Suggested Reading

Eseonu CI, ReFaey K, Garcia O, John A, Quinones-Hinojosa A, Tripathi P. Awake craniotomy anesthesia: a comparison of the monitored anesthesia care and asleep-awake-asleep techniques. World Neurosurg. 2017;104:679–86.
Ladino LD, Rizvi S, Tellez-Zenteno JF. The Montreal procedure: the legacy of the great Wilder Penfield. Epilepsy Behav. 2018;83:151–61.
Meng L, McDonagh DL, Berger MS, Gelb AW. Anesthesia for awake craniotomy: a how-to guide for the occasional practitioner. Can J Anaesth. 2017;64(5):517–29.
Milian M, Tatagiba M, Feigl GC. Patient response to awake craniotomy—a summary overview. Acta Neurochir. 2014;156(6):1063–70.

Management of the Patient with Trigeminal Neuralgia

21

Hilary Hott, Galal Gargodhi, and Eman Nada

Stem Case Terminology

A 55-year-old female complains of severe, shooting, electric shock-like pain in her right cheek. The pain occurs spontaneously or when she touches her face, chews, or upon brushing her teeth. The symptoms started suddenly about 1 year ago. She saw a neurologist 6 months ago and was diagnosed with trigeminal neuralgia (TN). The neurologist started her on medical treatment which initially provided some relief. However, few months later, her symptoms worsened again. The neurologist referred her to a pain management specialist, who recommended a nerve block. The block did not significantly help. She was then referred to a neurosurgeon, who recommended a trigeminal nerve decompression.

H. Hott · E. Nada (✉)
Department of Anesthesiology and Perioperative Medicine, University of Massachusetts Medical School, Worcester, MA, USA
e-mail: Eman.Nada@umassmemorial.org

G. Gargodhi
Department Anesthesiology and Pain Medicine, Camden Clark Medical Center, West Virginia University, Parkersburg, WV, USA

Question 1:
What is trigeminal neuralgia?

Answer:
Trigeminal neuralgia (TN) is a disorder characterized by recurrent unilateral, brief, electric shock-like pain. It is limited to the distribution of one or more divisions of the trigeminal nerve. TN is rare, with an incidence that ranges from 0.03 to 0.3%. The incidence increases with age, and the age distribution is usually between 37 and 67 years. Several studies have reported an increased incidence in women compared to men with a ratio 3–1 [1–3].

Question 2:
What is the etiology and pathogenesis of TN?

Answer:
TN can be divided into three categories:

- Classical: due to neurovascular compression of the trigeminal nerve.
- Secondary: due to an underlying disease, which can be a tumor (as in cerebellopontine angle tumor), arteriovenous malformation, or multiple sclerosis.
- Idiopathic: in which no abnormalities can be seen on magnetic resonance imaging or on electrophysiological testing.

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_21

The most common type is due to vascular compression, usually within a few millimeters of entry into the pons. Compression by an overlying artery or vein may result in demyelination. Other mechanisms have been proposed, including narrowing of the osseous canals transmitting the corresponding nerve branches and allergic-immune mechanisms.

The focal demyelination of the trigeminal nerve at its entry into the pons may lead to increased firing of the afferent fibers and increased excitability of the trigeminal brainstem complex, which could explain the triggering of symptoms in response to non-noxious stimuli. The "unified" theory combines the process involving ephaptic, ectopic transmission of axonal discharges and nuclear hyperactivity in the pathophysiology of TN. Ephaptic transmission occurs when the damaged axons in the area of focal demyelination become a source of ectopic generation of high-frequency discharges [4–7].

Question 3:
What is the anatomy of the trigeminal nerve?

Answer:
The trigeminal nerve is the largest cranial nerve. It emerges from the lateral aspect of the pons of the brainstem by a large sensory root and a small motor root. It is the chief nerve for general sensory innervation of the head. It originates from the lateral surface of the pons by motor and sensory roots, then the roots cross the medial part of the crest of the petrous part of the temporal bone and enter the trigeminal cave of the dura mater lateral to the body of the sphenoid and cavernous sinus. The sensory root leads to the trigeminal ganglion; the motor root runs parallel to the sensory root, bypasses the ganglion and becomes part of the mandibular nerve.

At the end it divides into three divisions that is the ophthalmic, mandibular, and maxillary. The trigeminal nerve provides sensory innervation to the dura of the anterior and middle cranial fossae, skin of the face, teeth, gingiva, mucosa of the nose, paranasal sinuses, and mouth. It also supplies somatic motor fibers and distributes postsynaptic parasympathetic fibers [8] Fig. 21.1.

Question 4:
What are the diagnostic criteria for TN?

Answer:
The International Classification of Headache Disorders ICHD-3 diagnostic criteria [9] include the following description:

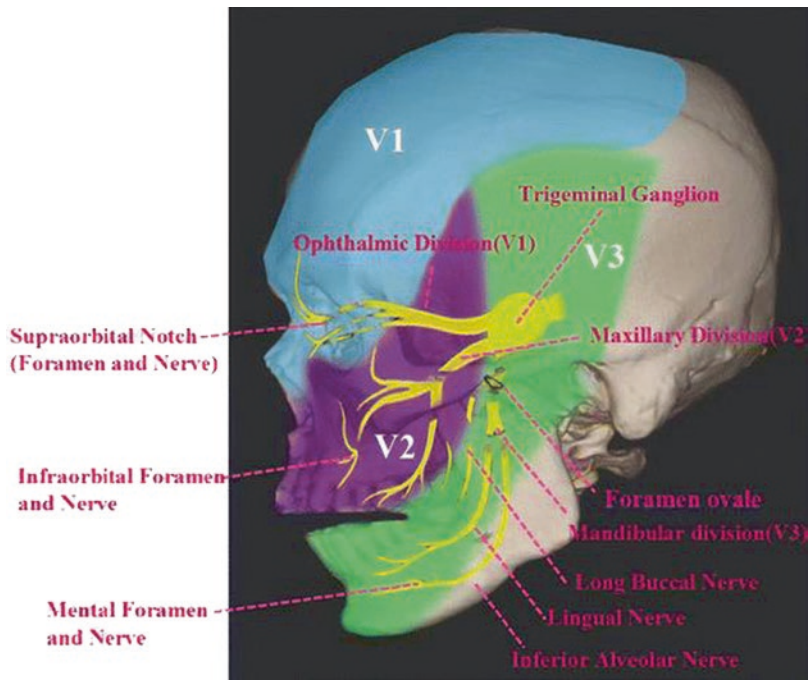


Fig. 21.1 Trigeminal nerve anatomy

TN develops without apparent cause other than neurovascular compression.

Diagnostic criteria:

(a) At least three attacks of unilateral facial pain fulfilling criteria B and C
(b) Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution
(c) Pain has at least three of the following four characteristics:
    1. Recurring in paroxysmal attacks lasting from a fraction of a second to 2 min
    2. Severe intensity
    3. Electric shock-like, shooting, stabbing or sharp in quality
    4. Precipitated by innocuous stimuli to the affected side of the face
(d) No clinically evident neurological deficit.
(e) Not better accounted for by another ICHD-3 diagnosis

Question 5:
What is the differential diagnosis of TN?

Answer:
The following conditions produce facial pain that can be confused with TN pain [10] (See Table 21.1).

Question 6:
How do you diagnose TN?

Answer:
Classic TN is usually diagnosed by history as per the ICDH-3 criteria—question 4. Clinical exam is usually normal in classic TN except for hyperalgesia. Hypoesthesia or hypoalgesia in the affected trigeminal region always indicates axonal damage and necessitates extensive diagnostic workup in cases of secondary TN. Traditionally, autonomic symptoms such as tearing and rhinorrhea have not been associated with TN [9–11].

Patients may have periods of remission without any attacks lasting months or years, but the attacks may become longer, and remissions may become shorter over time [12].

Question 7:
The patient sees a neurologist, who prescribes carbamazepine. What is carbamazepine, and what other medications can help in treating the pain of TN?

Answer:
Carbamazepine and oxcarbazepine are the first-line drugs for paroxysmal pain. When the full dose is limited because of the side effects, an add-on treatment with lamotrigine or baclofen

Table 21.1 Differential diagnosis of trigeminal neuralgia

Condition	Differentiating point
• Short-lasting unilateral neuralgiform headache attacks with autonomic symptoms (SUNA)	Pain may change sides
• Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)	
• Paroxysmal hemicrania	
• Migraine headache	Pain is different, brief, not as intense Photophobia, phonophobia, gastrointestinal symptoms
• Trigeminal neuropathy and atypical trigeminal neuralgia	Pain is preceded by trauma and/or clear-cut neurological abnormalities
• Persistent idiopathic facial pain	Pain is dull and persistent
• Herpes zoster infection	The presence of herpetic rash, tingling, and neurological abnormalities
• Cluster headache	Orbital, suborbital, or temporal pain with autonomic symptoms. Pain is much longer in duration: 15–180 min. Horner syndrome, conjunctival injection, epiphora
• Teeth pain (cracked, caries, pulpitis)	Can evoke shooting pain with chewing

is used. In patients with atypical TN, both gabapentin and antidepressants should be tried as an add-on to oxcarbazepine or carbamazepine. Carbamazepine carries the rare risk of agranulocytosis and aplastic anemia, while oxcarbazepine may carry the risk of hyponatremia. Because of the side effects, a new, better tolerated, selective sodium channel blocker is under development. Efficacy of medical treatment is approximately 75–80% initially, which then declines to approximately 50% over time [13, 14].

Topical intranasal or oral lidocaine used on the buccal mucosa and intravenous infusion are helpful to reduce the paroxysmal pain and simplify TN treatment [15–17]. Pimozide produces a significant reduction in TN symptoms, and BTX-A injection was recommended as a useful treatment for refractory TN [18, 19].

Question 8:
After few weeks on medical management, the patient feels the medication is not effective anymore. What are the other options available?

Answer:
Medications relieve pain in approximately 75–80% of patients, especially early on. However, medications often lose effectiveness over time. For patients with TN refractory to medical therapy, early surgical therapy or ablative interventions are considered [20, 21]. Ablative procedures are preferable in patients with multiple comorbidities that increase surgical risk or in patients who are not willing to undergo surgery [22]. They work by selectively damaging unmyelinated and myelinated pain fibers while ideally sparing the rest of the nerve fibers [23]. Ablation can be done percutaneously or stereotactically. Percutaneous ablation is done using radiofrequency thermocoagulation, physical pressure or chemically with glycerol. In balloon compression, the nerve is destroyed by pressing the nerve against the bone which results in mechanical nerve destruction. Stereotactic radiosurgery is a non-percutaneous ablative procedure which utilizes technologies that focus small high-dose radiation beams onto specific points within the trigeminal nerve root. The technologies include Gamma Knife, CyberKnife, and LINAC-MLC-based radiosurgery. However, these treatments are expensive [23, 24]. The success rate after the ablative procedures starts high and tends to decrease over time to 50% at 3–5 years. Sensory loss, dysesthesia, anesthesia dolorosa, and corneal numbness with risk of keratitis are common side effects [25–27].

Question 9:
The patient undergoes a diagnostic Gasserian ganglion block with little improvement. Now she is referred to a neurosurgeon. What are the surgical options?

Answer:
The main surgical treatment is microvascular decompression (MVD) of the trigeminal nerve. It is indicated when symptoms become refractory to medical therapy or when the medications are no longer tolerated. In some centers, it is considered the first option when patients are in good health [13, 28].

In the absence of neurovascular compression, a posterior fossa exploration may be done. In the case of negative posterior fossa exploration, one of the following can be considered:

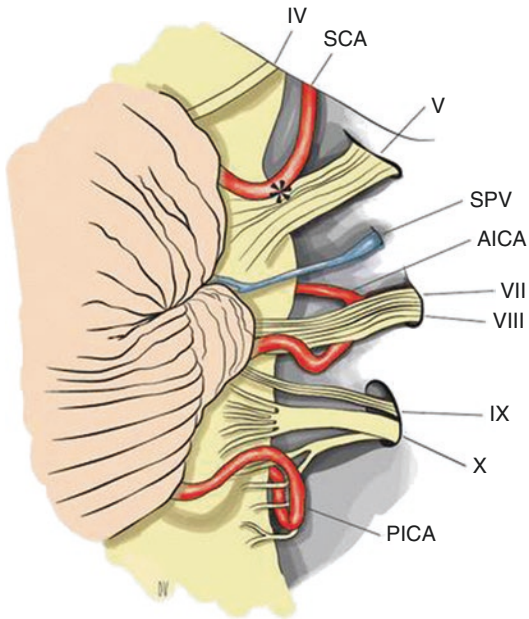
- Partial sensory rhizotomy entails the division of the lateral one-half to two-thirds of the sensory root. It has the drawback of producing sensory deficits.
- Internal neurolysis—also called nerve brushing or combing—entails separation of the nerve fascicles within the internal epineurium, which derives from the invagination of arachnoid and dura as the nerve exits the dura. As there is no injury to the nerves, sensory deficits may be less severe. Internal neurolysis is a safe, effective, and durable treatment for TN in the absence of neurovascular compression [29].
- Peripheral neurectomy targets the peripheral branches of the nerve external to the skull. It is generally not a recommended procedure [13]. However, it can be used in elderly patients or for those patients in areas with no access to a major surgical procedure [30].

Question 10:
What is MVD of the trigeminal nerve?

Answer:
MRI techniques are used to show the compression site and measure the volume and cross-sectional area of the nerve. The most common site of neurovascular compression is at the root entry zone, usually by the superior cerebellar artery [31]. In MVD, the trigeminal nerve root entry zone is freed and isolated from the vessels compressing it. This isolating material can be either Teflon and/or muscle. However, Teflon as an isolating material has been associated with a higher rate of TN recurrence than muscle [32] Fig. 21.2.

Question 11:
What are the pros and cons of MVD?

Answer:
MVD achieves the most sustained pain relief. Success rate is 90% initially, and 60–70% of patients remain pain free after 5 years [20, 33, 34]. However, it is a major surgical procedure that entails a craniotomy. Complications include incisional infection, facial palsy, facial numbness, cerebrospinal fluid leak, and hearing deficit with a postoperative mortality of about 0.1% [35] Fig. 21.3.



IV :The Trochlear Nerve
V: The Trigeminal Nerve
VII: Facial Nerve
VIII: The Vestibulocochlear nerve
IX: The Glossopharyngeal Nerve
X: The Vagus Nerve
SCA: Superior cerebellar artery
SPV: Superior Petrosal Vein
AICA: Anterior Inferior Cerebellar Artery
PICA: Posterior Inferior Cerebellar Artery

Fig. 21.2 Showing compression of the trigeminal nerve by the superior cerebellar artery (SCA)

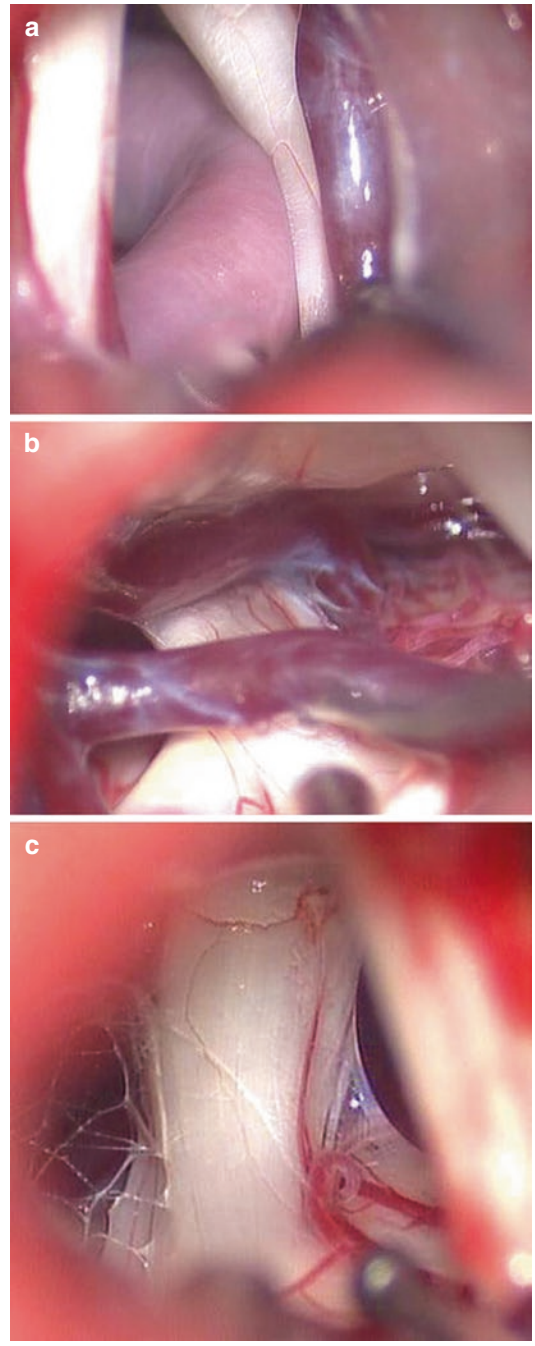


Fig. 21.3 Compression of the trigeminal nerve. Representative intraoperative images of **a** artery compression and vein close, **b** vein compression, and **c** arachnoid adhesions

Question 12:
Now the patient is scheduled for MVD of the trigeminal nerve. What are the anesthetic considerations of this procedure?

Answer:
The general anesthetic goals and considerations are the same as for any posterior fossa craniotomy is: to provide brain relaxation for good surgical exposure and to maintain adequate cerebral perfusion pressure to prevent cerebral ischemia from brain retraction.

Adequate intravenous access should be established, a type and screen should be performed, and any medications the patient is taking as for TN should be continued in the preoperative period. For patients who are on opioids preoperatively, postoperative pain management may be challenging and the use of intraoperative ketamine may be helpful.

During induction, face stimulation by application of a mask should be avoided, as it may induce the pain.

The position of the patient is usually supine with a "bump" and head turned or lateral park bench position [36]. The most common approach is the suboccipital retrosigmoid approach. The endoscopic-assisted procedure allows for a minimal incision, helps reduce the operative time, allows better exposure and is associated with reduced intra- and postoperative complications [37].

For endoscopic skull base surgery, it is important to have a stationary field; any patient movement carries the risk of intracranial injury by the endoscope or endoscopic instruments and to the head being fixed in the Mayfield frame [38, 39].

Question 13:
What type of monitoring is indicated for this procedure?

Answer:
Besides using the ASA monitors, invasive arterial blood pressure and urine output monitoring helps in tight control of the hemodynamics.

Brainstem auditory evoked potential (BAEP) and electromyographic (EMG) monitoring of the trigeminal and the facial nerves are also used. When neuromonitoring is used, anesthesia should be modified so as not to suppress the monitored waveforms [40, 41].

Some neurosurgeons are comfortable performing this procedure without neuromonitoring. If non-depolarizing muscle relaxants are to be used, the long-term use of antiepileptic medications results in resistance and increased requirements. Phenytoin and carbamazepine induce hepatic microsomal enzymes significantly, while oxcarbazepine induces them to a lesser though still clinically significant extent [42–44]. Topiramate induces hepatic microsomal enzymes in a dose-dependent manner. Valproate is an inhibitor of hepatic microsomal enzymes. Gabapentin, lamotrigine, levetiracetam, tiagabine, and vigabatrin do not induce hepatic enzymes [45].

Question 14:
What are the intraoperative complications specific to this procedure?

Answer:
Because the skull is opened next to the sigmoid sinus, bleeding and air embolus are potential hazards. Triggering of the trigeminocardiac reflex (TCR) is not uncommon with this procedure.

Question 15:
What is the trigeminocardiac reflex?

Answer:
TCR is the sudden occurrence of bradycardia, hypotension, apnea, and gastric hypermotility. The presentation ranges from sudden onset of sinus bradycardia, bradycardia terminating into asystole, asystole with no preceding bradycardia, arterial hypotension, and apnea. The drop in the mean arterial pressure and heart rate should be more than 20% from the baseline at the time of trigeminal nerve manipulations. The TCR is activated by central or peripheral stimulation of any of the sensory branches of the trigeminal nerve. It can be elicited even from

percutaneous compression of the trigeminal ganglion [46–50].

Factors that can predispose to TCR are hypercapnia, hypoxia, light anesthesia, children with high resting vagal tone, narcotics, preoperative beta-blockers, and calcium channel blockers. Avoidance of factors known to cause predisposition to the reflex and cessation or modulation of the surgical stimulus are usually all that is needed to halt the reflex [49]. Vagolysis using atropine may be needed. However, high doses of atropine may not completely prevent the bradycardia caused by TCR [51, 52]. The benefits and risks of temporary pacing should also be considered in cases of TCR especially in the presence of cardiac conduction problems [50].

Multiple Choice Questions

1. A 50-year-old female has a history of intermittent, sharp, and stabbing pain on her left side of the face that lasts only few seconds. It started about 1 year ago and has gotten worse since. The patient thought it was related to an infected tooth. However, the pain did not improve after the tooth extraction. The pain is aggravated by touching and brushing her teeth at times. There are no relieving factors. She denies any other associated symptoms with her facial pain. There is no family history of headaches. She had a workup done by her neurologist that showed normal laboratory results. What is the most likely diagnosis for this patient?
   (a) Cluster headaches
   (b) Migraine headaches
   (c) Herpes neuritis
   (d) Trigeminal neuralgia

   Answer: d

   For the classic TN developing without apparent cause other than neurovascular compression, the International Classification of Headache Disorders ICHD-3 diagnostic criteria include [9]:
   1. At least three attacks of unilateral facial pain fulfilling criteria B and C
   2. Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution
   3. Pain has at least three of the following four characteristics:
      (a) Recurring in paroxysmal attacks lasting from a fraction of a second to 2 min
      (b) Severe intensity
      (c) Electric shock-like, shooting, stabbing or sharp in quality
      (d) Precipitated by innocuous stimuli to the affected side of the face
   4. No clinically evident neurological deficit
   5. Not better accounted for by another ICHD-3 diagnosis
2. After the appropriate diagnosis was made, the neurologist decides to start the patient on carbamazepine. What lab values should be ordered and monitored prior to initiation of carbamazepine and during treatment?
   (a) Coagulation profile
   (b) Complete blood count
   (c) Frequent electrocardiographic monitoring
   (d) Serum creatinine and blood urea nitrogen

   Answer: b

   Carbamazepine can be well tolerated by most patients as a first treatment agent for TN. However, it have some serious although rare side effects such as leukopenia, aplastic anemia, and hepatic and pancreatic impairment [53].
3. Three days after starting carbamazepine, the patient started to have dizziness, vertigo, and intermittent diplopia. What would be the next medication option for this patient?
   (a) Amitriptyline
   (b) Oxcarbazepine
   (c) Ibuprofen
   (d) Duloxetine

   Answer: b

   Oxcarbazepine is a suitable alternative and more tolerated than carbamazepine. In 2008, the American Academy of Neurology and the European Federation of Neurological Societies issued the diagnostic evaluation and treatment of TN (an evidence-based review) that recommended the use of oxcarbazepine (level B evidence) [20].
4. In spite of the full dose of carbamazepine and the retrogasserian ganglion rhizotomy, the

condition does not improve. Her pain is getting worse with frequent attacks. MRI of the brain showed a pulsatile artery compressing the trigeminal nerve. What is the best next step to discuss with the patient?

(a) Repeat the glycerol rhizotomy one more time before deeming it a failure.
(b) We don't have any other interventions to offer and you will learn to live with the pain.
(c) Neurosurgical referral for MVD of the trigeminal nerve.
(d) Add more medications.

Answer: c

MVD of the trigeminal nerve achieves the most sustained pain relief. The success rate is 90%. After 5 years, 60–70% of patients remain pain free [20, 33, 34].

5. The patient decides to undergo MVD of the trigeminal nerve. The chronic use of carbamazepine may necessitate which changes of anesthesia?

(a) Lower doses of succinylcholine
(b) Lower doses of non-depolarizing muscle relaxants
(c) Higher doses of non-depolarizing muscle relaxants
(d) Lower MAC of inhalational anesthetics

Answer: c

Some neurosurgeons are comfortable performing this procedure without neuromonitoring. If non-depolarizing muscle relaxants are to be used, the long-term use of antiepileptic medications results in resistance and increased requirements. Phenytoin and carbamazepine induce hepatic microsomal enzymes significantly, while oxcarbazepine induces them to a lesser though still clinically significant extent [42–44].

6. The patient is fully anesthetized, and the surgeon starts manipulating the trigeminal nerve. The patient's heart rate drops suddenly to 37/min. What is the first measure to treat the condition?

(a) Alert the surgeon and ask them to stop immediately
(b) Give glycopyrrolate
(c) Give atropine
(d) Wait and it will correct itself

Answer: a

Avoidance of factors known to cause predisposition to the reflex and cessation or modulation of the surgical stimulus are usually all that is needed to halt the reflex [49]. Vagolysis using atropine may be needed. However, high doses of atropine may not completely prevent the bradycardia caused by TCR [51, 52].

References

1. MacDonald BK, et al. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. Brain. 2000;123(Pt 4):665–76.
2. De Toledo IP, et al. Prevalence of trigeminal neuralgia: a systematic review. J Am Dent Assoc. 2016;147(7):570–576 e2.
3. Katusic S, et al. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984. Ann Neurol. 1990;27(1):89–95.
4. Roth G, et al. Cryptogenic hemifacial spasm. A neurophysiological study. Electromyogr Clin Neurophysiol. 1990;30(6):361–70.
5. Love S, Coakham HB. Trigeminal neuralgia: pathology and pathogenesis. Brain. 2001;124(Pt 12):2347–60.
6. Sabalys G, Juodzbalys G, Wang HL. Aetiology and pathogenesis of trigeminal neuralgia: a comprehensive review. J Oral Maxillofac Res. 2013;3(4):e2.
7. Rozen TD. Trigeminal neuralgia and glossopharyngeal neuralgia. Neurol Clin. 2004;22(1):185–206.
8. Moore KL, Agur AMR, Dalley AF. Clinically oriented anatomy, vol. xxxv. 8th ed. Philadelphia: Wolters Kluwer; 2018, 1153p.
9. Headache Classification Committee of the International Headache Society. The international classification of headache disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629–808.
10. Maarbjerg S, et al. Trigeminal neuralgia - diagnosis and treatment. Cephalalgia. 2017;37(7):648–57.
11. Simms HN, Honey CR. The importance of autonomic symptoms in trigeminal neuralgia. Clinical article. J Neurosurg. 2011;115(2):210–6.
12. Zakrzewska JM, Linskey ME. Trigeminal neuralgia. BMJ. 2015;350:h1238.
13. Cruccu G, et al. AAN-EFNS guidelines on trigeminal neuralgia management. Eur J Neurol. 2008;15(10):1013–28.
14. Di Stefano G, Truini A, Cruccu G. Current and innovative pharmacological options to treat typical and atypical trigeminal neuralgia. Drugs. 2018;78(14):1433–42.
15. Kanai A, et al. Intranasal lidocaine 8% spray for second-division trigeminal neuralgia. Br J Anaesth. 2006;97(4):559–63.

16. Niki Y, et al. Immediate analgesic effect of 8% lidocaine applied to the oral mucosa in patients with trigeminal neuralgia. Pain Med. 2014;15(5): 826–31.
17. Stavropoulou E, et al. The effect of intravenous lidocaine on trigeminal neuralgia: a randomized double blind placebo controlled trial. ISRN Pain. 2014;2014:853826.
18. Turk Boru U, et al. Botulinum toxin in the treatment of trigeminal neuralgia: 6-month follow-up. Medicine (Baltimore). 2017;96(39):e8133.
19. Yang F, et al. Efficacy of 8 different drug treatments for patients with trigeminal neuralgia: a network meta-analysis. Clin J Pain. 2018;34(7):685–90.
20. Gronseth G, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the quality standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. Neurology. 2008;71(15):1183–90.
21. Di Stefano G, et al. Triggering trigeminal neuralgia. Cephalalgia. 2018;38(6):1049–56.
22. Sindou M, Keravel Y. Algorithms for neurosurgical treatment of trigeminal neuralgia. Neurochirurgie. 2009;55(2):223–5.
23. Zakrzewska JM, Linskey ME. Trigeminal neuralgia. BMJ Clin Evid. 2014;2014:1207.
24. Debono B, et al. Dedicated linear accelerator radiosurgery for classic trigeminal neuralgia: a single-center experience with long-term follow-up. World Neurosurg. 2019;121:e775–85.
25. Fujimaki T, Fukushima T, Miyazaki S. Percutaneous retrogasserian glycerol injection in the management of trigeminal neuralgia: long-term follow-up results. J Neurosurg. 1990;73(2):212–6.
26. Vadokas V, et al. [Experience with retrogasserian glycerol rhizotomy in the treatment of trigeminal neuralgia]. Schmerz. 1994;8(4):216–21.
27. Zakrzewska JM, Jassim S, Bulman JS. A prospective, longitudinal study on patients with trigeminal neuralgia who underwent radiofrequency thermocoagulation of the Gasserian ganglion. Pain. 1999;79(1): 51–8.
28. Cruccu G. Trigeminal neuralgia. Continuum (Minneap Minn). 2017;23(2, Selected Topics in Outpatient Neurology):396–420.
29. Ko AL, et al. Long-term efficacy and safety of internal neurolysis for trigeminal neuralgia without neurovascular compression. J Neurosurg. 2015;122(5):1048–57.
30. Ali FM, et al. Peripheral neurectomies: a treatment option for trigeminal neuralgia in rural practice. J Neurosci Rural Pract. 2012;3(2):152–7.
31. Tanrikulu L, et al. Preoperative MRI in neurovascular compression syndromes and its role for microsurgical considerations. Clin Neurol Neurosurg. 2015;129:17–20.
32. Haidar H, et al. Endoscopy-assisted microvascular decompression for trigeminal neuralgia: the prognostic impact of interposing material. J Int Adv Otol. 2014;10:107–12.
33. Tatli M, et al. Various surgical modalities for trigeminal neuralgia: literature study of respective long-term outcomes. Acta Neurochir. 2008;150(3):243–55.
34. Wei Y, et al. Clinical features and long-term surgical outcomes in 39 patients withtumor-related trigeminal neuralgia compared with 360 patients with idiopathic trigeminal neuralgia. Br J Neurosurg. 2017;31(1):101–6.
35. Xia L, et al. Effectiveness and safety of microvascular decompression surgery for treatment of trigeminal neuralgia: a systematic review. J Craniofac Surg. 2014;25(4):1413–7.
36. Forbes J, et al., Microvascular decompression: salient surgical principles and technical nuances. J Vis Exp. 2011;(53): e2590.
37. Alshukry A, et al. Trigeminal neuralgia (TN): a descriptive literature analysis on the diagnosis and management modalities. J Stomatol Oral Maxillofac Surg. 2017;118(4):251–4.
38. Amorocho MC, Fat I. Anesthetic techniques in endoscopic sinus and skull base surgery. Otolaryngol Clin N Am. 2016;49(3):531–47.
39. Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. Neurosurg Focus. 2002;12(5):e5.
40. Simioni V, et al. Intraoperative monitoring of sensory part of the trigeminal nerve using blink reflex during microvascular decompression for trigeminal neuralgia. Acta Neurochir. 2018;160(1): 165–9.
41. He X, et al. Alarming effect of intraoperative neuroelectrophysiological monitoring in microvascular decompression for primary trigeminal neuralgia. Zhonghua Yi Xue Za Zhi. 2015;95(21): 1651–4.
42. Spacek A, et al. Rocuronium-induced neuromuscular block is affected by chronic carbamazepine therapy. Anesthesiology. 1999;90(1):109–12.
43. Johannessen Landmark C, Patsalos PN. Drug interactions involving the new second- and third-generation antiepileptic drugs. Expert Rev Neurother. 2010;10(1):119–40.
44. Roth S, Ebrahim ZY. Resistance to pancuronium in patients receiving carbamazepine. Anesthesiology. 1987;66(5):691–3.
45. Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: interactions between antiepileptic drugs and other drugs. Lancet Neurol. 2003;2(8):473–81.
46. Bainton R, Lizi E. Cardiac asystole complicating zygomatic arch fracture. Oral Surg Oral Med Oral Pathol. 1987;64(1):24–5.
47. Loewinger J, Cohen M, Levi E. Bradycardia during elevation of a zygomatic arch fracture. J Oral Maxillofac Surg. 1987;45(8):710–1.
48. Brown JA, Preul MC. Percutaneous trigeminal ganglion compression for trigeminal neuralgia.

Experience in 22 patients and review of the literature. J Neurosurg. 1989;70(6):900–4.
49. Lang S, Lanigan DT, van der Wal M. Trigeminocardiac reflexes: maxillary and mandibular variants of the oculocardiac reflex. Can J Anaesth. 1991;38(6):757–60.
50. Schaller B. Trigemino-cardiac reflex during microvascular trigeminal decompression in cases of trigeminal neuralgia. J Neurosurg Anesthesiol. 2005;17(1):45–8.
51. Prabhakar H, Ali Z, Rath GP. Trigemino-cardiac reflex may be refractory to conventional management in adults. Acta Neurochir. 2008;150(5):509–10.
52. Schaller B, et al. Trigeminocardiac reflex during surgery in the cerebellopontine angle. J Neurosurg. 1999;90(2):215–20.
53. Pellock JM. Carbamazepine side effects in children and adults. Epilepsia. 1987;28(Suppl 3):S64–70.

Management of Patient with Scoliosis

22

Monica S. Tandon, Aastha Dhingra, and Vineeth Varma

Stem Case Terminology

- **History**

A 14-year-old boy is scheduled for a posterior spinal instrumentation and fusion procedure, for his right thoracic scoliosis. According to the medical records, he has a history of adolescent idiopathic scoliosis (AIS) that was detected when he was 12 years of age. At initial presentation, the Cobb angle of the thoracic curve was 30°, and he was advised to wear a brace to restrict further progression of AIS. But the deformity has progressively increased over the past 2 years, and on a recent examination, the Cobb angle was estimated to be 57°.

He is a healthy child and participates in school sports; but lately, he has noticed slight breathlessness when he plays basketball. He reports that his paternal aunt also has a slight deformity in her spine. He takes no regular medications and denies any allergy or previous adverse anesthetic events.

- **Physical examination**

The boy is 170 cm tall, weighs 62 kg, [Body mass Index (BMI)—21.5 kg/m^2) and has a normal gait. His heart rate (HR) is 76 bpm, blood pressure (BP) is 124/76 mmHg, and respiratory rate is 15/min. A right posterior rib hump and truncal asymmetry is noted in the standing position, with the right shoulder and right hemipelvis being higher as compared to the left side. There is no clinical leg-length discrepancy. The right thoracic hump becomes more prominent on forward bending.

Airway, cardiac, and respiratory examination is unremarkable; no abnormality is observed on skin examination. On neurological examination, he has full and symmetric strength, normal sensation, and symmetric deep tendon reflexes in all the extremities; gag reflex and symmetric abdominal reflexes are also normal.

- **Investigations**

His hemoglobin is 13 g/dL; other routine hematological, biochemical investigations and urinalysis reveal no abnormality; electrocardiogram (ECG) shows a normal sinus rhythm. His spirometry results are: forced vital capacity

M. S. Tandon (✉)
Department of Anesthesiology and Intensive Care, G.B. Pant Institute of Postgraduate Medical Education and Research, Maulana Azad Medical College and Affiliated Hospitals, Delhi University, New Delhi, India

A. Dhingra
Department of Anesthesia, Max Super-specialty Hospital, Ghaziabad, India

V. Varma
Department of Orthopedics, Lok Nayak Jai Prakash Narayan Hospital, Maulana Azad Medical College and Affiliated Hospitals, Delhi University, New Delhi, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_22

(FVC)—2.5 L (72% of predicted), forced expiratory volume in 1 s (FEV1)—2.05 L (65% of predicted), FEV1/FVC ratio—82% of predicted; oxygen saturation (SpO_2) on room air is 98%.

Standing anteroposterior (AP) radiograph of the spine demonstrates a single major thoracic scoliotic curve with a rightward convexity (dextroscoliosis) (Fig. 22.1a, b). The curve extends from the T1–L2 vertebra; its apex is at T8 vertebrae; and the Cobb angle measures 57°. The apical vertebra demonstrates a vertebral rotational deformity of 1 out of 4 (Nash and Moe classification) with less than 25% displacement of the pedicle towards the midline. There are no associated vertebral abnormalities. The ribs are pushed posteriorly and the rib cage is narrowed on the right side. Widening of intercostal spaces is maximally seen over the eighth to twelfth rib. The triradiate cartilage is open and the pelvis demonstrates a Risser 0 sign.

The magnetic resonance imaging (MRI) spine scan does not demonstrate any paraspinal soft tissue, vertebral, or spinal cord (SC) abnormality.

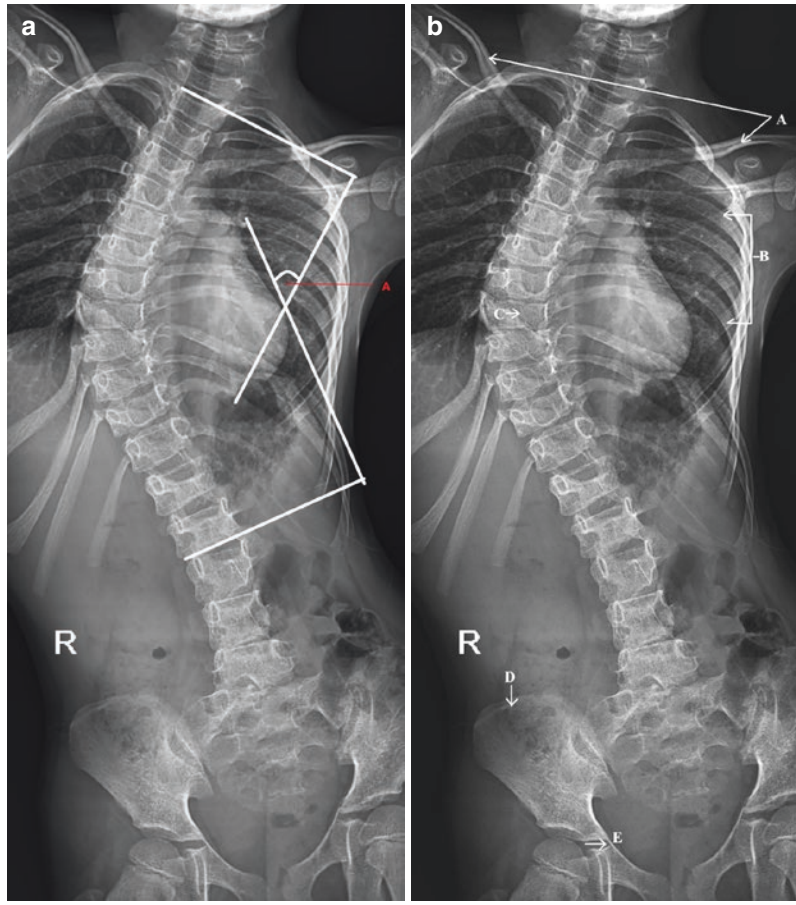


Fig. 22.1 (**a**) Standing radiograph of the spine (anteroposterior view) showing a single major thoracic scoliosis curve with rightward convexity (dextroscoliosis), extending from T1 to L2 vertebrae; apex of the curve is at T8 vertebra; Cobb angle of the curve (A) is 57° (measured from superior endplate of T1 and inferior endplate of L2 vertebrae). (**b**) Standing radiograph spine (anteroposterior view) showing, (A) left shoulder at a lower level than the right shoulder; (B) crowding of ribs on the concave side of thoracic curve; (C) right sided scoliosis curve extending from the T1 to L2 vertebrae; the apical vertebra (T8) demonstrates vertebral rotational deformity of 1 out of 4 (Nash and Moe classification). (D) Risser sign 0; (E) open triradiate cartilage

22.1 Basic Considerations

Question 1:
What is scoliosis?

Answer:
Normally, the spine is centered on the pelvis, has an S-shaped curvature (thoracic kyphotic curve; cervical and lumbar lordotic curves) when it is observed from the side (sagittal plane), and is more or less, vertically straight (<10° curvature) when viewed from behind (coronal/frontal plane). When the spine is laterally deviated from its central axis by more than 10° in the frontal plane, it is referred to, in simplistic terms, as scoliosis.

More specifically, scoliosis is a complex, three-dimensional deformities, which involves the spine as well as the thoracic cage. The spine deformity is characterized by an abnormal (>10°) lateral curvature of the spine in the coronal plane, lordosis of the thoracic spine in the sagittal plane, and rotation of the thoracolumbar vertebrae in the transverse plane [1].

As the lateral curvature of the spine increases, the affected vertebral bodies (VBs) and their spinous processes bend and rotate towards the convex part of the curve; consequently, the spine rotates or twists, and the curve becomes multidimensional. Furthermore, compression of the inter-vertebral (IV) discs and thinning of the pedicles on the concave side of the curve predispose to narrowing of the spinal canal on that side of the curve [2]. Since the ribs are attached to the vertebrae, they follow the rotational torque applied by the spine. On the convex side, they become widely separated and are pushed upwards and backwards; this leads to narrowing of the thoracic cage and development of a rib hump on the posterior chest wall [3]. Conversely, crowding of the ribs occurs on concave side of the curve, and an anterior rib hump is created as the ribs get pushed downwards as well as forwards [1, 3].

Besides a visible cosmetic deformity, these skeletal changes lead to truncal imbalance, altered spinal mechanics, and subsequently, degenerative changes in the spine. Further, the altered thoracic geometry impairs the functional biomechanics of the chest wall and causes secondary involvement of the respiratory and cardiovascular systems.

Question 2:
How is scoliosis measured?

Answer:
The "Cobb method" is used to determine the magnitude of scoliosis in the frontal plane [4, 5] (Fig. 22.1a). For this, the most tilted vertebrae at the cranial end [superior end vertebra (SEV)] and caudal end of the curve [inferior end vertebra (IEV)] are identified on an upright, AP spine radiograph (to define the upper and lower limits of the scoliotic curve). Lines are drawn along the upper and lower borders of the vertebral end plates of SEV and IEV, respectively. Another second line is drawn perpendicular to each of these lines; the angle formed by the intersection of these perpendicular lines is the "Cobb angle." The curve with the largest Cobb angle is called the "major curve"; all other curves noted on the X-ray are known as minor curves.

The Nash and Moe method is used to assess the extent of axial vertebral rotation, by examining the relationship of the pedicle to the center of the VB of the apical vertebra [vertebra which is the most laterally deviated from the central sacral line (vertical axis that passes through the patient's sacrum)], on an AP spine radiograph or a computerized tomography (CT) scan of the spine [4, 5]. There are four grades of axial rotation, ranging from Grade 0 (both pedicles are symmetric, no vertebral rotation is present) to grade 4 (the convex pedicle has moved past the midline of VB).

Question 3:
What are the various types of scoliosis in children? Which is the most common type?

Answer:
There are two types of pediatric scoliosis: idiopathic and nonidiopathic (Table 22.1). Approximately 80% of scoliotic children have Idiopathic Scoliosis (IS); these children are

Table 22.1 Etiology of scoliosis

Idiopathic (nearly 80% of all cases of scoliosis)
Infantile
Juvenile
Adolescent
Nonidiopathic
Neuromuscular scoliosis (approximately 15% of all cases of scoliosis)
Neuropathic (upper and lower motor neuron diseases): cerebral palsy, spinal muscular atrophy, poliomyelitis, syringomyelia
Myopathic: Duchenne muscular dystrophy (progressive muscle disorder), Friedreich ataxia
Congenital scoliosis (congenital abnormality of vertebrae/ribs)
Vertebral anomalies: Hemivertebrae, unilateral unsegmented bar
Rib anomalies: Congenital rib fusions
Neural tube defects: Spina bifida, diastematomyelia, myelomeningocele
Neurofibromatosis (von Recklinghausen disease)
Mesenchymal disorders
Marfan syndrome
Ehlers–Danlos syndrome
Morquio syndrome, Amyloplasia congenita, various types of dwarfisms
Rheumatoid arthritis
Osteogenesis imperfecta
Still disease
Scheuermann disease
Marfan syndrome
Trauma
Vertebral fracture, irradiation or surgery
Post-thoracic surgery
Neoplastic

otherwise healthy and do not have any discernible cause for their skeletal deformity [4, 6]. Nonidiopathic scoliosis develops as a result of an underlying pathology, mostly a neuromuscular, [neuromuscular scoliosis (NMS)] or congenital [congenital scoliosis (CS)], and occasionally, a mesenchymal, traumatic, neoplastic or syndromic condition [3, 4, 6, 7].

IS is further subdivided, on the basis of age at which it is diagnosed, into infantile (age less than 3 years), juvenile (age 4–9 years), adolescent (age 10–18 years), and adult IS (in patients older than 18 years) (Table 22.2) [8, 9]. AIS is the most common variant (approximately 90% of cases of IS), and also the most common type of scoliosis overall [9]. It has an incidence of 1–3% in children who are aged 10–16 years, and are at or near the onset of puberty, but have still not attained full skeletal maturity [6, 9–11]. Infantile idiopathic scoliosis (IIS) is the least common type and accounts for <1% cases of IS [4]. AIS and juvenile idiopathic scoliosis (JIS) are more prevalent in females and have a greater propensity for right thoracic curves [12, 13]. IIS, on the other hand, is more common in boys, is usually associated with left thoracic curves and is also the only type of IS which may resolve spontaneously [14]. Most of the children with IIS present within 6 months of birth; besides the scoliosis, they may also have other congenital abnormalities, e.g., plagiocephaly and congenital hip dysplasia [15, 16].

Table 22.2 Characteristic features of infantile, juvenile, and adolescent idiopathic scoliosis

	Infantile	Juvenile	Adolescent
Age at presentation	Birth to 3 years	4–9 years	10–18 years
Male:Female	1:1	1:3	1:6
Incidence (%)	<1	12–15	90
Associated findings	Mental deficiency, congenital heart defects, congenital hip dysplasia, plagiocephaly	None	None
Risk of cardiopulmonary compromise	High	Intermediate	Low
Risk of curve progression	<6 months: low >1 year: high	60–95%	10–20%
Possibility of curve resolution	<1 year: 90% >1 year: 20%	20%	Rare
Neural axis abnormalities	Yes (20%)	Yes (20%)	No
Surgical intervention	Yes, often an early surgical intervention in patients with rapidly progressive curves; high morbidity	Yes, in almost 95% of progressive curves	Uncommon, in 0.1% patients

NMS occurs in association with various neuropathic, myopathic, or connective tissue systems disorders; the most common conditions are cerebral palsy (CP), Duchenne muscular dystrophy (DMD), and spinal muscular atrophy. CP is characterized by a static, upper motor neuron lesion caused by an anoxic cerebral injury; its clinical manifestations range from normal cognition and minimal neurological deficits to severe mental retardation and spastic quadriparesis. Scoliosis affects nearly 25% of patients with CP [17]. Its severity correlates with the extent of their neurological impairment and functional decline, and approximately 66% of nonambulatory CP patients develop NMS [17]. DMD is a progressive myopathic, sex linked recessive disorder in which deficiency of "dystrophin" leads to gradual deterioration of the muscular system; cardiac, pulmonary, hematological, and gastrointestinal systems are also commonly involved.

CS occurs in approximately 1 of every 1000 live births as a result of vertebral or costal anomalies such as hemivertebrae, fused vertebrae, or fused ribs [7, 11]. Concomitant congenital anomalies especially those involving the cardiac (ventricular septal defect, patent ductus arteriosus, Tetralogy of Fallot), genitourinary system and neurological systems are also often present; occasionally, it may be part of a syndrome, e.g., Marfan, Rett, Klippel–Feil syndrome, osteogenesis imperfecta [7, 18].

Question 4:
How is IS classified?

Answer:
There are several categorization systems for IS; the International Scientific Society on Scoliosis Orthopaedic and Rehabilitation Treatment (SOSORT) endorses three classifications, which have a prognostic relevance: chronological, angular, and topographic (Table 22.3) [4].

The chronological classification is based on the age at diagnosis and categorizes IS into IIS, JS, and AIS.

In the topographic classification, the curves are described on the basis of their anatomical site (cervical, cervicothoracic, thoracic, thoracolumbar, lumbar), direction of their convexity (right or left), and location of their apical vertebra.

Table 22.3 Common classification systems for idiopathic scoliosis

Chronological classification	
Scoliosis research society classification	
Infantile	0–3 years
Juvenile	4–9 years
Adolescent	10–18 years
Adult	>18 years
Dickson and Archer classification	
Early onset scoliosis: Onset at <5 years of age Late onset scoliosis: Onset at >5 years of age	
Topographic classification	
Anatomical site of curve	*Location of curve apex*
Cervical	Disc C6–C7
Cervico-thoracic	C7–T1
Thoracic	Disc T1–T2 T11–T12
Thoracolumbar	T12–L1
Lumbar	Disc L1–L2
Angular classification	
Cobb angle (degrees)	*Classification of severity*
<20	Low
21–35	Moderate
36–40	Moderate–Severe
41–50	Severe
51–55	Severe to very severe
>55	Very severe
Other classifications	
Lenke classification 3D classifications Rigo classification King and Moe classification Ponseti and Friedman classification	

The angular classification is based on extent of the Cobb angle and grades IS into six categories ranging from low (<20°) to very severe (>55°). This classification not only provides a very good estimate of the severity of scoliosis, its likelihood of progression, and the risk of cardiopulmonary compromise, but also plays a very critical role in the treatment decisions for patients with IS.

Another age classification (Dickson and Archer classification) classifies IS into early onset scoliosis (EOS; patient age less than 5 years at presentation) and late onset scoliosis (children older than 5 years at presentation). It is based on the logic that curves which develop beyond 5 years of age are less likely to affect the pulmonary function; IIS and JIS are placed into one

category in this classification (though both may have a different prognosis) [19].

The Lenke classification is a complex classification system, which incorporates several objective criteria pertaining to the coronal and sagittal plane deformity and provides useful information for the surgeons regarding the appropriate surgical approach and the extent of instrumentation. In addition to six types of curves (I–VI), this classification also includes a lumbar curve modifier (A, B, or C; based on the central sacral vertical line) and a thoracic sagittal modifier (hypo-/hyper- or normokyphotic, based on the degree of kyphosis) [4, 20].

In addition, several 3D classifications have also been proposed recently; however, the most useful one in clinical practice is not yet defined.

Question 5:
What is the etio-pathogenesis of IS?

Answer:
While several plausible mechanisms have been proposed, a precise understanding of the etiology of IS still remains elusive. Given that a strong positive family history is often present and several potential genetic loci have also been identified, it is highly likely that it has a strong genetic component, with possibly a complex polygenic inheritance pattern [21, 22]. In addition, several other mechanisms such as hormonal theories (disturbance of growth hormone or estrogen, or melatonin deficiency due to altered calmodulin levels), connective tissue abnormality (collagen abnormalities in IV discs due to defects in mucopolysaccharide and lipoprotein synthesis), growth disorder theories (disorganized skeletal growth), and neuromuscular theories (primary muscle disorder) have also been implicated in its development [22, 23]. The pathophysiology of IS is also not very well established; the observation that curves tend to progress during periods of rapid growth appears to support a biomechanical contribution.

Hence, according to the current understanding, IS is most likely a multifactorial disorder which results from a complex interaction between genetic predisposing factors, the growth processes, and the patient's environment [4, 22, 23].

Question 6:
What is the natural history of IS?

Answer:
The behavior of curves in IS typically reflects the growth pattern of children. The curves progress rapidly during infancy (birth to 3–4 years) and adolescence (periods associated with rapid skeletal growth); their progression becomes slow during childhood and after attainment of skeletal maturity (or onset of menarche in girls) [4]. Since this pattern is observed in other types of scoliosis also, it appears to be independent of the etiology of IS.

The rate of curve progression is most marked during the adolescent growth spurt; during this "curve acceleration phase," the curves significantly change their behavior and separate into rapid, moderate, or slowly progressive curves. Rapidly progressive curves progress at an average rate of 1.6° per month and can reach a curve magnitude of 60° (rapidly progressive scoliosis); moderately progressive curves can grow up to 40–60°; curves with a low progression rate usually do not reach 40°. Among girls, the curves progress most rapidly during the peak height velocity (approximately 6 months before menarche).

The rate of curve progression decelerates gradually after attainment of maturity (or menarche); smaller curves (less than 30°) usually stabilize, those greater than 30° may continue to progress, but curves greater than 50°, especially thoracic curves, almost certainly continue to progress into adulthood [3, 24, 25].

If left untreated, the altered spinal mechanics and degenerative changes that develop as a consequence of the progressive osseous deformity lead to truncal decompensation, decreased spinal mobility, back pain, progressive functional limitation, and neurologic compromise [4]. Furthermore, the detrimental effect of the deformity on respiratory mechanics, gas exchange, and pulmonary vasculature predisposes to the development of respiratory failure and cor pulmonale in patients with very severe scoliosis [26]. The overall morbidity and mortality is strongly influenced by the type of IS, rate of

curve progression (at least 5° increase in the Cobb angle between two consecutive examinations, which are three to 6 months apart), and the genetic background of the patients [4, 19].

While the curves in AIS do progress and result in a surface deformity with cosmetic concerns and a slightly increased prevalence of low back pain, but the overall consequences over a lifetime are usually minimal, occasionally moderate, and very rarely, life-threatening. Nearly 10% and 0.1% of the children require some form of treatment and an operative intervention, respectively [8, 12, 27]. Generally, female gender, a larger curvature at presentation (>30°), lesser maturity (younger age at presentation, premenarchal, higher amount of remaining skeletal growth), thoracic curves, and thoracic dominant double curves are associated with a higher likelihood of curve progression; skeletally immature children with thoracic curves are the most vulnerable, with a 58–100% risk for curve progression [1, 9, 19, 28–31].

Unlike AIS, almost 95% of juvenile curves are progressive; while curve progression can be temporarily stabilized with conservative management, a high proportion of children with JIS (approximately 64%) ultimately require an operative intervention [13].

Infantile curves can either resolve spontaneously or may be progressive. Progressive IIS has the worst prognosis, with a high mortality rate due to the cardiopulmonary compromise and hence an early operative intervention is usually required. Features suggestive of progressive IIS include large curves (greater than 60°), double curves, a rib vertebral angle difference at the apical vertebra greater than 20° (difference of the angle between the rib and its corresponding VB), or a phase II rib (rib head overlaps the VB, due to spinal rotation) [16, 19, 32].

Question 7:
How does natural history of NMS and CS differ from IS?

Answer:
Generally, both NMS and CS are associated with a higher likelihood of curve progression, severe cardiopulmonary compromise and consequently, earlier surgical intervention than AIS [33].

In addition to the age-related curve progression, the natural history of NMS and its overall consequences are also highly influenced by the pathophysiology of the underlying neuromuscular condition (Table 22.4). The curves in NMS are usually large and stiff and are often associated

Table 22.4 Pertinent anesthetic considerations in patients with neuromuscular scoliosis

Scoliotic deformity:
Usually an early onset of scoliosis
Large, stiff, curves which continue to progress after skeletal maturity
Concomitant kyphosis often present
Comorbidities
Severe, progressive cardiorespiratory dysfunction; respiratory failure usually by second decade of life (DMD); many patients on NIPPV, preoperatively
High incidence of dilated cardiomyopathy in DMD patients [arrhythmias (patients may be on a pacemaker), ventricular dilatation, congestive cardiac failure]
Seizures in approximately 30% of patients with CP
Gastroesophageal disorders (especially in CP patients): gastroesophageal reflux disorder, hiatal hernia; and poor oropharyngeal control
Poor nutritional status
Increased bleeding risk:
Deficiency of coagulation factors (impaired production of Vitamin K dependent factors due to malnutrition); platelet dysfunction
DMD: vascular pathophysiological changes (vascular smooth muscle dysfunction and increased fibrinolysis due to leakage of muscle components secondary to muscle degeneration), osteopenia (impaired production of Vitamin K dependent factors due to the poor nutritional status; platelet function deficiency)

(continued)

Table 22.4 (continued)

CP: Drug induced osteopenia (valproate, eptoin), platelet dysfunction (valproate), von Willebrand factor type 1 deficiency (valproate)
Surgery
Usually performed at much lower curve magnitude as compared with idiopathic scoliosis, especially in patients with underlying cardiac and pulmonary dysfunction in order to improve the quality of life (maintain a straight spine to allow comfortable sitting and aid nursing care)
Surgery stops curve progression, but does not prevent the progressive decline in respiratory function
Most common procedure: Posterior spinal fusion; anterior/combined approach release reserved for very severe deformities
Large and stiff complex curves may require an osteotomy
Growing rod system, chest wall distraction system, growth modulation surgery may be required in children with progressive deformities
Perioperative risks
Prolonged extensive surgery (larger, stiffer curves; greater need for vertebral osteotomy)
Significantly increased risk of:
Severe blood loss
Iatrogenic neurological injury
Surgical wound infections
Postoperative pulmonary complications including pneumonia, respiratory failure, and prolonged mechanical ventilation
Preoperative evaluation
Special investigations:
Pulmonary function tests
Arterial blood gas analysis
Polysomnography/overnight oximetry to detect nocturnal hypoventilation/sleep apnea (in patients with morning headaches, daytime somnolence)
Stress echocardiography (exercise tolerance usually difficult to assess in wheelchair-dependent patients; resting echo normal study does not exclude significant pathology)
Holter monitoring (if arrhythmias present on ECG)
Serum albumin, transferrin; lymphocyte count (for assessment of nutritional status)
Antiepileptic drug level (phenytoin, valproate)
Consider CT lung volumes or a dynamic MRI (if PFT is not feasible)
Consider radionuclide imaging, if echocardiography is not feasible
Other considerations:
DMD patients on pacemaker for arrhythmias: ensure that pacemaker is working properly
CP patients with vagal nerve stimulation for seizure treatment: ensure proper working of the stimulator
Latex allergy in CP patients (due to multiple surgical exposures)
Poor vascular access due to deformities and contractures, multiple surgeries, prolonged ICU stays
Potential for malignant hyperthermia like syndrome in patients with DMD on exposure to succinylcholine or inhalational agents; features: hyperkalemia, rhabdomyolysis, and cardiac arrest usually in absence of signs of hypermetabolism seen in MH
Specialist consultations: cardiologist, pulmonologist, gastroenterologist, nutritionist; physiotherapist
Surgery contraindicated in DMD patients if LVEF <50%, FVC <25%
MEP monitoring contraindicated/used with caution in epileptic patients
Prudent to postpone the surgery, if the anitepileptic drug levels are in the subnormal range
Antiepileptic drugs (phenytoin, valproate): altered anesthetic drug metabolism

DMD Duchenne muscular dystrophy, CP cerebral palsy, NIPPV non-invasive positive-pressure ventilation, PFT pulmonary function test, ECG electrocardiogram, MRI magnetic resonance imaging, ICU intensive care unit, LVEF left ventricular ejection fraction, FVC forced vital capacity, MEP motor evoked potential

with kyphosis. In DMD, the progressive muscle weakness usually begins by 3–4 years of age and typically results in wheel chair dependence by 10–12 years of age. The scoliosis too manifests relatively early in life and progresses very rapidly once the patients become nonambulatory, especially during the adolescent growth spurt phase. Progressive imbalance due to the spasticity or muscle weakness often results in sweeping C-type or thoracolumbar curves, with consequent pelvic obliquity, truncal imbalance, and difficulty with wheelchair sitting and caregiving. Furthermore, while IS tends to stabilize after the patients have achieved skeletal maturity, the curves in DMD patients continue to progress with advancing age. Death usually occurs in the second decade as a result of significant respiratory compromise and/or due to development of cardiomyopathy; associated hematological and gastrointestinal dysfunction also contribute to the high morbidity associated with this condition (Table 22.4).

Patients with CP tend to be skeletally immature till late second or third decades of life and hence have a higher risk for curve progression than those with IS; specific factors which increase the risk for curve progression in these patients include thoracolumbar curves, skeletal immaturity at presentation, nonambulatory patients, and a poor functional status [34, 35].

Besides the growth-related curve progression, the natural history of CS is determined by several other factors, especially the geometry and location of the vertebral anomalies, and the associated multisystemic congenital abnormalities. Progression of scoliosis is negligible in patients with non-incarcerated hemivertebrae, but presence of hemivertebrae with a contralateral bar and fully segmented non-incarcerated hemivertebrae is usually associated with a high risk of curve progression. Vertebral malformations greatly predispose to the development of restrictive lung disease and thoracic insufficiency syndrome (TISS).

Question 8:
How is the "the remaining skeletal growth potential" of child assessed? What is its relevance in scoliotic children?

Answer:
There are several radiological indicators for assessment of the skeletal maturity of a child; the most commonly used indicators are Risser sign, maturity of the ring apophyses (annular apophyses), and closure of the triradiate cartilage of the pelvis.

The Risser staging assesses the extent of ossification of the iliac apophysis on a frontal plane radiograph (iliac apophysis is divided into four equal quadrants; ossification progresses from a lateral to medial direction). The Risser sign is graded from 0 to 5 (Risser 0: no evidence of ossification; Risser 1, 2, 3, 4: 25%, 50%, 75%, and 100% excursion, respectively; Risser 5: fusion of apophysis to the sacroiliac joint). Risser stages 0, 4, and 5 indicate skeletal immaturity, end of spinal growth, and full skeletal maturity, respectively. The risk for curve progression is as high as 70% if the Risser sign is 0 or 1 (due to significant remaining growth reserve), but declines to approximately 10% with a Risser sign of 3 [28].

Question 9:
What is the effect of the scoliotic deformity on the respiratory and cardiovascular function?

Answer:
Scoliosis affects the pulmonary function in several ways; the most significant consequence is the development of a restrictive lung defect due to both a direct reduction in the chest wall compliance which restricts normal inflation of lungs and an indirect decrease in the lung compliance which leads to reduced lung volumes. These changes manifest as a reduction in the total lung capacity (TLC), on pulmonary function testing (PFT).

The functional biomechanics of the thoracic cage is impaired in scoliotic patients owing to several factors, including restricted rib movements, decreased functional efficiency of intercostal respiratory muscles (suboptimal muscle stretch due to changes in intercostal spaces), and an increased mechanical dysfunction of diaphragm (torsion on diaphragm; decrease in its force generating capacity) [36, 37]. Consequently, the chest wall becomes stiffer, its compliance decreases, and the lung expansion becomes restricted. **T**his decrease in chest wall compliance correlates closely with the severity of the restrictive lung defect, and with the decrease in FVC. These changes are more pronounced in patients with EOS and also in those with CS (due to vertebral anomalies and fused ribs) [37].

Several factors contribute to the decrease in lung volumes. "True lung hypoplasia" plays an important role in infantile, CS, NMS and possibly, JIS. Children with IIS have a narrow, funnel-shaped, upper thoracic cage, which compresses the lungs and also interferes with their normal growth and development (most of the rapid alveolar multiplication and hypertrophy occurs till about 4 and 8 years of age, respectively) [26, 36, 38]. Hence there is a high risk of developing thoracic insufficiency syndrome [(TISS); pulmonary failure due to inability of the thorax to support normal breathing and lung growth]. While children with AIS also have a narrow rib cage that causes extrinsic lung compression, however, their lung parenchyma is almost fully developed before the onset of scoliosis, hence their respiratory impairment is less severe as compared to those with EOS, CS, or NMS [26, 36, 37].

Worsening of the scoliotic deformity also leads to an indirect decrease in the lung compliance (progressive atelectasis and air trapping due to compression of lungs by the rib cage deformity, reorientation of surface tension forces, and/or alteration of elastic properties of lungs). Ultimately, regardless of the initial causative mechanisms, irreversible lung atrophy due to chronic hypoinflation and atelectasis leads to a further decline in lung volumes [36].

Besides the reduced inspiratory capacity, patients with significant scoliosis also have an ineffective ventilatory pattern which relies on an increased frequency of respiration (rather than an increase in tidal volume) and is achieved at the cost of extra work by the rib cage and abdominal expiratory muscles; this pattern is evident at rest, on exertion as well as during sleep. Consequently, the work of breathing increases significantly; respiratory muscle fatigue sets in over time and predisposes to the development of respiratory failure [26, 36]. Further, the significant difference between geometry of each hemithorax leads to asymmetrical alveolar ventilation (overventilation on convex side and underventilation on concave side of the curve), especially in children with severe CS and infantile thoracic scoliosis [26, 36].

The gas exchange becomes impaired in extremely severe scoliosis; chronic hypoxemia and hypercapnia occur due to the ventilation-perfusion mismatch, alveolar hypoventilation, increased dead space and alveolar shunting. This predisposes to the development of respiratory failure, elevated pulmonary vascular resistance (PVR), pulmonary hypertension (PHT), cor pulmonale and eventually, right-ventricular failure (RVF) [26, 37, 39].

Though restrictive lung defects are most prevalent, obstructive lung disease with moderate to severe air trapping has also been observed in patients with severe scoliosis. Narrowing, rotation, compression, and/or displacement of the trachea and mainstem bronchi can occur in patients with severe rotational deformity and hypo-kyphoscoliosis of the thoracic spine [26, 36, 39]. Lower airway obstruction also develops as the disease worsens, possibly because of an increased bronchomotor tone (to compensate for the restricted chest wall movement and/or to resist compressive scoliotic forces) and/or due to airway hyper-responsiveness (chronic airway inflammation secondary to poor clearance of secretions); it usually responds to bronchodilators [36, 39].

The altered thoracic geometry also leads to subtle changes in the position and functioning of the heart and large vessels, which restricts the increase in stroke volume that may be necessary during conditions of increased metabolic demand,

such as during exercise [26]. In addition, impaired myocardial diastolic function and structural cardiac anomalies, especially mitral valve prolapse (MVP; in 25% of AIS patients) are also observed in patients with IS [40–42].

Question 10:
What are the factors that influence the extent of cardiorespiratory impairment in patients with IS?

Answer:
The severity of cardiorespiratory impairment in IS is largely linked to the age of onset of scoliosis (high risk of cardiopulmonary compromise in children with EOS), severity of the thoracic curve, number of vertebrae involved (7 or more), location of the curve in the proximal thoracic spine (more cephalad thoracic curves cause more severe lung compression), and the degree of thoracic hypo-kyphoscoliosis (thoracic kyphosis less than 10°) [26, 37, 43–46].

Significant respiratory impairment is relatively uncommon in AIS patients, except in those with extremely severe scoliosis [7, 12, 47]. Generally, patients with an AIS and a Cobb angle <35° (mild to moderate scoliosis) do not experience any respiratory symptoms, apart from a decrease in their exercise capacity [26]. A reduction in the work capacity and ventilatory reserve may be observed when the Cobb angle exceeds 40°; this is probably related to the generalized muscle dysfunction (particularly lower limb muscle dysfunction) often observed in patients with IS, rather than due to a ventilatory impairment induced by the spinal deformity [48].

Lung function abnormalities are usually detectable on PFT, when the curves reach a Cobb angle of 50–60°, and may be fairly significant when they progress beyond 70° [36, 44]. Significant pulmonary symptoms, such as dyspnea, inability to cough or clear secretions, usually appear when the thoracic curves exceed 65–80° [26]. Curvatures greater than 100° are associated with significant alveolar hypoventilation and arteriovenous shunting. Patients with curves more than 120° have a high risk of developing irreversible respiratory failure and cor pulmonale [3, 36, 42].

Question 11:
What are the common findings on PFT and arterial blood gas (ABG) analysis in patients with AIS?

Answer:
The PFT findings usually indicate a restrictive lung defect. The vital capacity (VC), FVC, and FEV1 are decreased; FEV1/FVC ratio is usually normal (unless there is coexisting obstructive airway disease). There is an inverse (though not linear) relationship between the severity of the curve and the decrease in the FVC as well as FEV1 [3, 37, 45, 49].

The TLC, functional residual capacity, inspiratory capacity, and expiratory reserve volume are also decreased. Residual volume (RV) is generally maintained; however, it may decline slightly in severe scoliosis. Due to the relative decrease in TLC, the RV/TLC ratio is increased. (due to incomplete exhalation because of expiratory respiratory muscle dysfunction, and/or due to lower airway obstruction) [26].

Maximum inspiratory pressure is decreased and its fall to less than 30 cmH_2O indicates a high likelihood of respiratory insufficiency and a need for prolonged ventilator support postoperatively. Maximum expiratory pressure is normal or may be low. Expiratory flow rates are decreased proportionally to the restricted lung volume [7].

Curves greater than 35° may cause mild hypoxemia (presumptively due to ventilation-perfusion mismatch) with normocapnia. Hypercapnia is generally observed when the curves exceed 100°.

Question 12
Why do patients with NMS develop severe respiratory failure and significant cardiovascular decompensation at an earlier age and at a much lesser curve magnitude, than those with AIS?

Answer:
Besides the scoliotic deformity, patients with DMD have progressive respiratory muscle weakness (due to the underlying muscular dystrophy), which starts in early infancy and results in a greater distortion of the relatively compliant thoracic cage, and consequently, a higher reduction in the chest wall compliance, and a more severe "true lung hypoplasia."

Further, while patients with IS can maintain a relatively adequate ventilation (albeit with a significantly increased work of breathing), patients with DMD are unable to do so because of their primary myopathy; this leads to an earlier and a more severe development of lung atelectasis.

In addition, abnormalities in the central respiratory drive, nocturnal hypoventilation, frequent respiratory infections, upper airway obstruction, poor cough reflexes, inability to clear secretions, and pulmonary fibrosis due to the recurrent pulmonary aspiration further aggravate the increased respiratory morbidity. Reactive airway disease is also fairly common in children with CP.

These changes lead to a steady deterioration in their respiratory function throughout life, with an average decrease in the vital capacity (VC) by about 4% every year and a further 4% reduction for every 10% increase in the Cobb angle [50]. Patients with curves that exceed 35% usually have less than 40% of the predicted VC [51]. Though the risk of mortality remains high, use of non-invasive positive-pressure ventilation (NIPPV) has been reported to significantly improve their survival; initially, NIPPV may be required only during sleep, but as the disease gradually worsens, daytime use also becomes necessary.

More than 90% patients with DMD have clinical or subclinical cardiac dysfunction. Dilated cardiomyopathy (fibrosis of posterior basal and lateral wall of left ventricle) develops in more than 50% patients, usually after 10 years of age; by 15 years of age, the ejection fraction may be lower than <45% [52]. The cardiomyopathy predisposes to occurrence of arrhythmias, ventricular dilatation, and congestive cardiac failure, and may also result in mortality in 10% of the patients [53]. Patients with CP are also at risk of developing RVF as a result of the increased PVR and PHT due to the chronic hypoxia.

22.2 Surgery-Related Considerations

Treatment recommendations for AIS (observation, physiotherapy, bracing, surgery) are largely driven by the curve magnitude and rate of curve progression. Surgery is usually indicated when the Cobb angle exceeds 50°; its aim is to correct and limit further progression of the deformity, restore the truncal balance, improve cosmesis and reduce the risk of cardiopulmonary complications later in life [4, 11]**. The surgery usually involves an instrumented fusion of the spine and occasionally, a thoracoplasty.**

Question 13:
What are the various surgical approaches through which this surgery can be performed? Which is the most commonly used approach?

Answer:
Surgery for correction of the scoliotic deformity can be performed through an anterior, posterior, or a combined anterior-posterior approach; the choice of approach is usually determined by the type of curve, degree of spinal flexibility, and preference of the surgeon.

Anterior approach: The anterior approach (standard open thoracotomy or thoracoscopic) is performed with the patient placed in the lateral decubitus position and is particularly useful for correction of stiff thoracic curves. However, it involves violation of the thoracic cavity and quite often requires use of one lung ventilation (OLV) (for selective collapse of the lung on the operative side) to facilitate access to the thoracic spine**.**

The standard open thoracotomy is performed through a large lateral skin incision on the flank and entails removal of portion of a rib, opening of the pleura, and placement of a postoperative chest drain. This approach is associated with a significant decline in postoperative pulmonary function and an increased risk of pulmonary complications including pneumonia, lobar collapse, pleural effusion, atelectasis, and prolonged ventilatory support [1]. Other potential complications include injury to heart, lungs, pleura, diaphragm, major vessels, and thoracic duct; spinal cord ischemia due inadvertent injury to the artery of Adamkiewicz (in left sided approach); and postoperative flank pain and scarring.

Video assisted thoracoscopy (VATS) is increasingly being used as an alternative to the traditional open thoracotomy. It is less invasive, poses fewer problems with pain and altered pulmonary function, and also requires a shorter hospital stay, but the extent of curve correction achieved is probably inferior, compared to the traditional approach [1, 54, 55]. Moreover, the smaller incision sometimes makes complications more difficult to manage; an inadvertent entry into a large blood vessel or a viscera may necessitate a rapid conversion to an open thoracotomy.

Posterior approach: The posterior approach (dorsal midline) surgery is performed with the patient placed in the prone position and relies on use of segmental thoracic pedicle screw and rod constructs to provide a robust three-column control of each vertebra. Its results are reported to be superior to the anterior approach surgery (higher fusion rates, superior curve correction, and better rib hump reduction) [19, 56]**.** Moreover, it is technically easier, does not require violation of the thoracic cavity or use of OLV and is associated with a lower complication rate, better preservation of pulmonary function, lesser risk of neurovascular compromise, and a shorter hospital stay, as compared with the anterior approach. Given these advantages, it is presently the preferred approach for management of majority of the scoliotic curves (with adequate flexibility), including most of the complex thoracic curves [56, 57].

Combined anterior and posterior approach: While the posterior only approach provides satisfactory results for most of the scoliotic curves, however a combined anterior-posterior approach may occasionally be necessary for correction of large curves (Cobb angle >70–80°), excessively rigid curves (usually not bending less than 50°), large thoracic curves with severe kyphosis, and for prevention of crankshaft phenomenon in skeletally immature adolescents [58, 59]. It involves an anterior release (usually including diskectomy and bone grafting) through an open or endoscopic approach, followed by a staged or same-day, posterior segmental instrumentation and fusion. Being technically more complex, it is associated with much greater blood loss and a higher incidence of complications than the anterior or posterior approach (reported incidence of postoperative complications with posterior, anterior, and combined approaches: 6.7%, 10.0%, and 19.8%, respectively) [60].

This patient has been advised to undergo a posterior spinal fusion (PSF) with pedicle screw fixation from T4 to T12 vertebrae, in view of his very severe (>55° Cobb angle), rapidly progressive, thoracic AIS, along with presence of factors that indicate a high likelihood of curve progression (large thoracic curve, significant remaining growth potential).

Question 14:
What are the pertinent steps of a PSF procedure, and what are their implications for the neuroanesthetist?

Answer:
The surgery is typically an extensive multi-level procedure, in which rods (most common instrumentation device) are anchored to the vertebral column (VC), by screws placed in the pedicles, in order to stabilize the spine, allow early postoperative mobilization, and facilitate a faster bony fusion. The surgery is broadly divided into four steps: spine exposure; anchor placement; instrumentation and deformity correction; arthrodesis and closure.

Exposure of the spine: A midline longitudinal skin incision is made over the spine, and the dissection is extended down through the dermis, subdermal adipose tissue, to the supraspinous ligament and spinous processes. Subperiosteal dissection is performed bilaterally at each level, along the spinous processes, laminae, and out to the tips of the transverse processes. The spinous processes are harvested, and laminae and transverse processes are decorticated to prepare the fusion bed; and generous facetectomies are performed at the levels that are to be fused [57]. This soft tissue dissection and bone decortication can result in considerable blood loss. Sometimes,

additional complex interventions such as Pontes/Smith-Peterson osteotomy, pedicle subtraction osteotomy, or vertebral column resection may also be necessary in patients with very severe, rigid curves (especially in patients with CS, NMS) or for correction of severe focal kyphoscoliosis. While these techniques are expected to improve the spinal mobility, they are also associated with a markedly increased risk of complications, including severe bleeding, iatrogenic neurological injury, and dural tears [56, 60, 61].

The surgeons take several measures to minimize the vascular oozing and improve the hemostasis during this stage of the surgery; these include avoidance of extraperiosteal dissection into paraspinal musculature; epinephrine infiltration in intradermal and subcutaneous tissues; use of an ultrasonic bone scalpel for performing the facetectomy and posterior column osteotomy; use of electrocautery/bipolar sealers, collagen shrinkers, or other hemostatic sponge agents; and placement of packing at each levels [62]. Use of controlled hypotension further helps to decrease the blood loss during this stage of the surgery.

Anchor fixation (bilateral segmental transpedicular thoracic screw fixation): During this stage, pedicle screws are inserted into the cancellous bone of the VBs ("safe area": just lateral to the middle aspect of superior facet) on the convex side of the curve, under CT or fluoroscopy guidance or by the free hand technique. Prior to the screw insertion, a probe is passed through a tract created by a gear shift into the cancellous bone in order to determine the length of the screw and also to ensure that the walls of the pedicle are intact. Insertion of the screws is associated with several risks including severe blood loss (bloodiest step of PSF), iatrogenic neurological injury, and dural tears [62]. An improperly positioned screw can breach the medial or inferior pedicle wall to impinge on the exiting nerve roots; anterior penetration of screw through the VB body cortex in the thoracic region can result in injury to the thoracic aorta [62]. Hence, recent consensus guidelines recommend use of intraoperative neurophysiological monitoring [IONM; motor evoked potentials (MEPs) and electromyography (EMG)] during and after placement of the pedicle screws to aid in avoidance or early detection of nerve root injury [57, 63].

Instrumentation and deformity correction: During this stage, two contoured or adjustable stainless steel rods are placed along the concavity of the curve (for hypokyphotic or normokyphotic sagittal alignment) to distract and straighten the spine. These rods are attached and tightened onto the pedicle screws, and then rotated in a 90° derotation maneuver, to correct the frontal and sagittal alignment and improve the spinal stability; a convex rod may also be placed to reduce the axial rotation. After satisfactory alignment is achieved, the locking bolts are finally tightened, and a final fluoroscopy is performed to check the correction as well as to exclude the possibility of an inadvertent pneumothorax.

This stage is associated with a high risk for neurophysiologic compromise; stretching of the cord predisposes to arterial spasm, and consequently, an ischemic neurological injury; even a minor change in the spinal alignment during distraction of the vertebral elements can result in a neurological deficit due to stress on the cord. IONM [somatosensory evoked potentials (SSEPs) & MEPs] is used to determine the safe extent of distraction of the spine; spinal cord protection measures are implemented to help preserve the neurological integrity during this phase of the surgery.

Arthrodesis and closure: In this stage, autologous bone graft (taken during decortication/harvested from the iliac crest/rib if thoracoplasty is being performed) is packed over the raw decorticated surfaces to promote spinal fusion; deep fascia and skin are closed in layers after performing a thorough irrigation.

Question 15:
Thoracoplasty may occasionally be performed in conjunction with a PSF, for reducing the rib hump deformity. What are its potential implications for the neuroanesthetist?

Answer:
Since thoracoplasty typically involves excision of prominent rib sections on the convex side of the thoracic deformity (from posterior axillary line to the junction with the transverse process), it can lead to severe pain in the rib area and a significant decline in the pulmonary function in the postoperative period; there is also a risk of inadvertent pleural injury. This procedure is typically not recommended if the preoperative FVC of the patient is less than 60% of predicted values.

22.3 Anesthetic Considerations

Question 16:
Enumerate the pertinent anesthetic considerations for management of AIS patients undergoing a multilevel PSF?

Answer:
Most AIS patients are healthy and have an acceptable functional status (except those with cardiorespiratory compromise due to extremely severe scoliosis); however, the surgeries are invariably complex, usually involve at least 6–8 vertebral levels and often last for several hours. The specific anesthetic concerns that may arise during the PSF are listed below.

- Major blood loss with risks of hemodynamic instability, increased blood transfusion requirement, coagulation disturbances, cardiopulmonary and renal dysfunction, infection, and postoperative mechanical ventilation.
- Risk of iatrogenic neurological injury.
- Provision of optimal conditions for IONM.
- Complications related to use of prone position.
- Risk of postoperative pulmonary dysfunction and an increase in the incidence of postoperative pulmonary complications (PPCs) including the need for prolonged ventilatory support (especially in patients with severe preoperative respiratory dysfunction).
- Risk of hypothermia.
- Risk of infection, especially surgical site infection (SSI).

Question 17:
What is the risk of major blood loss and transfusion requirements during the surgery?

Answer:
Various studies have evaluated the risk factors for major blood loss during corrective surgeries for IS; important factors include severity of the curve (>8 spinal levels), number of vertebrae to be fused (>6), hyper-kyphosis, surgical approach (combined and posterior approaches), prolonged duration of surgery, osteotomy and bone graft size, intraoperative mean arterial pressure (MAP), preoperative hematocrit and coagulation status, male gender, and a low BMI [64–66].

PSF results in greater blood loss as compared with ASF (PSF:275–907 mL; ASF: 323–171 mL), most likely due to the larger surgical exposure of the highly vascular paraspinal muscles, together with engorgement of the vertebral venous plexuses in the prone position; blood loss during combined approaches is even higher (821–1277 mL) [62, 64].

According to an analysis of a large Nationwide Inpatient Sample (NIS) database, by Yoshihara et.al, the incidence of autologous blood transfusion (ALBT) during spinal fusion procedures for children with IS was approximately 30%; children undergoing a posterior or combined approach surgery, fusion of nine or more spinal levels, and/or those with a Elixhauser comorbidity score >4 (most common comorbidities: chronic pulmonary disease, anemia, fluid and electrolyte disorder) were at an increased risk of receiving an ALBT [67, 68]. In another retrospective analysis by Kim et.al, a massive transfusion was deemed necessary in 9.7% of AIS patients undergoing PSF and was also associated with a poorer clinical outcome; the risk of a massive transfusion was higher in patients with a low BMI, higher number of fused vertebrae and Lenke type 4 curves [69].

Hence on basis of the abovementioned considerations, this patient has a significant risk of increased perioperative blood loss and transfusion [male gender, severe curve (T1–L2 vertebra, 57° Cobb angle) posterior approach surgery, spinal fusion of nine vertebral levels].

Question 18:
What is the risk of neurological injury during the surgery?

Answer:
Neurological injury (injury to nerve roots, spinal cord, peripheral nerves), though relatively uncommon [incidence of new neurologic deficits (NND) during PSF and combined approach surgery for AIS: 0.3% and 1.2%, respectively], is the most feared complication of scoliosis correction surgeries [70]. Risk factors for neurological injury include correction of curves that are large (Cobb angle >90°) or associated with significant kyphosis or require a vertebral osteotomy; revision surgeries; and combined surgical approaches [7, 11, 33].

The injury can occur due to direct mechanical trauma by the surgical implant, instrument, or bony structure, or indirectly as result of spinal cord ischemia. The ischemia can result from several mechanisms including excessive distraction of the SC or compression of blood vessels during a deformity correction maneuver; diminished perfusion due to intraoperative hypotension; interruption of radicular blood flow due to accidental ligation or damage to the vessel; or secondary to development of an epidural hematoma [71, 72].

Concomitant hypotension, significant hemorrhage, anemia, hypoxia, or hypothermia further worsen the neurological injury [70, 73, 74]. The thoracic SC is particularly vulnerable to ischemic injury because of several reasons, including its overall lower blood supply as compared to the cervical and lumbosacral cord; relatively scarcity of anterior radicular arteries in the midthoracic region; and presence of a "watershed zone" at the union of anterior spinal artery and anterior radicular arteries.

Question 19:
Why is important to be extremely careful while positioning these patients for PSF?

Answer:
These anesthetized patients are placed in the prone position for several hours during these extensive surgeries. This puts pressure on their soft tissues, which predisposes to development of local ischemic changes and in severe cases, even tissue necrosis of the weight bearing bony prominences; pressure sores of the breast and genitalia are extremely common injuries. More serious complications such as cardiorespiratory compromise, compression neuropraxia, and perioperative visual loss (POVL) are often the consequences of improper positioning. Oropharyngeal and conjunctival swelling due to venous congestion and interstitial edema in the dependent position; macroglossia because of inadvertent protrusion of the tongue between the teeth; and cervical spine injury and carotid or vertebral artery occlusion (less common) while shifting the positions, have also been reported in the literature. Furthermore, hypotension, excessive blood loss, obesity, and presence of comorbidities further increase the likelihood of these complications.

Cardiorespiratory complications: Abdominal compression due to improper prone positioning raises the intra-abdominal pressure. This puts direct pressure on the inferior vena cava leading to peripheral venous pooling, a decrease in venous return and cardiac output as well as an increase in the surgical bleeding due to engorgement of the valve-less epidural and para-vertebral venous plexuses. The increased intra-abdominal pressure also has a detrimental effect on ventilation owing to the cephalad displacement of abdominal contents, restriction of diaphragmatic movements, and increased airway pressures. Moreover, the increased thoracic pressure causes a decrease in the left ventricular volume, stroke volume, and a further reduction in the cardiac output, while raising the central venous pressure (CVP). Increased surgical blood loss in the setting of a suboptimal cardiac output markedly enhances the risk of intraoperative hypotension and organ hypoperfusion especially acute kidney injury; catastrophic cardiovascular collapse due to obstruction of inferior vena caval flow by improperly positioned supporting pads or operating table frame has been reported in the literature [75].

Compression neuropraxia: Peripheral neuropathy occurs due to intraneural capillary ischemia, resulting from overstretching or

compression of a nerve due to an improperly positioned limb, in combination with a prolonged period of intraoperative hypotension [33, 72]. The brachial plexus is particularly vulnerable, as it not only traverses across three mobile bony structures (clavicle, first rib, humeral head) but is also fixed at the cervical vertebrae and the axillary fascia [75]. Compression of the brachial plexus and subclavian vessels (in the costo-clavicular space) and/or stretching of the plexus (across the coracoids process and glenohumeral joint) can occur with hyper-abduction of the shoulder (beyond 90°); the risk though is lower as compared with hyper-abduction in the supine position, as reportedly, these positions have different effects on mobility of the shoulder and the brachial plexus [76].

Ulnar nerve injury may result from direct compression at the cubital tunnel (elbow) due to direct pressure by the arm boards, or because of excessive elbow flexion (>90°), or indirectly, because of ischemia, resulting from compression of the brachial artery (due to a malpositioned upper limb) [75]. Common peroneal N is vulnerable to direct compression at the fibular head; lateral femoral cutaneous N injury (Meralgia paresthetica) is related either to iliac crest bone harvesting or to anterior compression of the nerve by an improperly placed pelvic bolster, or resting pads of the spinal frame/table.

Ophthalmologic complications: POVL can occur due to several mechanisms, such as ischemic optic neuropathy (ION), central retinal artery occlusion (CRAO), and cortical blindness. ION is usually related to decreased oxygen delivery due to raised orbital venous pressures, during prolonged prone position surgeries; CRAO or horseshoe head rest syndrome occurs due to retinal ischemia caused by a direct compression on the eye globe as a result of improper positioning of the head in the head support device (usually a horseshoe head rest). Cortical blindness is caused by decreased perfusion to the visual cortex of the occipital lobes in the brain, typically due to prolonged hypotension, hypoxia, cardiac arrest, or a thromboembolic event [75].

POVL is a relatively rare complication of pediatric scoliosis correction surgeries, with an estimated incidence of 0.16%, as per a retrospective analysis of large NIS database, by Ramos et al. [77] However, while ION and CRAO usually account for most of the cases of POVL observed in adults, cortical blindness was responsible for all the cases of POVL in pediatric patients, in the abovementioned analysis [77]. A younger age, male gender, long segment fusions (eight or more spinal levels), anemia, and Medicaid as insurance were identified as independent risk factors for occurrence of POVL in this study.

Question 20:
What is the potential risk of PPCs in this patient?

Answer:
Postoperative pulmonary dysfunction in AIS patients results from both their preexisting scoliosis related respiratory impairment (with curves >60%) as well as the surgery induced immobility, pain, and atelectasis; use of a surgical approach that involves violation of the chest wall (anterior thoracotomy, VATS posterior approach with thoracoplasty) further increases the risk [78, 79]. Lung volumes can decrease by up to 60% in the immediate postoperative period; FEV1 and FVC values are reported to be the lowest on the third postoperative day and can continue to remain significantly low for up to a week after the surgery [80]. It may take up to 2–3 months for these values to return to the baseline, or even longer (up to 2–3 years) if the surgical approach involves violation of the thorax. The posterior only approach is reported to have the least detrimental effect on the postoperative pulmonary function [44, 45, 56, 81].

PPCs such as atelectasis, bronchospasm, pneumonia, hemothorax, pneumothorax, pleural effusion, and respiratory failure necessitating prolonged mechanical ventilation are not uncommon. The risk of postoperative respiratory failure with a need for prolonged mechanical ventilation is particularly high in patients with large scoliotic curves (>100°), and in those with severely deranged PFT values (preoperative FEV1 <40%,

FVC <30% (or less than 25 mL/kg body weight), VC <60%, inspiratory capacity <30 mL/kg, or TLC <60% of predicted values) [82].

This patient has normal respiratory parameters, with a mild restrictive lung defect on spirometry evaluation which highly precludes the likelihood of his developing respiratory failure in the postoperative period; however, concerns related to surgery induced hypoventilation and atelectasis are inevitable and merit appropriate attention.

Question 21:
What are the additional anesthetic concerns during spinal fusion in patients with NMS or CS?

Answer:
Patients with NMS and CS have a much higher incidence of morbidity (higher blood loss, SSI, and PPCs including pneumonia, respiratory failure, and prolonged mechanical ventilation), mortality, and new neurological deficits (NNDs) than those with IS [reported incidence of morbidity, mortality, NND—NMS: 17.9%, 0.3%,1.1%; **CS**: 10.6%, 0.3%, 2%; **IS**: 6.3%, 0.02%, 0.8%, respectively) [33]. Several factors contribute to their worse outcome: poor preoperative functional status (multiple systemic comorbidities and/or congenital anomalies; severe cardiopulmonary dysfunction, poor nutritional status); larger and stiffer curves which necessitate more prolonged and extensive surgeries (often involving osteotomies or a combined approach) (Table 22.4).

The estimated blood loss during PSF for NMS ranges from 2000 to 3500 mL; DMD patients are at the highest risk, with the blood loss sometimes even exceeding their estimated blood volume [7, 42, 83]. In addition to the inherent surgical technique related risk, several other DMD-related factors including osteopenia, vascular pathophysiological changes, and coagulopathy exacerbate the perioperative blood loss in these patients [7, 42, 83].

Patients with CP are often on antiepileptic drugs for concomitant seizure disorders, which further increase their bleeding risk [84]. Moreover, malnourishment as a result of a high metabolic demand (due to frequent illness) as well as a suboptimal oral intake [due to gastroesophageal problems: gastroesophageal reflux disorder (GERD), hiatal hernia, poor oropharyngeal control] leads to an impaired production of Vitamin K dependent factors. The incidence of their postoperative complications correlates with the extent of their spinal deformity (Cobb angle >70°), medical problems, neurological impairment, and nutritional status (weight for age below fifth percentile) [84, 85].

Patients with CS have a high incidence of intraspinal abnormalities (18–38% incidence) which greatly increases their risk for neurological injury during the surgery [18, 86].

22.4 Preoperative Considerations

Question 22:
What are the specific considerations during the preoperative evaluation of patients with IS for PSF? Is a PFT, ABG analysis and echocardiography necessary in all patients? What are the additional considerations for patients with NMS or CS?

Answer:
The preoperative evaluation (history of the patient and family, clinical examination, review of clinical records and investigations) focuses on identification of the patient-specific as well as surgery-related factors that can influence the perioperative course of the patients (Tables 22.5 and 22.6). Pertinent considerations include an assessment of the type and severity of scoliosis; cardiopulmonary and neurological status of the patient; presence of comorbidities and/or congenital anomalies; presence of factors associated with an increased bleeding risk; and the details of the surgery. Important aspects of this evaluation are discussed below.

Since the curves in AIS are usually right sided, presence of a left sided curve should raise the suspicion for other underlying conditions and congenital anomalies.

A good exercise tolerance and absence of respiratory symptoms are generally good predictors of an acceptable cardiorespiratory

Table 22.5 Preanesthetic evaluation of patients with adolescent idiopathic scoliosis for posterior spinal fusion: pertinent considerations regarding history and clinical examination

Assessment of the type and severity of the scoliosis
Age of onset of scoliosis
Type of scoliosis: Idiopathic: adolescent/juvenile/infantile
Anatomical site: cervical/cervicothoracic/thoracic/thoracolumbar/lumbar
Direction of the curve: right/left sided
Type of curve: single/double/major
Number of vertebral levels involved
Severity of the curve: Cobb angle, vertebral rotation
Pertinent surgical details
Proposed surgical procedure
Site, number of vertebral levels to be fused
Surgical approach and position of the patient
Anticipated surgical duration and blood loss
Type of instrumentation planned
Plan for osteotomy/vertebral column resection
Cardiopulmonary evaluation:
History: baseline exercise tolerance (to assess the cardiopulmonary reserve), dyspnea on exertion, tachypnea, cough, wheezing
Auscultation of lungs: Bilateral air entry (may be unequal and/or decreased in advanced scoliotic deformity); wheeze/crepitations (obstructive or parenchymal lung disease)
Cardiac evaluation: Heart sounds (pulmonary hypertension: accentuation of pulmonic component of second heart sound (loud P2); cardiac murmurs; signs of right ventricular failure (engorged neck veins, hepatomegaly, lower extremity edema)
Neurological evaluation
History: back pain, neurological deficits, gait problems, truncal imbalance
Examination: graded strength testing of all extremities; assessment of dermatomal sensation, and vibratory and position sense (proprioception); deep tendon reflexes, clonus, Babinski reflex, abdominal reflexes; gag reflex; supine straight leg raise test
Evaluation of bleeding risk
History of bleeding during prior surgical interventions/dental procedures; history of epistaxis, menorrhagia, hematuria, easy bruising
Presence of any congenital anomalies/comorbidities/increased bleeding risk
Past medical history, including detailed birth history, developmental milestones (to rule out other causes of spinal deformity)
Family history: scoliosis, other spinal deformities, major musculoskeletal conditions, bleeding disorders (family screened for any religious or cultural concerns regarding blood transfusion, i.e., Jehovah's Witness)
History of medications/allergies
Airway assessment
Skin examination:
Presence of lesions that may indicate other causes of scoliosis (e.g., hair patches, sinuses, dimples over lower back in neural tube defects; café au lait spots, axillary spotting subcutaneous nodules, and axillary freckles in neurofibromatosis)

reserve and the patient's ability to withstand the stress of a major operation; an adequate cough usually indicates a satisfactory forced expiratory volume [3].

The preoperative neurological assessment should be carefully documented as it serves as a baseline for identification of postoperative neurologic deficits. Patients with AIS usually have a normal neurological examination. Signs such as a positive supine straight leg raise test (impingement of a nerve root), abnormal gag reflex (underlying hindbrain anomaly, e.g., Arnold–Chiari malformation), asymmetrical or absent abdominal reflexes (intraspinal pathology, e.g., syringomyelia) are

Table 22.6 Preanesthetic evaluation for deformity correction surgery in patients with scoliosis: routine and special investigations

	Routine investigations	Special investigations[a]
Respiratory system	Plain chest radiograph Spirometry Baseline oxygen saturation	Pulmonary function tests (including bronchodilator reversibility) Arterial blood gas analysis Pulmonary diffusion capacity
Cardiovascular system	Electrocardiogram	Echocardiography/dobutamine stress echocardiography
Blood tests	Full blood count (hemoglobin, hematocrit, total and differential leucocyte count) Coagulation profile (platelet count, prothrombin time-international normalized ratio, partial thromboplastin time, bleeding time) Blood crossmatch Blood sugar serum electrolytes	Liver function tests Renal function tests
Radiological and other investigations	X-ray spine AP view X-ray chest PA view	MRI spine scan (for detecting intraspinal abnormalities in children with CS) Renal ultrasound (in children with CS) Cervical spine radiograph series with lateral flexion and extension (to rule out instability cervical spine anomalies in CS as many syndromes are associated with difficult intubation) Doppler ultrasound lower limbs Polysomnography/overnight pulse oximetry (in patients with very severe scoliosis)

MRI magnetic resonance imaging, CS congenital scoliosis, EOS early onset scoliosis, AP anteroposterior, PA posteroanterior

[a]May be indicated in children with EOS, CS, very severe AIS

suggestive of an associated neurological problem; these patients are at increased risk for developing SC injury during the surgery and require an MRI scan of spine (and brain, if indicated) for further evaluation.

In addition to the routine investigations, spirometry and a baseline SpO_2 should be performed in all patients. The spirometry aids in determining the severity of the restrictive lung disease, identifying obstructive airway disease, and also in assessing the risk of PPCs [3]. The baseline oxygen saturation SpO_2 (in the supine position, breathing room air) provides a simple and effective method for evaluating the risk of PPCs [87]. A low preoperative SpO_2 is a significant independent risk factor for development of PPCs; the risk is reported to be twice as high if it is 91–95% as compared with SpO_2 values greater than a >96%, and it increases tenfold with SpO_2 values lower than 90% [87].

While the routine use of PFT is slightly controversial, it is definitely indicated in patients who have EOS or a severe restrictive lung defect on spirometry evaluation. In addition, if routine spirometry testing reveals an obstructive airway disease (a decrease in FEV1/FVC ratio; or a decrease in forced expiratory flow (FEF 25–75%), then a bronchodilator should be administered to determine its reversibility.

An ABG analysis should be performed in patients with EOS, and in those who have a markedly reduced VC on PFT. Additionally, a formal sleep study or at least an overnight oximetry may be considered in patients with very severe scoliosis (even if reasonably normal levels of oxyhemoglobin saturation are maintained when they are awake) [88].

An echocardiography is required in patients with EOS, extremely severe scoliosis (>100°), significant exercise intolerance, poor respiratory function (for evaluation of biventricular function), clinical or ECG signs of right heart failure [jugular vein distension, hepatomegaly, hepatic

congestion, or lower extremity edema; ECG: right ventricular hypertrophy (right axis deviation, large R in V1 and V2), right atrial enlargement (P wave >2.5 mm)], evidence of a cardiomyopathy, and for detection of MVP, congenital or valvular heart disease (if suspected).

Patients with cervical or upper thoracic scoliosis should undergo an X-ray cervical spine, to detect a potentially difficult airway.

Patients with NMS or CS merit a more extensive evaluation; pertinent aspects are listed in Table 22.4.

Children with CS may require additional investigations, in accordance with their underlying pathology or syndrome, especially for evaluation of concomitant renal, cardiac, airway and intrathecal abnormalities (Table 22.5).

Question 23:
While this patient has an acceptable functional status (mild restrictive lung defect, no systemic comorbidities or congenital anomalies), however, several patients especially those with very significant spinal deformity, EOS, NMS, or CS have a poor functional status and may not be able to tolerate the surgery well. What preoperative measures can be taken to optimize their condition, and reduce the perioperative morbidity?

Answer:
Preoperative optimization focuses on correction/optimization of modifiable factors, such as cardiopulmonary dysfunction, anemia, and poor nutritional status. An intensive multidisciplinary approach (pulmonologist, physiotherapist, nutritionist, cardiologist, hematologist, anesthesiologist, spine surgeon) is vital and can result in a marked improvement in the clinical outcomes of these patients, including those with very severe pulmonary dysfunction (FVC <32%) [7, 89].

Optimization of the cardiopulmonary status: Initiation of an incentive spirometry based respiratory care program (e.g., I COUGH) helps to improve the preoperative pulmonary function and decrease the rates of postoperative pneumonia and unplanned re-intubation; it may be especially useful in patients with EOS, NMS and in those undergoing a thoracotomy. [87].

Reversible conditions such as asthma or respiratory infection should be controlled with steroids, bronchodilators, and antibiotics, as indicated.

An episode of a recent respiratory infection (within the last month) is associated a higher likelihood of developing a PPC; it may be prudent to postpone the surgery for 4–6 weeks to allow full recovery [3].

Patients, who are on NIPPV, should be referred to a pulmonologist and physiotherapist, for optimization of their respiratory condition. In addition, those who are likely to be transitioned to NIPPV [bi-level positive airway pressure (BIPAP)] in the postoperative period often benefit from preoperative training in the use of BIPAP and mechanically assisted coughing (facilitates an earlier tracheal intubation with a smoother transition to NIPPV, postoperatively) [90].

Patients with NMS, CS and those with severe cardiopulmonary compromise due to IS and/or an MVP require a consultation with a cardiologist for further evaluation and optimization of their cardiac status.

Correction of anemia: Preexisting anemia (<10 mg %) is associated with an increased risk of postoperative pneumonia, increased length of hospital stay, and a higher mortality; hence it should be investigated and corrected, in consultation with the hematologist.

Treatment options for iron deficiency anemia include dietary supplements, such as folate, vitamin B12, and iron therapy. Preoperative intravenous iron supplementation replenishes the iron stores in 7–14 days and is a safe option for increasing the hematocrit; recombinant erythropoietin (ESA), though effective, is reported to be associated with an increased risk of deep vein thrombosis (DVT) [91].

Preoperative autologous blood donation may be considered; however, recent "consensus-based best practice guidelines" for perioperative management of blood loss recommend against its routine use during PSF for AIS because of reports of reduced blood loss as well as of significant

wastage of unused autologous donor units, during these surgeries [92–94].

Nutritional optimization: Patients with CP require a preoperative evaluation of their gastroesophageal problems and poor nutritional status. The GERD can worsen after the surgery and exacerbate their aspiration risk. A Nissen fundoplication procedure should be considered prior to the scoliosis surgery, in patients with severe GERD not responsive to medical management, as it has been shown to result in a considerable reduction in their postoperative morbidity [95]. In addition, they may require aggressive measures for optimization of their nutritional status including insertion of a gastrostomy tube especially if they have a low plasma albumin (<3.5 g/dL) or lymphocyte levels ($<1.5 \times 10^3/\mu L$); optimization of these parameters has been reported to lower the SSI rate and shorten their length of hospital stay [96, 97].

Question 24:
What are the other pertinent preoperative considerations for scoliosis correction surgeries?

Answer:
In addition to the optimization measures, the preoperative preparation should also include psychological preparation of the child and the parents. In particular, the process of intraoperative wake-up test (if planned) should be explained as it helps to ameliorate the anxiety of the patients and also ensures their cooperation during the assessment. They should be assured that while they will be awakened briefly during the surgery and will be asked to respond to commands (e.g., move the feet or hands), they will neither feel pain nor remember being awake during surgery.

Planning for large volume hemorrhage is a vital component of preoperative planning. Blood should be cross matched and reserved; if indicated, it should be available in the operating room, before commencement of the surgery [62]. Adequate quantities of other blood products [e.g., fresh frozen plasma (FFP), platelets, cryoprecipitate, coagulation factors] should also be readily available, especially in patients with nonidiopathic scoliosis.

Patients with NMS may be on preoperative medications (e.g., baclofen, diazepam for spasticity, corticosteroid therapy in DMD patients, antiepileptic drugs in CP patients), which should be continued perioperatively. Preoperative sedation with oral midazolam (0.5 mg/kg) may be considered.

Antibiotics are administered prior to the surgery to reduce the risk of SSI (cefazolin 20 mg/kg (maximum 2000 mg) given 30 min prior to incision; or in case of serious penicillin/cephalosporin allergy, vancomycin 10 mg/kg, given 150 min prior to incision) [72].

22.5 Intraoperative Management

Question 25:
What monitoring modalities and vascular accesses should be considered for the surgery?

Answer:
In addition to the standard monitoring (ECG, noninvasive blood pressure, SpO_2 end tidal carbon dioxide temperature, fluid input, urine output), insertion of two large bore peripheral venous cannulae (secured on the upper extremities for easier access); an arterial and a central venous access; monitoring of evoked responses, depth of anesthesia (Bispectral index, Patient State Index etc.) and extent of neuromuscular blockade should be considered during these extensive multilevel procedures. Further, point-of-care viscoelastic assays, if available, may be useful for guiding the blood component transfusion strategy in patients with severe intraoperative bleeding.

The arterial catheter allows continuous assessment of the BP and fluid responsiveness (pulse pressure variation), along with measurement of ABG, blood glucose, electrolytes and serum lactate levels; in fact, given the need for maintaining different BP targets during various phases of the surgery and the high risk of hypotension due to the extensive perioperative blood losses, it is a very vital component of the perioperative monitoring strategy.

A central venous access is useful for rapid transfusion of fluids and blood, infusion of vaso-

active medications; for monitoring the mixed venous saturation (SvO2) and the CVP (absolute CVP values are not an accurate indicator of the true preload in prone position surgeries, however the CVP trend provides adequate inputs for guiding the hemodynamic management).

Temperature monitoring is very important as these patients are prone to develop hypothermia because of the prolonged operating times and exposure of a large surface area. This not only increases the risk of complications (impaired platelet function, coagulopathy, increased blood loss, metabolic complications, impaired wound healing with an increased risk of SSI) but also delays the clearance of anesthetic drugs by prolonging their metabolism, interferes with correct interpretation of IONM, and significantly increases the likelihood of ventilation in the early postoperative period [98, 99].

Monitoring of the anesthetic depth and extent of neuromuscular blockade enable a precise titration of anesthetic drug dosages; this not only helps to reduce the risks of intraoperative awareness and inadvertent patient movement but also facilitates proper interpretation of IONM as well as a rapid emergence at the end of the surgery or for a "wake up" test.

Question 26:
How is the prone position achieved for a PSF in scoliotic patients? What measures should be taken to prevent the positioning-related complications?

Answer:
The patients are usually anesthetized in the supine position, and then turned prone, using a log roll technique (head, body rotated in unison while maintaining a neutral neck position), onto the positioning system [specialized table, e.g., Jackson Frame; radiolucent table with a specialized frame, e.g., Wilson, Relton-Hall; or bolsters which provide support to the sternum, iliac crest, and lower legs]. This transition should be well coordinated in order to avoid accidental dislodgement/kinking of the tracheal tube, the vascular accesses, and the monitoring lines; in some centers, the circuits and tubings are briefly disconnected during this transition. Patients with CS, Marfan syndrome, and neurofibromatosis may have concomitant cervical spine anomalies and must be turned and positioned with great care.

The patient's head and neck are placed in a neutral position on a soft foam/gel pad with preconfigured cutouts or a horseshoe headrest; their position may change during surgical manipulation of the spine and should be inspected frequently during the procedure. Eyes are closed; care is taken to avoid any external compression of the eyes, ears, nose, and face; soft mouth guards are inserted to prevent injury to the tongue and lips during intraoperative MEP monitoring. Use of specially designed facemasks and devices that allow periodic inspection of the face during surgery in the prone position, (e.g., prone View) provides increased safety in the prone position [100].

The patient's chest and abdomen should hang freely, with the legs at the level, and the head, above the level of the heart, respectively; a 10° reverse Trendelenburg position should be considered, if feasible. These maneuvers optimize the cardiac preload and respiratory function, minimize perioperative blood loss, and reduce the risk of POVL (high hydrostatic pressure in the eyes predisposes to reduced blood perfusion).

The arms are placed in an "air planed" position (<90° abduction at the shoulder and elbow) to allow intraoperative fluoroscopy and avoid compression neuropraxia; axillae are inspected to ensure that the frame does not compress the axillary sheath. In female patients, the breasts are positioned medially and caudal to the supporting pads to avoid direct pressure on the nipples; in males, the genitalia are allowed to hang freely. The patient's knees are flexed, feet are placed in the neutral position, and pelvic bolsters are carefully positioned to prevent inadvertent compression of the lateral femoral cutaneous nerve. All bony prominences and pressure points (elbows, pelvis, knees, and ankles) should be well padded. Further, utilization of IONM can help in early detection of positioning-related compression neuropathies.

While the overall aim during the prone positioning of these patients is to maintain/increase thoracic kyphosis and optimize the lumbar

lordosis of the spine, however, this optimal position is often elusive, owing to the scoliotic deformity. A combination of built-up thoracolumbar supports and a leg sling are often helpful; additional pillows can be used to elevate the legs, to improve the extension at the hip joint, during the correction of deformity.

Question 27:
Given the increased risk of major blood loss, what intraoperative strategies can be implemented to minimize the severe bleeding and the transfusion requirements in these patients?

Answer:
Recent "consensus-based best practice guidelines" recommend the administration of antifibrinolytics use of controlled hypotension during specific phases of the surgery, and avoidance of hemodilution, to decrease the blood loss and transfusion requirements during these surgeries [62]. In addition, simple measures such as avoidance of abdominal compression during prone positioning and a good surgical technique also contribute to a considerable reduction in the intraoperative blood loss. While other techniques such as acute normovolemic hemodilution and intraoperative red blood cell salvage with cell saver have also been used, however, the higher costs, logistic challenges, and above all the low evidence regarding their efficacy preclude their routine use during these surgeries [72]. Intraoperative cell salvage may probably be considered if the anticipated surgical duration is more than 6 h and estimated blood loss is greater than 30% of total blood volume; however, it is prudent to remember that this blood has heparin, and significant volumes of the re-transfused blood may induce a coagulopathy [101].

Antifibrinolytic drugs: Antifibrinolytics such as tranexamic acid (TXA) and epsilon aminocaproic acid (EACA) are synthetic lysine analogs, which reversibly bind to lysine-binding sites on plasminogen to prevent its conversion to plasmin and hence directly inhibit the degradation of fibrin (by plasmin).

Results of several studies demonstrate that these drugs are an effective, safe, and cost-effective option for mitigating the perioperative blood loss and transfusion requirements not only for PSF for AIS but also for the more complex spinal fusions in patients with NMS [102–105]. TXA is 6–10 times more potent than EACA and is more widely used because of its easy availability. Its optimal dose regimen, however, is not very well established (loading dose ranges from 10 to 30 mg/kg; subsequent continuous infusion dose: 1–10 mg/kg/h) [106, 107]. EACA is usually administered as 100–150 mg/kg i.v loading dose, followed by an i.v infusion at a rate of 10–15 mg/kg/h.

Controlled hypotension: Use of deliberate hypotension at the time of incision (lowering of the MAP to <65 mmHg) is reported to be a safe and effective technique to decrease the intraoperative blood loss, improve visualization during spine exposure, and reduce the operative time of these surgeries [108]. In a retrospective analysis of over 300 AIS patients, Verma et.al reported a 33% reduction in the blood loss by lowering the BP at the time of skin incision, without the occurrence of any hypotension-related complications. Several other studies also report a 29–49% reduction in the perioperative blood loss, with use of this technique [108–111].

However, in view of the potential risks of ischemic cord injury and POVL, the current consensus guidelines recommend limiting the use of "controlled hypotension" and using a "targeted MAP approach" according to the phase of the surgery. In this approach, the MAP is typically lowered to 60–65 mm of Hg during the spine exposure, with the help of anesthetic agents and/or specific hypotensive drugs (e.g., esmolol, labetalol), but is subsequently increased to maintain adequate SC perfusion during the instrumentation [72].

Question 28:
What should be the goals for intraoperative fluid and blood management?

Answer:
A meticulous fluid and blood management strategy is crucial not only for maintaining normal

plasma volumes and hemodynamic stability in the face of severe intraoperative bleeding but also to reduce the risk of hypoperfusion-related ischemic SC injury.

The fluid management plan should address the fluid deficits, maintenance requirements as well as the ongoing losses. Typically, isotonic crystalloids, e.g., Ringers Lactate, are the primary fluids of choice during pediatric spine surgeries; there are also some preliminary reports of the beneficial effect of sterofundin in preventing major acid base imbalance and preserving the plasma biochemistry, during these surgeries [112]. Colloids, e.g., low and medium molecular weight hetastarches (Pentastarch, Voluven; lesser coagulopathic potential than high molecular weight hetastarches), may be used as resuscitation fluids.

Glucose containing solutions are not routinely administered in children; they can result in significant hyperglycemia, which may potentially exacerbate an ischemic neurological injury. Nevertheless, children can develop hypoglycemia during these prolonged surgeries, and it may be prudent to monitor blood glucose levels intraoperatively, and infuse a dextrose containing solution if required.

Fluid therapy should be guided by static parameters (e.g., CVP, HR, BP) as well as dynamic estimates of fluid responsiveness (e.g., pulse pressure variability/systolic pressure variability) and the urine output; in addition, the adequacy of end organ perfusion should be also assessed (blood lactate, mixed venous oxygen saturation).

Ongoing blood losses are managed with administration of fluids (crystalloids, colloids), blood products, and if required, vasopressors (e.g., phenylephrine, norepinephrine). It is prudent to calculate the maximal allowable blood loss [EBV × (H0−H1)/H0; EBV—Estimated blood volume (70 mL/kg for children >2 years of age; H0—hematocrit at beginning of the surgery, H1—lowest acceptable/target hematocrit]. The transfusion trigger usually ranges from 25 to 30% hematocrit (or 7–9 g/dL hemoglobin) depending on the rapidity and amount of the blood loss, the hemodynamic parameters, adequacy of end organ perfusion, and the patient's general medical condition especially the cardiorespiratory reserve and coexisting cardiac/pulmonary morbidities.

Generally, blood transfusion is required if the blood loss exceeds 20% of the patient's EBV; typically, transfusion of 15 mL/kg packed red blood cells (PRBC) raises the hemoglobin concentration by about 3 g/dL. Blood component therapy, e.g., platelets FFP (dose—10–15 mL/kg), may be required if the predicted blood loss is greater than 40% of the circulating blood volume [113]. Technologies such as Sonoclot (Sienco, Inc), thromboelastogram (TEG), or Rotem have also been used to reduce the massive blood loss and precisely guide the transfusion strategy during these surgeries [114]. These technologies analyze the in-vitro rheological changes in the blood during the coagulation process, to identify the specific cause of bleeding, e.g., thrombocytopenia, depletion of clotting factors, hypofibrinogenemia, and fibrinolysis. Specific blood components are administered accordingly (platelet concentrates: platelet levels <100,000/m^3; cryoprecipitate: fibrinogen levels <150 mg/dL with microvascular/active bleeding or massive blood transfusion (dose: 1 unit per 5–10 kg body weight); desmopressin (0.3 μg/kg) for oozing despite a platelet count >100,000 U/μL) [113, 115].

Question 29:
What measures should be taken to reduce the risk of intraoperative neurologic injury?

Answer:
Use of SC protection measures, together with implementation of IONM and a careful attention to the positioning of the patient, is recommended for decreasing the risk of intraoperative iatrogenic neurologic injury [72].

SC protection measures: The risk of SC injury is particularly high during the instrumentation and deformity correction maneuvers. Ensuring optimal physiological conditions by maintaining normotension, normothermia, normal oxygenation, and an optimal hematocrit can minimize the risk of ischemia-related SC injury during this

critical phase; the surgeon should inform the anesthetist approximately 15 min prior to the spine distraction and straightening maneuvers so as to allow a sufficient time for physiologic optimization. The MAP target is generally >70 mmHg (>80 mmHg in high-risk cases) and is achieved by administration of fluids and if required, vasopressors [72]. Normothermia is maintained by administration of warm intravenous fluid and use of two forced warm air blankets (placed on upper extremities; and lower extremities below the buttocks).

IONM: IONM (SSEP, MEP, EMG) provides a real-time feedback about the integrity of the SC, nerve roots, and peripheral nerves (Table 22.7). The EP waveforms are monitored for latency and amplitude; a significant change in these parameters (as per predefined warning criteria; usually a decrease in amplitude and increase in latency/loss of signal) indicates a potential neurological injury and gives the managing team an opportunity to reverse or correct a potential neurological deficit. Individually, these techniques have false-negative as well as false-positive results; however, when used simultaneously, they are reported to have a fairly high sensitivity (100%) and specificity (88%) for detecting a true neurologic deficit [57, 63, 72, 116]. Hence a multimodality monitoring approach using SSEP, MEP, and EMG (rectus abdominis EMG) is highly recommended; the wake-up test should be considered only if these modalities are not available [57, 63, 72].

Question 30:
What do SSEPs monitor? How are they monitored during the surgery? What are their advantages and disadvantages?

Answer:
SSEPs monitor integrity of the posterior cord (dorsal columns: ascending proprioceptive sensory pathways) (Table 22.7). They can identify mechanical, ischemic (hypotension: decreased amplitude, increased latency), and physiological insults to the SC (hypothermia: increased latency); they are also very useful for detecting a positioning-related neuropraxia (Ulnar N SSEP for detection of brachial plexopathy); however, they do not provide any information regarding the integrity of motor tracts or nerve roots [11, 72].

In SSEP monitoring, repetitive low intensity electrical stimuli are applied to afferent peripheral nerves (via needle electrodes). The resulting EEG responses (microvolt range signals) are recorded at the scalp (cortical SSEPs), proximal spinous process (subcortical SSEPs), and extremities (peripheral SSEPs). The recording is continuous, but there is a time lag in the feedback because of the time required for averaging of the low amplitude signals.

Cortical SSEPs monitor the entire sensory pathway, but are sensitive to anesthetic effects and tend to fade gradually in amplitude during the surgery; in comparison, subcortical SSEPs though electrically less reliable, are relatively resistant to the effect of inhalational anesthetics.

Table 22.7 Intraoperative neuromonitoring techniques during posterior spinal fusion

	Somatosensory evoked potentials (SSEPs)	Transcranial motor evoked potentials (TcMEPs)	Electromyography (EMG)
Monitor	Posterior cord (dorsal columns: ascending proprioceptive sensory pathways)	Anterior spinal cord (descending motor pathways)	Peripheral nerve integrity and function
Common stimulation sites	Peripheral sensory nerves, e.g., Posterior tibial nerve (proximal to ankle) Ulnar/median nerve (proximal to wrist)	Transcranial scalp electrodes [over an area that overlies the motor cortex [1–2 cm anterior to C1–C2 (international 10–20 system)]]	Free running: none Triggered: bipolar stimulation of specific structure, e.g., Pedicle track/pedicle screw @5–30 mA for 0.2 ms
Stimulation intensity	Stimulus intensity:5–45 mA Stimulus duration: 0.2 ms Stimulation rate: 4.7/s	Stimulus intensity: 80–100 mA Stimulus duration: 50 μs; 2–4 pulses; interstimulation interval-1–5 ms	

Table 22.7 (continued)

	Somatosensory evoked potentials (SSEPs)	Transcranial motor evoked potentials (TcMEPs)	Electromyography (EMG)
Recording sites	*Peripheral nerve* Median/ulnar N (Epi/Epc: contralateral and ipsilateral Erb's point—2 cm superior to midpoint of clavicle) Popliteal N: Popliteal fossa *Spinal Cord*: Median/ulnar N:C5S-Fpz (5th cervical spine–frontopolar midline) Popliteal N:T12 S-REF (12 thoracic spine–noncephalic reference) *Subcortical:* Median/ulnar N: Cpi–REF (Cpi—ipsilateral centroparietal) Popliteal N:Fpz-C5S *Cortical:* Median/ulnar N: Cpc–Cpi (Cpc—contralateral centroparietal) Popliteal N: Cpz-Fpz (Cpz—midway between Cz and Pz)	D wave recording: spinal cord Neurogenic MEP: Nerves CMAP: (compound muscle action potential): Muscle Typical recording sites: first dorsal interosseous, abductor pollicis brevis (upper extremity muscles); quadriceps, tibialis anterior abductor digiti minimi and gastrocnemius (lower extremity muscles)	Myotome specific C8–T1 Adductor pollicis T2–T6 Intercostals T6–T12 Rectus abdominis L3–L4 Vastus lateralis L4–L5 Anterior tibialis S1–S2 Gastrocnemius
Warning signs	Unilateral or bilateral >50% reproducible decrease in amplitude from the baseline (voltage of the response) Or Complete loss of waveform	Unilateral or bilateral >65% reproducible decrease in amplitude from the baseline (voltage of the response) Or Complete loss of waveform	Spontaneous EMG: Sustained neurotonic discharges (>2 s) Triggered EMG: action potential with low stimulation intensity (<10 mA)
Advantages	High specificity and sensitivity to sensory deficits Continuous monitoring (no interruption of surgery required) Easy to implement No contraindication	Specific and sensitive to motor deficits Large signal amplitude Instantaneous feedback	Allows surgical correlation with specific nerve roots Continuous monitoring with spontaneous EMG Instantaneous feedback
Disadvantages	Do not evaluate motor pathways Low signal amplitude multitrace averaging required, delayed response (seconds to minutes)	Intermittent monitoring (interruption in surgery required) Sensitive to muscle relaxants, inhalational anesthetics Caution in patients with seizures Difficult to obtain responses in young children (developing nervous system, patients with preexisting neurological deficits)	Sensitive to muscle relaxants Monitors only nerve roots Not useful in cases with preexisting neurological disorders Sensitivity and specificity not very high

Usually, both cortical and subcortical SSEPs are monitored to help distinguish between true neurological and systemic events (hypotension, hypothermia, anesthetic effect); if cortical responses are lost, but subcortical responses remain, a systemic etiology should be suspected. Peripheral recording sites detect impending or evolving peripheral nerve problems and also help to distinguish between a peripheral and a central event. In a peripheral event, the impulse is lost in

a distal to proximal fashion, and hence the EP response fades and eventually disappears; a spinal cord event, on the other hand, has no effect on peripheral site recordings (both stimulation and recording occur below the level of injury).

In thoracic surgeries, SSEPs are usually monitored in the upper limbs (serve as control signals because they are not affected by surgical manipulation in the thoracic spine) as well as lower extremities (monitor dorsal cord integrity). The upper extremity data provide a good measure of the systemic function, hence if lower extremity data meets warning criteria, checking the upper extremity data quickly helps to identify whether the cause is focal systemic or technical (loss of responses in both extremities usually indicates a systemic and not a neurological etiology).

Question 31:
What do Transcranial MEPs (TcMEPs) monitor? What is the technique of monitoring? What are their advantages and disadvantages, as compared with SSEPs?

Answer:
TcMEPs monitor the integrity of the anterior SC (descending motor pathways) (Table 22.7). They are very sensitive to ischemic insults and are considered to be superior to SSEPs for detection of hypoperfusion-related cord injury [Anterior Spinal Artery (ASA) is the primary source of blood supply to the anterior cord, and also to nearly 75% of the SC]; they are also useful for detection of positioning-related neuropathy of the peroneal and femoral nerves.

TcMEPs are generated by application of high frequency multipulse electrical stimulation through needle or corkscrew electrodes inserted into the scalp; corresponding MEP waveforms are recorded at the level of the spinal cord (D wave recording), nerve (neurogenic MEPs), or muscle [compound muscle action potential (CMAP) or myogenic MEPs].

Unlike SSEPs, MEPs are monitored intermittently after each event that can compromise the cord integrity (stimulation necessitates interruption of the surgery for 15–30 s in order to obtain adequate readings) but have the advantage of providing instant feedback [a higher response amplitude (millivolt range) as compared with SSEPs obviates the need for averaging].

CMAPs monitor the entire motor pathway including the neuromuscular junction. The distal muscle recordings are made through surface, subdermal or intramuscular needle electrodes, inserted bilaterally in the upper and lower extremities. They are sensitive to anesthetic agents and in particular, muscle relaxants (generated by synaptic transmission of corticospinal impulses to the ventral motor neurons) [11].

Question 32:
What is the role of EMG monitoring in scoliosis correction surgeries?

Answer:
EMG (spontaneous or triggered) is particularly useful for evaluation of cortical integrity and detection of potential nerve root injury during placement of pedicle screws (nerve root injuries account for almost 60% of all postoperative NNDs) (Table 22.7) [11, 116]. In this technique, EPs generated by muscle fibers are recorded through paired needle electrodes (inserted transdermally into or in proximity to muscles innervated by the nerve roots of interest); the difference in electrical activity between the two electrodes is displayed as a waveform on the monitor; an audible feedback may also be provided. EMG is relatively resistant to anesthetic effects, but can be abolished by neuromuscular relaxants. It has a high sensitivity but a low specificity for predicting neurological deficits, but nevertheless is a very useful component of multimodality monitoring during scoliosis correction surgeries.

Spontaneous or free running EMG: Normally, EMG is quiet (inactive) under anesthesia; continuous low amplitude, high frequency activity may be recorded during light anesthesia, and is audible as a continuous noise. A high frequency (30–100 Hz) "neurotonic burst pattern" on EMG along with an audible short "blurp" occurs, when irritation of a nerve root due to retraction, mechanical stimulation (nearby dissection, drilling, or ultrasonic aspiration), or electrocautery

(thermal irritation) produces spontaneous firing of the nerve with activation of its corresponding myotome [116]. Generally, this EMG pattern is a cause for concern only if it is sustained and/or has a high amplitude. But, a long train of neurotonic activity, with popping corn ("popcorn") or an aircraft engine "bomber" type sound, implies potential neural injury, and a need for prompt reassessment by the surgeon.

In triggered/evoked EMG monitoring, each pedicle track or screw is electrically stimulated with increasing intensity (5–30 mA). With a correctly positioned pedicle screw, no action potential should be observed at the recording electrode with a stimulation intensity of less than 10 mA. But, appearance of an action potential at this low intensity stimulation (6–10 mA) is highly suggestive of a breach in the cortical integrity (the significantly reduced impedance allows the current to depolarize the nerve root) or damage/irritation of the nerve root [decrease in electrical threshold (<10 mA)] by the malpositioned pedicle screw [117].

Question 33:
What is the effect of anesthetic drugs on IONM?

Answer:
The effect of various anesthetic agents on IONM are as follows:

Inhalational agents: Volatile anesthetic agents (desflurane, sevoflurane, isoflurane) inhibit both cortical SSEPs and TcMEP (dose-dependent decrease in amplitude and increase in latency), but have a negligible effect on subcortical SSEP and EMG responses. Doses greater than 0.5 MAC may result in suppression of SSEPs; TcMEPs are exquisitely sensitive and may be abolished at concentrations as low as 0.2 MAC [11].

Nitrous oxide also suppresses these EPs (reduction in amplitude), albeit to a lesser extent, but has a synergistic effect when co-administered with other inhalational agents. In view of this synergism, as well as the high degree of inter-individual response variability, optimal SSEPs may not be obtained if an N_2O-volatile anesthetic (0.5–1 MAC) combination is used during anesthetic maintenance.

Intravenous anesthetic agents: Conventional doses of propofol, opioids, and dexmedetomidine typically have very little effect on SSEP and TcMEP responses; propofol may cause a transient decrease in amplitude when given in large doses [11, 118]. Thiopentone does not interfere with SSEP monitoring though a bolus dose may transiently suppress cortical SSEPs. A bolus dose of midazolam has a minimal effect, but its continuous infusion can suppress the SSEP responses. In contrast, MEPs, however, are significantly depressed by midazolam and may be completely abolished by thiopentone, necessitating caution if these drugs are used during induction [11].

Etomidate [g-aminobutyric acid (GABAA) receptor inhibition) and ketamine (*N*-methyl-D-aspartate receptor inhibition) have neuroexcitatory properties, and unlike most other anesthetic drugs, they cause an increase in the amplitudes of SSEP and MEP [11].

Muscle relaxants: Neuromuscular blocking agents suppress TcMEPs and EMG responses, but improve SSEP recordings by reducing the noise produced by muscle activity.

Question 34:
What should be the choice of anesthetic drugs for spinal fusion for AIS?

Answer:
Most AIS patients are healthy adolescents who can tolerate a wide range of anesthetic regimens, but the choice of anesthetic drugs is usually limited by their compatibility with IONM; short acting drugs (allow a rapid titration of anesthetic depth with a faster emergence, especially if an intraoperative "wake up test" becomes necessary) that cause minimal interference with IONM are usually preferred. Since EPs are more resistant to the effect of intravenous agents as compared to volatile anesthetics, a total intravenous anesthesia (TIVA) based technique is most commonly used; low concentrations of volatile agents [<0.5 MAC (minimum inhalational concentration)] can be used as an adjunct to intravenous drugs.

Anesthetic induction is usually achieved with propofol and an opioid (remifentanil/fentanyl) along

with a nondepolarizing muscle relaxant (NDMR) to facilitate tracheal intubation. Anesthesia can be maintained with propofol-opioids or propofol-dexmedetomidine-opioid combination or a propofol-sevoflurane-opioid combination, in air-oxygen mixture; N_2O is usually excluded during IONM. Propofol infusion (up to 200 μg/kg/min) is usually well tolerated, but it may cause a slightly delayed emergence; hence dexmedetomidine (up to 0.6 μg/kg/h) or sevoflurane in low doses (<0.5 MAC) can be used as an adjunct to reduce the propofol requirement and facilitate a faster awakening [119].

TIVA without a muscle relaxant provides the ideal environment during MEP monitoring; however, a partial neuromuscular blockade (infusion titrated to two twitches on the train-of-four monitor) is also acceptable as it improves surgical retraction, provides a cleaner background, improves the SSEP quality, decreases patient movement and also, the risk of injuries following stimulation.

Ketamine (initial dose of 0.15 mg/kg followed by 2 μg/kg/min) can be used to augment EPs if there is a difficulty in obtaining reliable intraoperative signals [this problem is more common in EOS (because of immature neurologic development) and in NMS (preexisting neurologic deficits)]. Etomidate can also be considered, but its potential for enhanced seizure activity and adrenal suppression may limit its use during these procedures.

Question 35:
Besides choosing the appropriate anesthetic drugs, what other measures can be taken to provide optimal conditions for IONM?

Answer:
Anesthetic agents can confound the interpretation of EPs; hence it is imperative to maintain a constant anesthetic depth, especially during the critical periods when risk of neurological injury is high. Infusions are preferable to bolus doses, as they avoid a deceptive intermittent "worsening" or "improvement" of EPs. At the same time, the body movements that may occur during transcranial or peripheral N electrical stimulation should not be misinterpreted as spontaneous movements due to decreased anesthetic effect.

Maintenance of physiological homeostasis is extremely important; hypotension, anemia, hypoxia, hypocarbia, hypo/hyperthermia, besides being detrimental for the patient, also suppress the EPs. It is also pertinent to remember that IONM can cause motion artifacts in ECG, BP or SpO_2 waveforms and numerical values; in these instances, it is prudent to manually check the pulse, or request for a temporary cessation of stimulation, to avoid any confusion between an actual and a "mimicked" hemodynamic disturbance.

Last, but not the least, a collaborative team approach is crucial. The anesthetic technique as well as the IONM protocol (what EPs to monitor, when to monitor, strategy for loss of EPs) must be devised preoperatively, in consensus with the surgeon and the electrophysiologist.

Question 36:
What is a significant change on neurophysiological monitoring? How is it managed?

Answer:
A neurophysiological change is defined as an "alert" or a "significant change" when there is a unilateral or bilateral reduction in the amplitude of ≥50% for SSEP and ≥65% for TcMEP from the baseline (change in latency is not considered significant unless accompanied by a change in the amplitude) [120–122].

The "alert" can be due to surgical, physiological, or technical reasons or secondary to abnormal limb positioning and requires a prompt, collaborated response by the team.

The electrophysiologist evaluates the technical causes, and the anesthetist manages anesthetic physiological and positioning related factors, while the surgeon reassesses and may reposition or remove the instrumentation, to ease off the correction and reverse any pressure on the neural elements. Usually, bilateral changes (especially in tests which use controls) are suggestive of anesthetic effects or physiological changes (though they do not exclude the possibility of a surgical etiology), and unilateral changes indicate a surgical event. A response strategy is suggested in Table 22.8.

Table 22.8 Suggested response strategy for loss/"significant change" in neurophysiological signals during intraoperative neuromonitoring

Prompt communication between the anesthetist, neurophysiologist, and surgeon *Determine the pattern and timing of the signal change (by asking the electrophysiologist):* What is the signal change: increase in latency or decrease in amplitude or both or complete loss of signal When did it occur? Was there a change in MEPs, SSEPs, or both? Where is the signal change?: unilateral/bilateral; one/both extremities	
Determine the possible etiology	Management
Consider anesthetic effect Was there was a concurrent change in the anesthetic depth due to increase in MAC of volatile agent; administration of a bolus/increase in infusion rate of intravenous sedative or anesthetic drug/increase in the depth of neuromuscular blockade *Consider physiological factors* Did the change in the EP signal coincide with occurrence of hypotension, hypothermia, or anemia *Consider technical problems with recording* Malpositioning of electrodes and connections Change in the position of the neck Change in the position of the limbs on the table *Consider surgical factors* Discuss events and actions prior to the change in signal (e.g., during osteotomy/pedicle screw placement/distraction during rod placement)	*Measures taken by the anesthetist* Turn off volatile anesthetics and nitrous oxide, if administered, and convert to TIVA Decrease anesthetic depth, if necessary Increase mean arterial pressure to >90 mmHg to improve the spinal cord perfusion (volume expansion with blood products preferable to exclusive use of fluids and vasopressors) Ensure normothermia Optimize oxygen delivery: Administer 100% oxygen; correct hypovolemia; confirm adequate hemoglobin Consider small bolus of ketamine or etomidate to increase signal amplitude *Measures taken by the neuroelectrophysiologist* Correct electrode/connection related problems Reposition the neck/limbs, if malpositioned *Measures taken by the spine surgeon* Warm saline irrigation of surgical field (to remove blood and metabolites from local tissue damage as they may act as potent axonal blocking agents) Check position of implant (consider intraoperative imaging) Assess osteotomy sites; evaluate for spinal cord compression If the amplitude does not recover with the abovementioned actions, over the course of 10 min, then consider reversing surgical actions, e.g., remove rod/remove pedicle screw and evaluate for cortical breach
Ongoing considerations *If signals do not improve, discuss the following options* 1. Wake-up test: patient is allowed to awaken to demonstrate neurologic function, then the surgery is resumed 2. Aborting the procedure: distracting rods are removed the back is closed and a staged procedure is considered 3. Administration of methylprednisolone: 30 mg/kg IV in first hr. followed by 5.4 mg/kg/h for the next 23 h (limited data to support efficacy)	

MEP motor evoked potential, SSEP somatosensory evoked potential, MAC minimum alveolar concentration, TIVA total intravenous anesthesia

Question 37: What are the factors that influence the decision regarding the timing of tracheal extubation (post-surgery after emergence from anesthesia or a planned delayed tracheal extubation) after PSF for AIS?

Answer:

The timing of tracheal extubation after PSF for AIS is influenced by several factors such as the patient's airway, preoperative functional status, number of spinal levels fused, duration of surgery,

temperature of the patient, and the intraoperative blood loss and transfusion requirements.

While tracheal extubation can be performed in a significant proportion of the patients, mechanical ventilation in the early postoperative period may be required in some situations to allow the temperature, volume, metabolic, and coagulopathic abnormalities to be corrected and the airway edema to subside. These include a difficult airway [preexisting difficult airway/intraoperative airway edema (macroglossia, facial swelling, laryngeal and pharyngeal edema)] due to prolonged prone positioning/transfusion of large volumes of fluid; poor preoperative cardiorespiratory status; longer fusion segments (>8); long duration of surgery (>8 h); intraoperative hypothermia; and significant blood loss (>30 mL/kg) [7, 98, 99, 123].

22.6 Postoperative Management

Question 38:
What are the pertinent considerations for postoperative care of AIS patients following a PSF?

Answer:
The postoperative care regimen typically has several components including monitoring of vital parameters, pain severity, and volume status of the patient; management of fluids, blood loss, anemia, and hemodynamic instability; prevention and treatment of pain, nausea, vomiting, and constipation; early resumption of an oral regimen (diet as well as medications); encouraging early mobilization; and prevention of DVT and pulmonary dysfunction by early initiation of physical and respiratory therapy (Table 22.9).

A meticulous postoperative care strategy plays a vital role in facilitating a faster functional recovery, a shorter hospital stay, and reduced hospitalization costs. Hence, the recent "Consensus-Based Best Practice Guidelines" encourage the formulation of evidence-based, hospital-specific protocols, for postoperative management of AIS patients, following a PSF [124]. Implementation of such standardized protocols, for instance, the "Rapid Recovery Program" by Melhy et al. (multimodal pain management and early mobilization strategy) and "Perioperative Surgical Home" by Kim et al. (standardized preoperative planning, intraoperative anesthetic and surgical management, and immediate to long-term postoperative medical management) has shown promising results [65, 66, 125, 126].

Postoperative pain relief: Given the large skin incision and the extensive tissue dissection involved during the surgery, the patients tend to suffer from severe, debilitating pain in the postoperative period, which not only delays their mobilization, physical therapy, and return of normal bowel function but also increases their risk of developing several complications such as pulmonary dysfunction due to hypoventilation DVT and urinary tract infection. Hence an effective postoperative analgesia strategy is important; it provides optimal pain relief, minimizes the risk of PPCs as well as accelerates the functional recovery of patients.

Intravenous patient-controlled analgesia (IV PCA) with opioids (morphine/fentanyl) has been the mainstay of postoperative pain relief after PSF. However, given the high incidence of opioid-related side effects (somnolence, nausea, vomiting, pruritus, urinary retention, ileus), recent "consensus-based best practice guidelines" for postoperative care recommend the use of a multimodal perioperative approach that includes a combination of opioid (systemic intrathecal) and nonopioid analgesics (Table 22.10). This approach improves the quality of analgesia, reduces opioid dosages as well as side effects, and also facilitates early discontinuation of intravenous opioids [124].

Commonly used nonopioid drugs include anti-inflammatories (acetaminophen, ketorolac), neuroleptics (gabapentin), and antispasmodics (i.e., diazepam) [124–127]. Though there have been some concerns with the use of ketorolac (bleeding due to platelet dysfunction; pseudoarthrosis due to impaired bone healing), several studies have demonstrated its efficacy and safety in pediatric spinal fusion procedures [124].

Table 22.9 Postoperative care in patients with adolescent idiopathic scoliosis, following a posterior spinal fusion

Monitoring
Vital parameters: heart rate, blood pressure, respiratory rate, pulse oximetry (while on PCA)
Fluid intake, urine output, blood loss in the drain, central venous pressure (if CVP line in situ, on POD 0)
Pain score
Neurological examination: new neurological deficits, peripheral neuropathy
Investigations
Hemogram
Coagulation profile
Serum electrolytes
Cardiovascular system
Hypotension[a]: Manage with fluids[b] and, if required blood transfusion[c]
Respiratory system:
Supplemental low flow oxygen therapy to maintain SpO_2 >92% on POD 0
Optimal pulmonary hygiene
Prevention of postoperative atelectasis: respiratory therapy, early mobilization, pain relief
Pain relief
IV PCA (morphine/fentanyl)[d] supplemented with a combination of nonopioid analgesics (gabapentin/ketorolac/acetaminophen/tramadol) and intrathecal morphine
Gastro-intestinal system
Antiemesis:
Ondansetron 0.1 mg/kg/dose IV, maximum 4 mg every hours on POD 0
Shift to oral medication (same dose) PRN, for rest of the hospital stay
Bowel regimen:
Stool softener/laxative (e.g., docusate, 100 mg twice daily, bisacodyl—10 mg twice daily), start on POD 1
Assess daily (possible causes of constipation: opioids, decreased mobility, dehydration)
Diet:
Clear liquid diet on POD 0
High-fiber diet on POD 1
DVT prophylaxis
Log roll on bed every 2 h, till patient can attempt himself/herself
Sequential compression device × 3 days (continuously while in bed)
Mobilization and physical therapy
Encourage:
Sitting on edge of the bed on POD 0 if feasible (after 12 h of surgery)/or on POD 1
Sitting on chair and ambulating, 2–3 times on POD 1
Walking for a longer distance (goal—500 feet) and climbing stairs (goal-one flight of stairs), if tolerated, on POD 2
Urinary system
Removal of Foleys catheter by POD 2

AIS adolescent idiopathic scoliosis, PSF posterior spinal fusion, POD postoperative day, DVT deep vein thrombosis, IV PCA intravenous patient-controlled analgesia, PRN as needed, PO per orally, CVP central venous pressure, ADH antidiuretic hormone, Hb hemoglobin, SpO_2 oxygen saturation

[a]Most probable etiology: acute anemia (postoperative bleeding may equal or exceed the intraoperative blood loss)

[b]Isotonic fluids (avoid hypotonic fluids, high postoperative ADH levels may lead to hyponatremia and hypo-osmolality)

[c]Transfusion trigger: Hb < 7 g/dL or higher, if acute hemodynamically instability/coexisting cardiac morbidities

[d]Removal of IV PCA preferably by POD 1, latest by POD 3; Shift to oral analgesics by POD 1, if feasible

Perioperative intrathecal opioids are used as an adjuvant to the analgesia regimen. They are administered after anesthetic induction and prior to the surgical incision, and help to reduce the intraoperative as well as early postoperative pain (till 24 h) and the systemic opioid consumption; interestingly, some studies also document a reduction in the intraoperative blood loss although the exact mechanism of their blood-sparing effect is unclear [127].

While opioid-based epidural analgesia (single/double epidural catheter) is an effective and also a widely used technique, however recent "consensus-based best practice guidelines" do not seem to approve of its use because of its potentially restrictive impact on the mobilization

Table 22.10 Drugs for pain relief following posterior spinal fusion for adolescent idiopathic scoliosis

Morphine	*IV PCA* Continuous basal infusion: 0–20 μg/kg/h Demand dose: 10–20 μg/kg Lockout interval: 6–15 min 4 h limit: 250–400 μg/kg [a]*Intrathecal* 5–20 μg/kg (maximum of 300 μg), diluted in 2–4 mL of saline Avoid ≥20 μg/kg (risk of respiratory depression) [a]*Caudal* 50 μg/kg; maximum dose: 3 mg
Fentanyl	*IV PCA* Continuous basal infusion: 0–0.5 μg/kg/h Demand dose: 0.5 μg/kg Lockout interval: 6–10 min 4 h limit: 7–10 μg/kg
Gabapentin	Preoperative: 15 mg/kg PO on the morning of surgery Postoperative: 5 mg/kg PO, TID, for 2 days
Ketorolac	0.5 mg/kg IV q 6 h, for up to 5 days Maximum dose: 30 mg/dose, 120 mg/day
Acetaminophen	10–15 mg/kg q4–6h orally; maximum 90 mg/kg/day
Tramadol	1–2 mg/kg orally, q4–6 h Maximum single dose: 100 mg Maximum daily dose: lesser of either 8mg/kg or 400 mg
Diazepam	0.1 mg/kg every 6 h PRN (for muscle spasms); maximum 5 mg

IV PCA intravenous patient controlled analgesia, PRN as needed, PO per orally

[a]Morphine IV PCA added to this regimen, initially with a small bolus dose of 10 μg/kg; after 12–24 h, the bolus dose can be increased and a background infusion started, if required

of patients, as well as due to the distressing opioid-related adverse effects [124].

Question 39:
What are the potential postoperative complications after spinal fusion for AIS?

Answer:
Several large databases have analyzed the postoperative complications after scoliosis correction procedures [33, 60, 70, 128]. The overall incidence of complications after instrumented spinal fusion for AIS ranges from 5 to 23%, with acute respiratory failure re-intubation, implant-related complications (neurological injury, dural tear, screw loosening pneumothorax, pleural effusion, wound complications), and infections being the most commonly reported complications (incidence >1%) [71]. Other major, though less common complications include pancreatitis, disseminated intravascular coagulation, visual loss, death, cardiac arrest, hyperthermia, venous thromboembolism, and superior mesenteric artery syndrome (individual incidence ≤0.2%) [60, 70, 128].

The risk of complications is reported to be higher in younger patients, male patients, in those with comorbidities (anemia, hypertension, or hypothyroidism), and after revision procedures, anterior or combined approaches surgeries and corrective osteotomies [33, 60].

Multiple Choice Questions

1. Pattern of SSEP response change seen in Ulnar N neuropraxia is:
   (a) Global cortical loss, intact subcortical signals
   (b) Unilateral loss of Erb's point, subcortical and cortical signals
   (c) Intact Erb's point potential and subcortical signals; unilateral loss of cortical responses
   (d) Intact Erb's point potential, prolongation or loss of subcortical and cortical signals

   Answer: b
2. Pattern of SSEP response change observed with spinal cord injury is:
   (a) Global cortical loss, intact subcortical signals
   (b) Unilateral loss of Erb's point, subcortical and cortical signals
   (c) Intact Erb's point potential and subcortical signals; unilateral loss of cortical responses
   (d) Intact Erb's point potential, prolongation or loss of subcortical and cortical signals

   Answer: d
3. Pattern of SSEP response change observed with use of sevoflurane at 1.5 MAC is:

(a) Global cortical loss, intact subcortical signals
(b) Unilateral loss of Erb's point, subcortical and cortical signals
(c) Intact Erb's point potential and subcortical signals; unilateral loss of cortical responses
(d) Intact Erb's point potential, prolongation or loss of subcortical and cortical signals

Answer: a

4. Which of the following patients is likely to have the maximal blood loss during a PSF?
   (a) 13-year-old patient with AIS for PSF from T3–L2
   (b) 11-year-old patient with cerebral palsy for PSF from T3–L2
   (c) 11-year-old patient with Duchenne muscular dystrophy for PSF from T3–L2
   (d) 10-year-patient with JIS for PSF from T3–L2

   Answer: c

5. A 17-year-old girl with cerebral palsy and severe scoliosis is referred for pre-op evaluation. Arterial blood gas demonstrates a pO_2 = 60 mmHg and a pCO_2 = 47 mmHg. Which of the following PFT test reports is most likely to correspond to her respiratory disorder?

	FVC	FEV1	FEV1/FVC (%)	FEF 25–75	TLC	DLCO/VA
(a)	3.1 L (73%)	0.7 L (23%)	23	0.2 LPS (6%)	9.7 L (150%)	0.9 (19%)
(b)	1.1 L (36%)	0.8 L (29%)	78	0.7 LPS (22%)	2.1 L (54%)	7.0 (120%)
(c)	2.9 L (83%)	1.8 L (60%)	61	0.9 LPS (23%)	4.9 L (100%)	6.8 (122%)
(d)	1.7 L (51%)	1.4 L (49%)	78	1.3 LPS (35%)	2.7 L (52%)	2.6 (51%)

Answer: b

6. Which of the following statements is true about intraoperative intrathecal morphine administration for postoperative pain relief after PSF?
   (a) Its analgesic effect lasts for 48–72 h.
   (b) It interferes with somatosensory evoked potential monitoring.
   (c) It can cause delayed respiratory depression.
   (d) It is associated with an increased intraoperative blood loss.

   Answer: c

Bibliography

1. Saltikov JB, Weiss HR, Chockalingam N, et al. A comparison of patient-reported outcome measures following different treatment approaches for adolescents with severe idiopathic scoliosis: a systematic review. Asian Spine J. 2016;10(6):1170–94.
2. Farady JA. Current principles in the nonoperative management of structural adolescent idiopathic scoliosis. Phys Ther. 1983;63(4):512–23.
3. Gambrall MA. Anesthetic implications for surgical correction of scoliosis. AANA J. 2007;75(4):277–85.
4. Negrini S, Donzelli S, Aulisa AG, et al. 2016 SOSORT guidelines: orthopaedic and rehabilitation treatment of idiopathic scoliosis during growth. Scoliosis Spinal Disord. 2018;13(1):3.
5. Yaman O, Dalbayrak S. Idiopathic scoliosis. Turk Neurosurg. 2014;24(5):646–57.
6. Scoliosis Research Society Terminology Committee. A glossary of scoliosis terms. Spine. 1976;1(3):57–8.
7. Gibson PR. Anaesthesia for correction of scoliosis in children. Anaesth Intensive Care. 2004;32:548–59. PubMed: 15675216.
8. Dunn J, Henrikson NB, Morrison CC, et al. Screening for adolescent idiopathic scoliosis, evidence report and systematic review for the US preventive. JAMA. 2018;319(2):173–87.
9. Bunnell WP. The natural history of idiopathic scoliosis before skeletal maturity. Spine. 1986;11:773–6.
10. Konieczny MR, Senyurt H, Krauspe R. Epidemiology of adolescent idiopathic scoliosis. J Child Orthop. 2013;7(1):3–9.
11. Glover CD, Carling NP. Neuromonitoring for scoliosis surgery. Anesthesiol Clin. 2014;32:101–14.
12. Asher MA, Burton DC. Adolescent idiopathic scoliosis: natural history and long-term treatment effects. Scoliosis. 2006;1(1):2. https://doi.org/10.1186/1748-7161-1-2./1.
13. Robinson CM, McMaster MJ. Juvenile idiopathic scoliosis. Curve patterns and prognosis in one hundred and nine patients. J Bone Joint Surg Am. 1996;78(8):1140–8.
14. McMaster M. Infantile idiopathic scoliosis: can it be prevented? J Bone Joint Surg Br. 1983;65:612–7.

15. Lloyd-Roberts GC, pilcher MF. Structural idiopathic scoliosis in infancy: a study of the natural history of 100 patients. J Bone Joint Surg Br. 1965;47:520–3.
16. Ceballos T, Ferrer-Torrelles M, Castillo F, Fernandez-Paredes E. Prognosis in infantile idiopathic scoliosis. J Bone Joint Surg Am. 1980;62(6):863–75.
17. Hodgkinson I, Bérard C, Chotel F, et al. Pelvic obliquity and scoliosis in non-ambulatory patients with cerebral palsy: a descriptive study of 234 patients over 15 years of age. Rev Chir Orthop Reparatrice Appar Mot. 2002;88:337–41.
18. Basu PS, Elsebaie H, Noordeen MH. Congenital spinal deformity: a comprehensive assessment at presentation. Spine (Phila Pa 1976). 2002;27:2255–9.
19. Polly WD Jr, Larson Noel A. Pediatric and adult scoliosis. In: Ellenbogen RG, Abdulrauf SI, Sekhar LN, editors. Principles of neurosurgery. 3rd ed. Philadelphia: Elsevier Saunders; 2012. p. 497–508.
20. Lenke LG, Betz RR, Harms J, et al. Adolescent idiopathic scoliosis: a new classification to determine extent of spinal arthrodesis. J Bone Joint Surg Am. 2001;83:1169–81.
21. Grauers A, Einarsdottir E, Gerdhem P. Genetics and pathogenesis of idiopathic scoliosis. Scoliosis Spinal Disord. 2016;11:45.
22. Fadzan M, Saltikov JB. Etiological theories of adolescent idiopathic scoliosis: past and present. Open Orthop J. 2017;11(Suppl-9, M3):1466–89.
23. Newton Ede MM, Jones SW. Adolescent idiopathic scoliosis: evidence for intrinsic factors driving aetiology and progression. Int Orthop. 2016;40(10):2075–80.
24. Weinstein SL, Dolan LA, Spratt KF, Peterson KK, Spoonamore MJ, Ponseti IV. Health and function of patients with untreated idiopathic scoliosis: a 50-year natural history study. JAMA. 2003;289(5):559–67.
25. Negrini S, Grivas TB, Kotwicki T, Maruyama T, Rigo M, Weiss HR, et al. Why do we treat adolescent idiopathic scoliosis? What we want to obtain and to avoid for our patients. SOSORT 2005 consensus paper. Scoliosis. 2006;1:4.
26. Koumbourlis AC. Scoliosis and the respiratory system. Paediatr Respir Rev. 2006;7:152–60.
27. Saltikov JB, Turnbull D, Ng SY, et al. Management of spinal deformities and evidence of treatment effectiveness. Open Orthop J. 2017;11:1521–47.
28. Lonstein JE, Carlson JM. The prediction of curve progression in untreated idiopathic scoliosis during growth. J Bone Joint Surg Am. 1984;66(7):1061–71. https://doi.org/10.2106/00004623-198466070-00013.
29. Weinstein SL, Zavala DC, Ponseti IV. Idiopathic scoliosis: long-term follow-up and prognosis in untreated patients. J Bone Joint Surg Am. 1981;63(5):702–12. https://doi.org/10.2106/00004623-198163050-00003.
30. Weinstein SL, Ponseti IV. Curve progression in idiopathic scoliosis. J Bone Joint Surg Am. 1983;65(4):447–55. https://doi.org/10.2106/00004623-198365040-00004.
31. Tan KJ, Moe MM, Vaithinathan R, Wong HK. Curve progression in idiopathic scoliosis: follow-up study to skeletal maturity. Spine (Phila Pa 1976). 2009;34(7):697–700.
32. Mehta MH. The rib-vertebra angle in the early diagnosis between resolving and progressive infantile scoliosis. J Bone Joint Surg Br. 1972;54(2):230–43.
33. Reames DL, Smith JS, Fu KMG, Polly DW, Ames CP, Berven SH, et al. Complications in the surgical treatment of 19,360 cases of pediatric scoliosis: a review of the scoliosis research society morbidity and mortality database. Spine. 2011;36(18):1484–91. https://doi.org/10.1097/BRS.0b013e3181f3a326.
34. Saito N, Ebara S, Ohotsuka K, et al. Natural history of scoliosis in spastic cerebral palsy. Lancet. 1998;351:1687–92. https://doi.org/10.1016/S0140-6736(98)01302-6.
35. Thometz JG, Simon SR. Progression of scoliosis after skeletal maturity in institutionalized adults who have cerebral palsy. J Bone Joint Surg Am. 1988;70:1290–6.
36. Tsiligiannis T, Grivas T. Pulmonary function in children with idiopathic scoliosis. Scoliosis. 2012;7:7.
37. Johari J, Sharifudin MA, Rahman AA, et al. Relationship between pulmonary function and degree of spinal deformity, location of apical vertebrae and age among adolescent idiopathic scoliosis patients. Singap Med J. 2016;57(1):33–8. https://doi.org/10.11622/smedj.2016009. PubMed PMID: 26831315; PubMed Central PMCID: PMC4728701.
38. Muirhead A, Conner AN. The assessment of lung function in children with scoliosis. J Bone Joint Surg Br. 1985;67-B:699–702.
39. Kulkarni AH, Ambareesha M. Scoliosis and anesthetic considerations. Indian J Anaesth. 2007;51:486–95.
40. Hirshfield S, Rudner C, Nash CL Jr, et al. Incidence of mitral valve prolapse in adolescent scoliosis and thoracic hypokyphosis. Pediatrics. 1982;70:451.
41. Primiano FP Jr, Nussbaum E, Hirschfeld SS, Nash CL, Horowitz JG, Lough MD, et al. Early echocardiographic and pulmonary function findings in idiopathic scoliosis. J Pediatr Orthop. 1983;3:475–81.
42. Entwistle MA, Patel D. Scoliosis in children. Cont Educ Anaesth Crit Care Pain. 2006;6:13–6.
43. Johnston CE, Richards BS, Sucato DJ, Bridwell KH, Lenke LG, Erickson M. Correlation of preoperative deformity magnitude and pulmonary function tests in adolescent idiopathic scoliosis. Spine. 2011;36(14):1096–102.
44. Newton PO, Faro FD, Gollogly S, Betz RR, Lenke LG, Lowe TG. Results of preoperative pulmonary function testing of adolescents with idiopathic scoliosis. A study of six hundred and thirty-one patients. J Bone Joint Surg Am. 2005;87(9):1937–46.
45. Kearon C, Viviani GR, Kirkley A, Killian KJ. Factors determining pulmonary function in adolescent idiopathic thoracic scoliosis. Am Rev Respir Dis. 1993;148(2):288–94.

46. Upadhyay SS, Mullaji AB, Luk KD, Leong JC. Evaluation of deformities and pulmonary function in adolescent idiopathic right thoracic scoliosis. Eur Spine J. 1995;4(5):274–9.
47. Branthwaite MA. Cardiorespiratory consequences of unfused idiopathic scoliosis. Br J Dis Chest. 1986;80(4):360–9.
48. Martínez-Llorens J, Ramírez M, et al. Muscle dysfunction and exercise limitation in adolescent idiopathic scoliosis. Eur Respir J. 2010;36(2):393–400.
49. Lin MC, Liaw MY, Chen WJ, Cheng PT, Wong AM, Chiou WK. Pulmonary function and spinal characteristics: their relationships in persons with idiopathic and postpoliomyelitic scoliosis. Arch Phys Med Rehabil. 2001;823:335–41.
50. Kurz LT, Mubarak SJ, Schultz P, Park SM, Leach J. Correlation of scoliosis and pulmonary function in Duchenne muscular dystrophy. J Pediatr Orthop. 1983;3:347–53.
51. Smith AD, Koreska J, Moseley CF. Progression of scoliosis in Duchenne muscular dystrophy. J Bone Joint Surg Am. 1989;71:1066–74.
52. Ames WA, Hayes JA, Crawford MW. The role of corticosteroids in Duchenne muscular dystrophy: a review for the anaesthetist. Paediatr Anaesth. 2005;15:3–8.
53. Eagle M, Baudouin SV, Chandler C, Giddings DR, Bullock R, Bushby K. Survival in Duchenne muscular dystrophy: improvements in life expectancy since 1967 and the impact of home nocturnal ventilation. Neuromuscul Disord. 2002;12:926–9.
54. Tarpada SP, Morris MT. Minimally invasive surgery in the treatment of adolescent idiopathic scoliosis: a literature review and meta-analysis. J Orthop. 2016;14(1):19–22. https://doi.org/10.1016/j.jor.2016.10.006. PubMed PMID: 27818581; PubMed Central PMCID: PMC5080743.
55. Newton PO, Marks M, Faro F, et al. Use of video-assisted thoracoscopic surgery to reduce perioperative morbidity in scoliosis surgery. Spine (Phila Pa 1976). 2003;28:S249–54.
56. Olgun ZD, Yazici M. Posterior instrumentation and fusion. J Child Orthop. 2013;7(1):69–76. https://doi.org/10.1007/s11832-012-0456-5.
57. de Kleuver M, Lewis SJ, Germscheid NM, et al. Optimal surgical care for adolescent idiopathic scoliosis: an international consensus. Eur Spine J. 2014;23:2603–18. https://doi.org/10.1007/s00586-014-3356-1.
58. Muschik MT, Kimmich H, Demmel T. Comparison of anterior and posterior double-rod instrumentation for thoracic idiopathic scoliosis: results of 141 patients. Eur Spine J. 2006;15:1128–38.
59. Maruyama T, Takeshita K. Surgery for idiopathic scoliosis: currently applied techniques. Clin Med Pediatr. 2009;3:39–44.
60. De la Garza Ramos R, Goodwin CR, Abu-Bonsrah N, et al. Patient and operative factors associated with complications following adolescent idiopathic scoliosis surgery: an analysis of 36,335 patients from the Nationwide Inpatient Sample. J Neurosurg Pediatr. 2016;25(6):730–6.
61. Koerner JD, Patel A, Zhao C, Schoenberg C, Mishra A, Vives MJ, et al. Blood loss during posterior spinal fusion for adolescent idiopathic scoliosis. Spine. 2014;39(18):1479–87.
62. Fletcher ND, Marks MC, Asghar JK, Hwang SW, Sponseller PD, Harms Study Group, Newton PO. Development of consensus based best practice guidelines for perioperative management of blood loss in patients undergoing posterior spinal fusion for adolescent idiopathic scoliosis. Spine Deform. 2018;6(4):424–9. https://doi.org/10.1016/j.jspd.2018.01.00.
63. Vitale MG, Skaggs DL, Pace GI, et al. Best practices in intraoperative neuromonitoring in spine deformity surgery: development of an intraoperative checklist to optimize response. Spine Deform. 2014;2:333–9.
64. Ialenti MN, Lonner BS, Verma K. Predicting operative blood loss during spinal fusion for adolescent idiopathic scoliosis. J Pediatr Orthop. 2013;33(4):372–6.
65. Fletcher ND, Shourbaji N, Mitchell PM, Oswald TS, Devito DP, Bruce RW. Clinical and economic implications of early discharge following posterior spinal fusion for adolescent idiopathic scoliosis. J Child Orthop. 2014;8(3):257–63.
66. Fletcher ND, Andras LM, Lazarus DE, et al. Use of a novel pathway for early discharge was associated with a 48% shorter length of stay after posterior spinal fusion for adolescent idiopathic scoliosis. J Pediatr Orthop. 2017;37:92–7.
67. Yoshihara H, Yoneoka D. National trends in spinal fusion for pediatric patients with idiopathic scoliosis: demographics, blood transfusions, and in-hospital outcomes. Spine (Phila Pa 1976). 2014;39:1144–50.
68. Yoshihara H, Yoneoka D. Predictors of allogeneic blood transfusion in spinal fusion for pediatric patients with idiopathic scoliosis in the United States, 2004-2009. Spine (Phila Pa 1976). 2014;39:1860–7.
69. Kim HJ, Park HS, Jang MJ, et al. Predicting massive transfusion in adolescent idiopathic scoliosis patients undergoing corrective surgery: association of preoperative radiographic findings. Medicine (Baltimore). 2018;97(22):e10972.
70. Coe JD, Arlet V, Donaldson W, et al. Complications in spinal fusion for adolescent idiopathic scoliosis in the new millennium. A report of the Scoliosis Research Society Morbidity and Mortality Committee. Spine (Phila Pa 1976). 2006;31(3):345–9.
71. Murphy RF, Mooney JF 3rd. Complications following spine fusion for adolescent idiopathic scoliosis. Curr Rev Musculoskelet Med. 2016;9(4):462–9. https://doi.org/10.1007/s12178-016-9372-5.
72. Borden TC, Bellaire LL, Fletcher ND. Improving perioperative care for adolescent idiopathic scoliosis patients: the impact of a multidisciplinary care approach. J Multidiscip Healthc. 2016;9:435–45. https://doi.org/10.2147/JMDH.S95319. PubMed

PMID: 27695340; PubMed Central PMCID: PMC5028162.
73. Vitale MG, Moore DW, Matsumoto H, et al. Risk factors for spinal cord injury during surgery for spinal deformity. J Bone Joint Surg Am. 2010;92:64–71.
74. Devlin VJ, Schwartz DM. Intraoperative neurophysiologic monitoring during spinal surgery. J Am Acad Orthop Surg. 2007;15(9):549–60.
75. DePasse JM, Palumbo MA, Haque M, Eberson CP, Daniels AH. Complications associated with prone positioning in elective spinal surgery. World J Orthop. 2015;6(3):351–9.
76. Practice Advisory for the Prevention of Perioperative Peripheral Neuropathies 2018: an updated report by the American Society of Anesthesiologists Task Force on Prevention of Perioperative Peripheral Neuropathies. Anesthesiology. 2018;128(1):11–26. https://doi.org/10.1097/ALN.0000000000001937.
77. De la Garza-Ramos R, Samdani AF, Sponseller PD, Ain MC, Miller NR, Shaffrey CI, et al. Visual loss after corrective surgery for pediatric scoliosis: incidence and risk factors from a nationwide database. Spine J. 2016;16:516–22.
78. Lao L, Weng X, Qiu G, Shen J. The role of preoperative pulmonary function tests in the surgical treatment of extremely severe scoliosis. J Orthop Surg Res. 2013;8:32.
79. Zhang JG, Wang W, Qiu GX, et al. The role of preoperative pulmonary function tests in the surgical treatment of scoliosis. Spine (Phila Pa 1976). 2005;30:218–21.
80. Yuan N, Fraire JA, Margetis MM, Skaggs DL, Tolo VT, Keens TG. The effect of scoliosis surgery on lung function in the immediate postoperative period. Spine. 2005;30(19):2182–5.
81. Yaszay B, Jazayeri R, Lonner B. The effect of surgical approaches on pulmonary function in adolescent idiopathic scoliosis. J Spinal Disord Tech. 2009;22(4):278–83.
82. Yuan N, Skaggs DL, Dorey F, Keens TG. Preoperative predictors of prolonged postoperative mechanical ventilation in children following scoliosis repair. Pediatr Pulmonol. 2005;40:414–9.
83. Shapiro F, Sethna N. Blood loss in pediatric spine surgery. Eur Spine J. 2004;13(Suppl 1): S6–S17.
84. Cloake T, Gardner A. The management of scoliosis in children with cerebral palsy: a review. J Spine Surg. 2016;2(4):299–309. https://doi.org/10.21037/jss.2016.09.05.
85. Lipton GE, Miller F, Dabney KW, et al. Factors predicting postoperative complications following spinal fusions in children with cerebral palsy. J Spinal Disord. 1999;12:197–205.
86. Bradford DS, Heithoff KB, Cohen M. Intraspinal abnormalities and congenital spine deformities: a radiographic and MRI study. J Pediatr Orthop. 1991;11(1):36–41. https://doi.org/10.1097/01241398-199101000-00009.
87. Miskovic A, Lumb AB. Postoperative pulmonary complications. Br J Anaesth. 2017;118:317–34.
88. Kafer ER. Respiratory and cardiovascular functions in scoliosis and the principles of anesthetic management. Anesthesiology. 1980;32:339–51.
89. Wazeka AN, DiMaio MF, Boachie-Adjei O. Outcome of pediatric patients with severe restrictive lung disease following reconstructive spine surgery. Spine. 2004;29:528–34.
90. Bach JR, Sabharwal S. High pulmonary risk scoliosis surgery: role of noninvasive ventilation and related techniques. J Spinal Disord Tech. 2005;18: 527–30.
91. Laupacis A, Ergusson D. Erythropoetin to minimize perioperative blood transfusion. A systematic review of randamozed trials. The international study of Peri-Operative Transfusion (IPSOT) Investigators. Transfus Med. 1998;8:309–17.
92. Moran MM, Kroon D, Tredwell SJ, Wadsworth LD. The role of autologous blood transfusion in adolescents undergoing spinal surgery. Spine (Phila Pa 1976). 1995;20:532–6.
93. Bess RS, Lenke LG, Bridwell KH, et al. Wasting of preoperatively donated autologous blood in the surgical treatment of adolescent idiopathic scoliosis. Spine (Phila Pa 1976). 2006;31:2375–80.
94. Verma RR, Williamson JB, Dashti H, et al. Homologous blood transfusion is not required in surgery for adolescent idiopathic scoliosis. J Bone Joint Surg Br. 2006;88:1187–91.
95. Drvaric DM, Roberts JM, Burke SW, King AG, Kenneth FS. Gastroesophageal evaluation in totally involved cerebral palsy patients. J Pediatr Orthop. 1987;7:187–90.
96. Rappaport DI, Adelizzi-Delany J, Rogers KJ, et al. Outcomes and costs associated with hospitalist comanagement of medically complex children undergoing spinal fusion surgery. Hosp Pediatr. 2013;3(3):233–41.
97. Jevsevar DS, Karlin LI. The relationship between preoperative nutritional status and complications after an operation for scoliosis in patients who have cerebral palsy. J Bone Joint Surg Am. 1993;75:880–4.
98. Gurajala I, Ramachandran G, Iyengar R, Durga P. The preoperative and intraoperative risk factors for early postoperative mechanical ventilation after scoliosis surgery: a retrospective study. Indian J Anaesth. 2013;57:14–8. PMCID: PMC3658328; PubMed: 23716760.
99. Issac E, Menon G, Vasu BK, George M, Vasudevan A. Predictors of postoperative ventilation in scoliosis surgery: a retrospective analysis. Anesth Essays Res. 2018;12(2):407–11. https://doi.org/10.4103/aer.AER_18_18.
100. Mollmann M, Henning M, Liljenqvist U, Wenk M. A foam-cushion face mask and a see-through operation table: a new set-up for face protection and increased safety in prone position. Br J Anaesth.

2007;99(4):597–8. https://doi.org/10.1093/bja/aem248.
101. Bowen RE, Gardner S, Scaduto AA, Eagan M, Beckstead J. Efficacy of intraoperative cell salvage systems in pediatric idiopathic scoliosis patients undergoing posterior spinal fusion with segmental spinal instrumentation. Spine (Phila Pa 1976). 2010;35(2):246–51.
102. McNicol ED, Tzortzopoulou A, Schumann R, Carr DB, Kalra A. Antifibrinolytic agents for reducing blood loss in scoliosis surgery in children. Cochrane Database Syst Rev. 2016;(9):CD006883. https://doi.org/10.1002/14651858.CD006883.pub3.
103. Dhawale AA, Shah SA, Sponseller PD, et al. Are antifibrinolytics helpful in decreasing blood loss and transfusions during spinal fusion surgery in children with cerebral palsy scoliosis? Spine (Phila Pa 1976). 2012;37:E549–55.
104. Newton PO, Bastrom TP, Emans JB, et al. Antifibrinolytic agents reduce blood loss during pediatric vertebral column resection procedures. Spine (Phila Pa 1976). 2012;37:E1459–63.
105. Sethna NF, Zurakowski D, Brustowicz RM, Bacsik J, Sullivan LJ, Shapiro F. Tranexamic acid reduces intraoperative blood loss in pediatric patients undergoing scoliosis surgery. Anesthesiology. 2005;102(4):727–32.
106. Verma K, Errico T, Diefenbach C, et al. The relative efficacy of antifibrinolytics in adolescent idiopathic scoliosis: a prospective randomized trial. J Bone Joint Surg Am. 2014;96(10):e80.
107. Grant JA, Howard J, Luntley J, Harder J, Aleissa S, Parsons D. Perioperative blood transfusion requirements in pediatric scoliosis surgery: the efficacy of tranexamic acid. J Pediatr Orthop. 2009;29(3):300–4.
108. Verma K, Lonner B, Dean L, Vecchione D, Lafage V. Reduction of mean arterial pressure at incision reduces operative blood loss in adolescent idiopathic scoliosis. Spine Deform. 2013;1(2):115–22.
109. Lawhon SM, Kahn IIIA, Crawford AH, et al. Controlled hypotensive anesthesia during spinal surgery: a retrospective study. Spine (Phila Pa 1976). 1984;9:450–3.
110. Patel NJ, Patel BS, Paskin S, Laufer S. Induced moderate hypotensive anesthesia for spinal fusion and Harrington-rod instrumentation. J Bone Joint Surg Am. 1985;67:1384–7.
111. Grundy BL, Nash CL Jr, Brown RH. Deliberate hypotension for spinal fusion: prospective randomized study with evoked potential monitoring. Can Anaesth Soc J. 1982;29:452–62.
112. Sharma A, Yadav M, Kumar BR, Lakshman PS, Iyenger R, Ramchandran G. A comparative study of Sterofundin and Ringer lactate based infusion protocol in scoliosis correction surgery. Anesth Essays Res. 2016;10(3):532–7. https://doi.org/10.4103/0259-1162.181425.
113. Bharadwaj A, Khandelwal M, Bhargava SK. Perioperative neonatal and paediatric blood transfusion. Indian J Anaesth. 2014;58(5):652–7. https://doi.org/10.4103/0019-5049.144679.
114. Cao X, Zhang X, Li Q. Efficacy of thromboelastography to monitor the clinical massive transfusion in scoliosis: a randomized controlled trial. Zhonghua Wai Ke Za Zhi. 2016;54(2):137–41.
115. Halpin RJ, Sugrue PA, Gould RW, Kallas PG, Schafer MF, Ondra SL, et al. Standardizing care for high-risk patients in spine surgery: the northwestern high-risk spine protocol. Spine. 2010;35(25):2232–8.
116. Laratta JL, Ha A, Shillingford JN, et al. Neuromonitoring in spinal deformity surgery: a multimodality approach. Global Spine J. 2018;8(1):68–77. https://doi.org/10.1177/2192568217706970.
117. Glassman SD, Dimar JR, Puno RM, et al. A prospective analysis of intraoperative electromyographic monitoring of pedicle screw placement with computed tomographic scan confirmation. Spine. 1995;20:1375–9.
118. Bala E, Sessler DI, Nair DR, et al. Motor and somatosensory evoked potentials are well maintained in patients given dexmedetomidine during spine surgery. Anesthesiology. 2008;109:417–25.
119. Ngwenyama NE, Anderson J, Hoernschemeyer DG, et al. Effects of dexmedetomidine on propofol and remifentanil infusion rates during total intravenous anesthesia for spine surgery in adolescents. Paediatr Anaesth. 2008;18:1190–5.
120. Pastorelli F, Di Silvestre M, Plasmati R, et al. The prevention of neural complications in the surgical treatment of scoliosis: the role of the neurophysiological intraoperative monitoring. Eur Spine J. 2011;20(Suppl 1):S105–14. https://doi.org/10.1007/s00586-011-1756-z.
121. MacDonald DB, Al Zayed Z, Khoudeir I, et al. Monitoring scoliosis surgery with combined multiple pulse transcranial electric motor and cortical somatosensory-evoked potentials from the lower and upper extremities. Spine. 2002;28:194–203.
122. Schwartz DM, Auerbach JD, Dormans JP, Flynn J, Drummond DS, Bowe JA, Laufer S, Shah SA, Bowen JR, Pizzutillo PD, Jones KJ, Drummond DS. Neurophysiological detection of impending spinal cord injury during scoliosis surgery. J Bone Joint Surg. 2007;89A:2440–9.
123. Almenrader N, Patel D. Spinal fusion surgery in children with non-idiopathic scoliosis: is there a need for routine postoperative ventilation? Br J Anaesth. 2006;97:851–7. PubMed: 17035337.
124. Fletcher ND, Glotzbecker MP, Marks M, Newton PO, Harms Study Group. Development of consensus-based best practice guidelines for postoperative care following posterior spinal fusion for adolescent idiopathic scoliosis. Spine. 2017;42:E547–54.
125. Muhly WT, Sankar WN, Ryan K, Norton A, Maxwell LG, DiMaggio T, et al. Rapid recovery pathway after spinal fusion for idiopathic scoliosis. Pediatrics. 2016;137(4):e20151568.

126. Kim E, Lee B, Cucchiaro G. Perioperative surgical home: evaluation of a new protocol focused on a multidisciplinary approach to manage children undergoing posterior spinal fusion operation. Anesth Analg. 2017;125:812–9.
127. Seki H, Ideno S, Ishihara T, Watanabe K, Matsumoto M, Morisaki H. Postoperative pain management in patients undergoing posterior spinal fusion for adolescent idiopathic scoliosis: a narrative review. Scoliosis Spinal Disord. 2018;13:17. https://doi.org/10.1186/s13013-018-0165-z.
128. Menger RP, Kalakoti P, Pugely AJ, Nanda A, Sin A. Adolescent idiopathic scoliosis: risk factors for complications and the effect of hospital volume on outcomes. Neurosurg Focus. 2017;43(4):E3.

Part II

Neurology

Management of Patient with Guillain-Barré Syndrome

23

Jesse T. Lester

Stem Case Terminology

A 56-year-old man with a history of coronary artery disease which is medically managed, diabetes mellitus (non-insulin dependent), and recently diagnosed Guillain-Barré syndrome (GBS) presents for surgical management of acute cholecystitis. He is transferred to the preoperative area from the medical step down unit. On your arrival at the bedside for preoperative evaluation, you note that he is on 2 L of oxygen via nasal cannula and appears mildly dyspneic.

23.1 Preoperative

Question 1:
What is the epidemiology and pathogenesis of Guillain-Barré syndrome?

Answer:
Guillain-Barré syndrome (GBS) is an acute fulminant polyradiculoneuropathy of autoimmune origin. The incidence of GBS is approximately 1–4 cases per 100,000 annually. Males are slightly more commonly affected than females. Approximately 70% of cases of GBS occur 1–3 weeks after an acute infectious process, most often respiratory or gastrointestinal. Commonly implicated antecedent infections include Campylobacter jejuni, Cytomegalovirus, Epstein-Barr virus, HIV, Hepatitis E, and Mycoplasma pneumoniae. More recently, Zika virus has also been implicated as a possible precursor. Several vaccinations have been investigated as possible precursors to GBS, including swine influenza, H1N1, and Influenza vaccines in the early 1990s, although this contribution seems to be minimal at most. More recent influenza vaccines appear to have an even lesser effect on incidence of GBS.

Although there are thought to be both cellular and humoral components to the pathophysiology of GBS based on cerebrospinal fluid (CSF) studies, the primary mechanism is thought to be a form of molecular mimicry. Antibodies formed against the above mentioned infectious agents cross react against gangliosides located on the plasma membranes of neural cells. This leaves the nerve cells susceptible to autoimmune-induced damage and results in the clinical symptoms of neuropathy.

Question 2:
What is the clinical presentation of GBS?

Answer:
As noted above, GBS is often preempted by a respiratory or gastrointestinal infection several weeks prior to symptom onset. Clinical manifestations include a rapidly evolving areflexic motor

J. T. Lester (✉)
Department of Anesthesiology, The Ohio State University Wexner Medical Center, Columbus, OH, USA
e-mail: jesse.lester@osumc.edu

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_23

weakness/paralysis. This can be with or without sensory disturbance, with patients commonly endorsing tingling dysesthesias. Deep tendon reflexes generally dissipate or disappear altogether in the first few days of illness. Weakness typically evolves over hours to days and is typically ascending and symmetric. The lower extremities are often more affected than uppers. While cases vary in their severity, severe cases can result in complete tetraplegia as well as weakness of the intercostal muscles, impairing oxygenation and ventilation. Up to 30% of patients will require mechanical ventilatory support during the course of illness. The lower cranial nerves are also commonly affected, impairing clearance of secretions and potentially necessitating a secure airway.

Other symptoms include autonomic dysfunction, manifested as general loss of vasomotor control, exaggerated blood pressure responses, and severe postural hypotension. Cardiac dysrhythmias are also frequent in GBS patients, likely also secondary to loss of autonomic regulation. Diffuse pain in the neck, shoulders, back, or over the spine are common complaints. Fevers are generally absent in GBS and febrile episodes should prompt providers to search for alternative clinical explanations.

When the patient's symptoms plateau (usually within 4 weeks of onset) further progression is unlikely. Complete recovery can be expected within a few weeks when segmental demyelination is the predominant pathologic feature. However, when axonal degeneration is present, recovery can be significantly prolonged, often leaving a degree of permanent weakness. Mortality rate is 3–8%, most often secondary to complications of prolonged hospitalization (pulmonary embolus, sepsis, respiratory failure.) However, more rarely, autonomic dysfunction can result in lethal cardiac dysrhythmias, also contributing to the mortality of GBS.

Question 3:
How is a diagnosis of GBS established?

Answer:
GBS is a clinical diagnosis. As such, it is made by recognition of a rapidly evolving ascending paralysis, diminished or absent reflexes, all in a setting of appropriate clinical history (recent infectious symptoms) and absence of fever or other systemic symptoms which would point toward alternative diagnoses. The Brighton Collaboration developed a set of criteria for diagnosis of GBS in 2011 which have since been validated.

Brighton collaboration diagnostic criteria
Bilateral/flaccid weakness of limbs
Diminished/absent deep tendon reflexes in affected limbs
Monophasic clinical course of 28 days or less
Absence of alternative diagnosis for weakness
CSF cell count <50/μL
CSF protein concentration > normal value
Nerve conduction studies consistent with GBS

The more criteria satisfied, the more likely the diagnosis of GBS. Generally, if CSF has not been obtained, nerve conduction studies must be consistent with GBS.

Question 4:
What is the treatment for GBS?

Answer:
Treatment for GBS can be thought of as two separate strategies: therapeutic and supportive. Both plasma exchange and IVIG administration have been shown to be effective for therapeutic treatment of GBS. Plasma exchange is generally performed as five sessions over approximately 2 weeks. IVIG in a total dose of 2 g/kg of body weight is usually administered over 2–5 days. Neither plasma exchange nor IVIG are thought to be more effective than the other, and combining the two treatments is not thought to be more effective than either treatment alone. Selection of therapy generally is based on cost and availability. Although IVIG is generally better tolerated and more widely available compared to plasma exchange, it is also more expensive. Both oral and IV steroid administration has been proven ineffective for treatment of GBS, and as such steroids are not considered as a therapeutic option. There are monoclonal antibodies currently under clinical investigation as possible therapeutic adjuncts for GBS treatment.

Although both plasma exchange and IVIG have proven effective treatments for GBS, many patients still have prolonged clinical courses, with sometimes incomplete recovery, and a not insignificant mortality rate. This underscores the importance of supportive care in patients with GBS. Early recognition of potential need for mechanical ventilatory support is essential, via trending vital capacity and/or ABG values, and transitioning to care in an ICU when appropriate. Early and aggressive mobilization and physical therapy are essential, along with appropriate methods of preventing pressure ulcers, DVTs, ventilator-associated pneumonia, and provision of adequate nutritional support. Psychologic support is also important in this patient population.

Question 5:
Is this patient at risk for perioperative complications due to his diagnosis of GBS?

Answer:
GBS patients present with several clinical issues which are of concern when considering provision of an anesthetic. GBS carries a substantial risk of inability to wean safely from the ventilator postoperatively, given the inherent muscle weakness which is often the primary clinical component. GBS patients are also at risk of aspiration, especially if lower cranial nerve involvement is present on preoperative evaluation. This may necessitate use of a rapid sequence induction of anesthesia for safely securing the patient's airway as well as further complicate weaning safely from mechanical ventilation postoperatively. This is exacerbated if the ongoing use of pharmacologic neuromuscular blockade will be necessary for the procedure.

An exaggerated hyperkalemic response to succinylcholine administration is possible in GBS patients, given that these patients often have decreased mobility and are frequently bedbound. Both sensitivity and resistance to nondepolarizing neuromuscular blocking drugs has been reported, necessitating avoidance of these drugs when possible or at least meticulous monitoring with a peripheral nerve stimulator if these drugs are necessary for safe surgical technique.

The prevalence of autonomic dysfunction and cardiac dysrhythmias in GBS patients necessitates close hemodynamic monitoring intraoperatively, especially during periods of intense stimulation (direct laryngoscopy, surgical incision) or during changes of position intraoperatively.

As with any preoperative evaluation, a frank discussion and appropriate documentation as such regarding perioperative risks with the patient and family members is appropriate.

23.2 Intraoperative

Question 6:
How does the diagnosis of GBS affect your anesthetic plan?

Answer:
As discussed above, GBS patients often have lower cranial nerve involvement affecting their pharyngeal muscle function. This places them at higher risk of aspiration, and as such a rapid sequence induction should be considered in these patients.

Given the prevalence of autonomic dysfunction and cardiac dysrhythmias in GBS patients, arterial catheterization for continuous hemodynamic monitoring is strongly recommended. Particular attention should be paid to the patient' hemodynamics during periods of increased stimulation (direct laryngoscopy, surgical stimulation) as well as during positional changes to facilitate surgical approach and on initiation of abdominal insufflation if this will be utilized for the procedure. Exaggerated responses should be anticipated with treatment at the ready. Thoughtful placement of the transducer for an arterial catheter is also important. For example, if patient will be in steep reverse Trendelenburg position, it may be prudent to place the transducer at ear level to better approximate cerebral perfusion and promote early recognition and treatment of relative hypotension.

This also highlights the need for close communication between the anesthetic and surgical teams so that problems can be anticipated and dealt with in a timely manner. There are times

when the most appropriate treatment for an exaggerated hemodynamic response may simply be stopping the stimulus while other measures are instituted.

Regional anesthesia is used by some practitioners in GBS patients although this remains controversial, as there are case reports of worsened symptoms.

Question 7:
Will the diagnosis of GBS affect your choice of pharmacologic agents?

Answer:
Succinylcholine is best avoided in GBS patients due to a potential for excessive potassium release from denervated skeletal muscle. Nondepolarizing neuromuscular blocking drugs can be used if necessary in GBS patients, but both sensitivity and resistance have been reported, making meticulous nerve stimulator monitoring essential. Given the hemodynamic side effects associated with pancuronium administration, it is best avoided in GBS patients who are already at risk for hemodynamic instability. Sugammadex can be used as necessary to ensure adequate reversal of neuromuscular blockade if rocuronium or vecuronium were the agent used.

Given the high prevalence of autonomic dysfunction with GBS, it would be prudent to keep short acting and easily titratable vasoactive medications readily available.

23.3 Postoperative

Question 8:
How can you best assess readiness for extubation postoperatively?

Answer:
Given their muscular weakness at baseline, GBS patients are at higher risk to require postoperative ventilation. Many commonly used anesthetic drugs exacerbate this weakness, especially in the setting of neuromuscular blocking drugs. Ensuring adequate reversal of neuromuscular blockade is essential. Traditional extubation parameters such as NIF less than −20 cm H_20 and vital capacity of 15 mL/kg apply. In addition, the potential for pharyngeal muscle dysfunction makes assurance of adequate airway protective reflexes pertinent prior to extubation.

Multiple Choice Questions

1. A 60-year-old female presents with complaint of bilateral lower extremity weakness which has gradually progressed over several days. All of the following are consistent with a diagnosis of GBS except:
   (a) Upper respiratory infection 2 weeks previously
   (b) Mild fevers
   (c) Loss of deep tendon reflexes
   (d) Elevated CSF protein levels
   Answer: b

   GBS is a clinical diagnosis. The Brighton Collaboration developed diagnostic criteria for GBS which have since been validated. Answers A, C, and D would all support a diagnosis of GBS. The presence of fevers would actually prompt a practitioner to pursue other clinical explanations for the patient's symptoms
2. In the patient from question 1, you suspect GBS as the most likely diagnosis. What is the most appropriate treatment?
   (a) Steroid pulse followed by 7 day taper
   (b) IVIG
   (c) Broad spectrum antibiotics tailored to CSF culture results
   (d) Aggressive physical therapy
   Answer: b

   IVIG and therapeutic plasma exchange have proven effective in the treatment of GBS. With neither therapy thought to be superior and a combination of both generally thought to not be superior to either one alone, the choice generally comes down to availability and cost. Corticosteroids have not proven effective in treatment of GBS. While GBS is associated with a recent history of infection, antibiotics are not helpful in treatment as GBS is an autoimmune disorder. Aggressive physical therapy can help limit long-term morbidity associated with GBS and is an important part of supportive care but is not therapeutic in and of itself

3. A GBS patient requires a rapid sequence induction for safe airway management during an anesthetic. What is the appropriate choice of drug for neuromuscular blockade?
   (a) Succinylcholine
   (b) Pancuronium
   (c) Rocuronium
   (d) Vecuronium

   Answer: c

   Although succinylcholine provides rapid onset of ideal intubating conditions, it is best avoided in GBS patients due to the potential for exaggerated hyperkalemic response in denervated skeletal muscle. Rocuronium, if given at an appropriate dose (1 mg/kg or more) can result in optimal intubating conditions in roughly the same timeframe as succinylcholine. Rocuronium, as a non-depolarizing agent, is not associated with acute hyperkalemia. In addition to being slower in onset, pancuronium is associated with increases in heart rate and blood pressure via vagolytic and sympathomimetic properties. As such, pancuronium is not ideal in GBS patients who are already at risk for autonomic dysfunction. Vecuronium is slower in onset compared to rocuronium and is thus not an ideal choice for a rapid sequence induction
4. A GBS patient is undergoing an anesthetic prior to exploratory laparotomy and becomes acutely hypertensive and tachycardic with direct laryngoscopy. After assuring adequate level of anesthesia and analgesia, what would be the most appropriate medication to treat the hypertension and tachycardia?
   (a) Hydralazine
   (b) Labetalol
   (c) Nitroglycerin
   (d) Esmolol

   Answer: d

   Assuming adequate anesthesia and analgesia in this patient, acute hypertension and tachycardia are best treated with short acting and easily titratable vasoactive agents. Hydralazine is associated with a reflex tachycardia as well as a longer than ideal half-life. Labetalol would appropriately treat both the tachycardia and hypertension but the half-life is longer than is desirable for this likely acute issue. Nitroglycerin is short acting and titratable but is a primary venous dilator especially at lower doses and as such is not an ideal intervention in an acutely hypertensive patient. Esmolol will treat both the hypertension and tachycardia and has a very short half-life and as such is very titratable

References

Question 1

1. Jameson JL, et al. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill Education; 2018. (Ch. 439)

Question 2

2. Jameson JL, et al. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill Education; 2018. (Ch. 439)
3. Miller RD. Miller's anesthesia. 8th ed. Philadelphia: Saunders; 2014. (Ch. 42)
4. Stoelting RK, et al. Anesthesia and co-existing disease. 4th ed. London: Churchill Livingstone; 2002. p. 274–5.

Question 3

5. Fokke C, et al. Diagnosis of Guillain-Barré syndrome and validation of the Brighton criteria. Brain. 2014;137:33–43.

Question 4

6. Willison HF, et al. Guillain Barré syndrome. Lancet. 2016;29:717–27.

Question 5

7. Miller RD. Miller's anesthesia. 8th ed. Philadelphia: Saunders; 2014. (Ch. 42)
8. Stoelting RK, et al. Anesthesia and co-existing disease. 4th ed. London: Churchill Livingstone; 2002. p. 274–5.

Question 6

9. Miller RD. Miller's anesthesia. 8th ed. Philadelphia: Saunders; 2014. (Ch. 42)

10. Stoelting RK, et al. Anesthesia and co-existing disease. 4th ed. London: Churchill Livingstone; 2002. p. 274–5.

Question 7

11. Miller RD. Miller's anesthesia. 8th ed. Philadelphia: Saunders; 2014. (Ch. 42)
12. Stoelting RK, et al. Anesthesia and co-existing disease. 4th ed. London: Churchill Livingstone; 2002. p. 274–5.

Question 8

13. Barash PG, et al. Clinical anesthesia. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2013. p. 785.

Multiple Choice Question 1

14. Fokke C, et al. Diagnosis of Guillain-Barré syndrome and validation of the Brighton criteria. Brain. 2014;137:33–43.

Multiple Choice Question 2

15. Jameson JL, et al. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill Education; 2018. (Ch. 439)

Multiple Choice Question 3

16. Barash PG, et al. Clinical anesthesia. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2013. p. 785.
17. Miller RD. Miller's anesthesia. 8th ed. Philadelphia: Saunders; 2014. (Ch. 42)

Multiple Choice Question 4

18. Miller RD. Miller's anesthesia. 8th ed. Philadelphia: Saunders; 2014. (Ch. 42)

24 Management of Patient with Myasthenia Gravis

Sanchit Ahuja and Ashish K. Khanna

Question 1:
A 34-year-old woman with myasthenia gravis (MG) diagnosed 2 years ago is scheduled for an elective hysterectomy. She is currently on pyridostigmine 60 mg TID. Her vitals are normal for her age. Preoperative hematocrit is 30 g%. You are in pre-anesthesia clinic. Discuss the etiology, clinical features, and diagnostic tests for MG and its differential diagnosis? (Table 24.1)

Clinical Pearl

- Both MG and Lambert–Eaton myasthenic syndrome (LEMS) are diseases of the NMJ. However, in LEMS, muscle weakness improves with exercise, is usually associated with malignancy and caused by of antibodies to *presynaptic* voltage-gated P/Q-type calcium channels at NMJ. Patients with LEMS are sensitive to muscle relaxants. Since LEMS is characterized by an absence of the release of ACh, anticholinesterases such as pyridostigmine (edrophonium) do not appreciably increase the amount of ACh, nor do they affect weakness as a symptom. Patients with LEMS are more sensitive to non-depolarizers than patients with MG.
- Factors that may aggravate MG includes emotional stress, systemic illness, pregnancy, menstrual cycle, and increased temperature.
- The severity of MG is done according to Osserman classification system that classifies based on the muscle groups involved [10].

  Class I—ocular weakness alone

  Class II—mild weakness in muscle groups other than ocular

  Class III—moderate weakness in muscle groups other than ocular

  Class IV—severe weakness in other muscle groups other than ocular

  Class V—intubation necessary secondary to respiratory failure

Question 2:
What treatment options are available for this patient?

Answer:
Treatment goals must be individualized according to severity and functional impairments and are based on the predicted response to a specific form of therapy. Additionally, response to any form of treatment is difficult to access because

S. Ahuja
Department of Anesthesiology, Pain management and Perioperative Medicine, Henry Ford Health Systems, Detroit, MI, USA

A. K. Khanna (✉)
Department of Anesthesiology, Section on Critical Care Medicine, Wake Forest School of Medicine, Winston-Salem, NC, USA
e-mail: ashish@or.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_24

Table 24.1 Comparing differential diagnosis of the conditions mimicking myasthenia gravis

Disease	Etiology/pathophysiology	Clinical features	Diagnosis
Myasthenia gravis (MG) [1, 2]	Commonly caused by autoantibodies to acetylcholine receptors (AchR) on the *post-junctional* membrane of neuromuscular junction. These antibodies block neuromuscular transmission and initiate a complement-mediated inflammatory response which reduces the number of AchR and damages the end plate A minority have other autoantibodies to other epitopes, such as muscle-specific kinase (MuSK), an agrin receptor involved in the regulation/maintenance of the Ach receptors	Relapsing/remitting course. Usually presents between 15–50 years, female predominance in younger ages and reverse at older ages Cardinal symptoms are abnormal fatigable, fluctuating weakness of voluntary muscles, often involving facial and eye muscles; worsening towards the end of the day or following exercise is characteristic. Initial symptoms include intermittent ptosis or diplopia, but weakness of chewing, swallowing, speaking, or limb movement also occurs. Any limb muscle may be affected, most commonly those of the shoulder girdle. Respiratory muscles may also be involved No sensory signs or signs of CNS involvement, although weakness of the oculomotor muscles may mimic a central eye movement disorder	Diagnosis primarily based on history and physical examination, along with serological tests for autoantibodies (anti-AcR-Ab, anti-MuSK Ab) and electrophysiological studies (single fiber EMG) Positive antibody titre can be found in 85% of patients
Guillain–Barré syndrome [3, 4]	Cause unknown; may be autoimmune and theory supports acute infection triggered by virus. Invasion of myelin sheath by inflammatory cells	Acute inflammatory demyelinating polyneuropathy affecting the peripheral nervous system. Patients present with an acute neuropathy with ascending symmetric paralysis, hyporeflexia, or areflexia	Diagnosis primarily clinical. Supportive tests include CSF analysis and electrodiagnostic studies (electromyograph nerve conduction velocity) Positive findings include raised protein concentrations in CSF (albuminocytological dissociation) and decreased amplitude in distal motor or sensory nerves
Transverse myelitis [5–7]	Caused by inflammation across both sides of one level, or segment, of the spinal cord	Pain is the primary presenting symptom 1/3rd–1/2 of all patients. Symptoms include a loss of spinal cord function occurring over several hours to several weeks. Begins as a sudden onset of lower back pain, muscle weakness, or abnormal sensations in the toes and feet, and can rapidly progress to more severe symptoms, including paralysis, urinary retention, and loss of bowel control. Clearly defined sensory level without signs of compressive lesion. A bandlike tightness around the chest or abdomen, weakness, tingling, numbness of the feet and legs. Bladder and bowel dysfunction are common	Diagnosis based on exclusion of any compressive lesion Brain MRI helpful to rule out intracranial lesions. Spinal MRI typically shows cord swelling CSF analysis may show signs of inflammation-monocytes, raised protein content, and IgG index is elevated (normal, ≤ 0.85) EMG and neurological studies are normal

Table 24.1 (continued)

Disease	Etiology/pathophysiology	Clinical features	Diagnosis
Motor neuron disease [8, 9]	Progressive neurodegenerative disease that attacks the upper and lower motor neuron	Degeneration of the motor neuron leads to weakness and wasting of muscles, causing increasing loss of mobility in the limbs, and difficulties with speech, swallowing, and breathing	Clinical diagnosis along with EMG, NCV, and PET scan. EMG studies shows active (positive sharp waves, fibrillation potentials) and chronic denervation patterns (increased amplitude and duration of action potential). PET scan may represent reduced glucose consumption in precentral gyrus

Table 24.2 Available treatment options for a patient presenting with MG

Treatment options available [11]	Therapy	Comments
Symptomatic treatments Medical	*Acetylcholinesterase* (AChE) inhibitors • Pyridostigmine • Neostigmine	– Need for AChE inhibitors varies from day to day and also within same day – Different muscles respond differently with any dose, certain muscles get stronger, others do not change while others become weaker – Drug schedule should be titrated according to the patients workload
Chronic immunomodulating treatments [12]	*Steroids* • Prednisone *Immunomodulators* • Azathioprine • Cyclosporine • Mycophenolate	– Marked improvement or complete relief of symptoms occurs in 75% of cases – Improvement in first 6–8 weeks, but strength may increase to total remission over months – Best responses noted patients with recent disease – Presence of thymoma has excellent response
Rapid immunomodulating treatments	• Plasmapheresis • IV immune globulin	– Quick onset and generally reserved for myasthenic crisis – Preoperative use to maintain remission – Not recommended for long-term treatment
Surgical treatment	Thymectomy	– Presence of thymoma regardless of status except for those with only ocular features – Absence of thymoma in patients with generalized MG and AChR antibodies

the severity of symptoms fluctuates. Table 24.2 demonstrates available treatment options for a patient presenting with MG.

Question 3:
You began to review this case and completed a thorough history and physical exam, including the consideration of several problems such as severity of MG, prior history of exacerbations or myasthenic crisis, treatment regimen, open vs. laparoscopic procedure, anemia, and the possibility of positioning such as steep Trendelenburg. General anesthesia is planned. You specifically want to know how well this patient will perform after surgery and focus specific attention to the patient's ability to protect her airway. Routine preoperative laboratory work up including an EKG, and thyroid function tests is sent along with pulmonary function test is ordered to check baseline status. What is the utility of preoperative pulmonary function tests in this patient?

Answer:
Preoperative assessment should be individualized. Pulmonary function test is a helpful modality in assessing baseline lung parameters

Table 24.3 Spirometry pattern in restrictive lung disease

Value	Restrictive disease
FVC	↓↓↓
FEV1	↓↓↓
FEV1/FVC	Normal
FEF25–75%	Normal
FRC	↓↓↓
TLC	↓↓↓

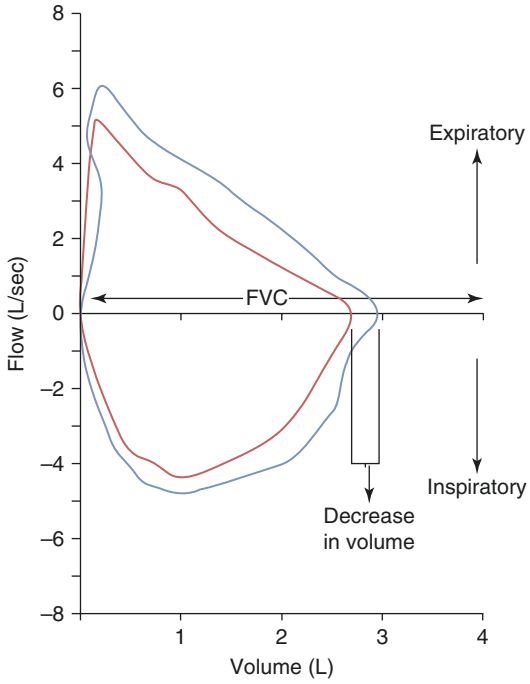


Fig. 24.1 Flow volume curve; blue line represents normal lung and red line represents restrictive ventilatory defect

including strength and endurance. In an ideal scenario, the decision should be collective and coordinated with the patient's neurologist. These are not always indicated but are helpful in assessing the baseline parameters or if respiratory impairments at all exist. A restrictive pattern is usually found in MG patients where all lung volumes are decreased (Table 24.3, Fig. 24.1). FEV1 and FVC both are decreased, therefore FEV1/FVC ratio may be normal to increased. Flow volume loops in supine and upright position are also helpful to determine any likelihood of extra- or intra-luminal, fixed or dynamic thoracic obstruction (in cases of occult thymoma) which may become evident immediately after induction of anesthesia [13]. Peak inspiratory flow requires active patient strength and is predictive for postoperative pulmonary complications. Elective surgery should be performed during a stable or quiescent disease phase, preferably early in the day when the patient's muscle strength is at its best. Primary focus should be on bulbar and respiratory symptoms and exacerbation of myasthenic crisis. Importantly, anesthesiologists should determine the extent of bulbar or respiratory involvement and frequency, and severity of recent myasthenic weakness attacks. The dosage of anticholinesterase drugs should be readjusted to obtain optimal symptomatic relief preoperatively.

Clinical Pearl

- Myasthenic crisis is the most common cause of death in MG patients. It can be precipitated by surgery itself [14]. Although insufficient evidence exists, nonetheless, a retrospective study done on thymomatous MG demonstrated a strong association between FVC and myasthenic crisis after thymectomy [15]. Another study also showed an association of a lower preoperative FVC with postoperative myasthenia crisis in patients undergoing transsternal thymectomy [16].
- Routine thyroid function tests should be ordered in all MG patients, since almost 3–8% have hyperthyroidism which may potentiate respiratory muscle weakness [17].
- Consider preoperative CT scan to look for occult compression and measure tracheal diameter if a thymoma is present. Normal tracheal diameter is 2.2 cm for men and 1.7 cm for women. The external diameter of 7.5 F tracheal tube corresponds to 1.1 cm and 6.5 F corresponds to 0.9 cm [18]. Preoperative assessment may not always be predictive of ease of intubation and ventilation. Sometimes flow volume loops lack clinical significance. Hence, anesthesiologists should always be prepared for a difficult airway situation.
- MG is an autoimmune disease and may be associated with other autoimmune disorders,

for example, diabetes, autoimmune thyroiditis, SLE, rheumatoid arthritis, etc.
- Preoperative hypokalemia may be detrimental as it may exacerbate muscle weakness.

Question 4:
Preoperative laboratory values are normal. You have instructed the patient to continue her usual dose of pyridostigmine on the day of surgery. The surgeon and the patient's neurologist are contacted, and surgery is scheduled as the first case of the day. Her PFTs show a vital capacity of 2.5 L and a diffusion capacity for carbon monoxide (DLCO) 70% of predicted. The patient is counselled for a possible need for postoperative mechanical ventilation. What risk factors for the MG patient determine the need for postoperative ventilatory support?

Answer:
A set of four risk factors also known as the *Leventhal criteria* for postoperative ventilation were identified that predicted an increased likelihood for the need for postoperative mechanical ventilation in patients with MG following transcervical thymectomy [19, 20].

These risk factors include:

1. Duration of disease ≥72 months (≥6 years) [12 points]
2. History of a chronic respiratory disease [10 points]
3. Pyridostigmine dose of >750 mg/day [8 points]
4. Vital capacity <2.9 L (or <40 mL/kg) [4 points]

A total score of ≥10 predicts likely need of postoperative ventilation >3 h.

These clinical markers were established in 1980 and are commonly considered applicable to MG patients undergoing other surgeries; however, subsequent data found them to have little or no actual significance. Concurrent disease processes, especially pulmonary diseases are associated with an increased risk for postoperative intubation in patients with MG. These risk factors are not absolute but nonetheless help the anesthesiologists to focus on important patient characteristics and may be useful in preoperative evaluation and postoperative care decision-making.

Pulmonary function tests are often performed to monitor pulmonary function of patients with MG. When the vital capacity falls below 2.9 L (<40 mL/kg), there is an increased risk for postoperative ventilatory support. Vital capacity is the maximum amount of air expelled after a maximal inhalation. Vital capacity decreases slightly with age and is normally 3–5 L.

Additionally, congestive heart failure and Clostridium difficile diarrhea are also associated with prolonged intubation. Clostridium difficile causes a metabolic acidosis, and respiratory compensation (increased minute ventilation) is difficult for MG patients [21].

This patient is taking 180 mg/day of pyridostigmine, which is below the doses typically associated with an increased risk for postoperative ventilatory support (>250–750 mg/day). Pyridostigmine is a cholinesterase inhibitor that increases the amount of acetylcholine at the NMJ and competes with the Ach-Ab, hence improving muscle strength. This patient should continue pyridostigmine in perioperative period, and missed doses may lead to increased neuromuscular weakness and may cause failed extubation. In addition, having MG for <72 months (as in our case) predicts a decreased likelihood that postoperative mechanical ventilation will be required compared to patients with a disease duration of ≥72 months.

In total, a low preoperative vital capacity (often defined as <2.9 L) has been one of the factors most strongly associated with the need for postoperative mechanical ventilation, whereas the predictive ability of factors like disease duration or pyridostigmine dosage has been inconsistent across studies [22]. Age and sex are also not as predictive.

Clinical Pearl
- In patients who have poorly controlled MG, a course of plasmapheresis prior to surgery is helpful typically when vital capacity is <2 L [23].

Steroid-dependent patients should be continued on steroid in the perioperative period. Thymectomy is the only definitive treatment for MG. Unfortunately, the indications for thymectomy are few. These includes new onset generalized MG, presence of thymoma, and failure of long-term treatment.

- Some clinicians may choose to hold anticholinesterase on the morning of surgery in anticipation of decrease need of muscle relaxants [24]. However, majority of practice patterns and protocols encourage a continuation of anticholinesterase on the day of surgery.

Question 5:
Patient arrived on the day of surgery per instructions, and the acute pain service was consulted to manage pain control. The service is considering an epidural catheter for intra- and postoperative pain control. What are the benefits of regional anesthesia and analgesia in this patient?

Answer:
Regional anesthetic technique including neuraxial and peripheral nerve blocks are safe and confer many benefits including intra- as well as postoperative pain control with minimal or no opioid use [25, 26]. MG has never been shown to cause an increased sensitivity to local anesthetics [27]. It offers two advantages at least, first by minimizing opioids the risk of respiratory depression can be prevented, secondly it provides better analgesia with improvement of respiratory mechanics. Esters—local anesthetics—are metabolized by pseudocholinesterase and may have a theoretical concern of prolonged effects due to anticholinergic treatment. Local anesthetics such as bupivacaine, and ropivacaine are potentially safe to use in epidurals [28]. Whenever local anesthetics are used in MG patients, a judicious use of drug dose is imperative.

MG patients have respiratory muscle weakness, and peripheral nerve blocks such as interscalene block (possibility of phrenic nerve involvement) can be a concern [29]. Anxiolytic drugs should also be minimized and potentially avoided in patients who have bulbar involvement since these patients have little reserve. If necessary, smallest effective dose of BZD can be given under close monitoring. For patients who are maintained on corticosteroids, blood glucose should be monitored in perioperative period.

Question 6:
A low thoracic epidural is placed and the patient is taken to surgery. General endotracheal anesthesia is planned considering the need for relaxation and the type of surgery. Standard ASA monitors are placed. What additional monitoring would you consider throughout this case?

Answer:
Standard ASA monitors with additional monitoring as dictated by patient comorbidities along with neuromuscular monitoring is the basic minimal requirement [30]. In MG, there can be a possibility of overestimation of NMB at one site which may not correlate the same relaxation to other sites. A standard peripheral nerve stimulator to objectively assess degree of neuromuscular blockade such as TOF ratio may be helpful to some extent. Recent data also suggests that severity of MG impacts the relationship between TOF ratio and T1, hence it may not be fully accurate in MG patients [31]. Also, no standard TOF ratio is established in literature for safe recovery [32]. Other adjuncts to monitor possible residual block may be used such as accelerography, mechanomyography, or electromyography. Peripheral nerve stimulators should be used to record baseline even if skeletal muscle relaxants are not used. An arterial line may be helpful to draw blood gases and monitor hemodynamics.

Question 7:
What medications should be avoided in this patient?

Answer:
There are several medications that have some muscle relaxing properties and may exacerbate weakness. Important among these are some specific antibiotics. These medications should be avoided as prophylaxis however must be used to treat specific infections, only if needed. Table 24.4 represents commonly used drugs that should be avoided in MG patients.

Table 24.4 Commonly used drugs that should be avoided in MG patients

Medications that may worsen myasthenia symptoms	Medications may be associated with exacerbation occasionally
1. Antibiotics [33] (a) Aminoglycosides—impair neuromuscular transmission • Gentamycin • Kanamycin • Neomycin • Streptomycin (b) Tetracyclines [34]—potentiate neuromuscular blockade of succinyl choline (c) Macrolides [35] • Erythromycin • Azithromycin (d) Fluoroquinolones [36] (e) Vancomycin [37] 2. Corticosteroids—reduce acetyl choline release and alter choline transport	1. Anticonvulsants [38] • Carbamazepine • Ethosuximide • Gabapentin • Phenobarbital • Phenytoin 2. Butyrophenones • Haloperidol 3. Phenothiazines • Chlorpromazine/prochlorpromazine 4. Calcium channel blockers [39] 5. Iodinated contrast agent [40] 6. Local anesthetics [41]—potentiate the effect of neuromuscular agents and reduce sensitivity of the post-junctional membrane to acetylcholine

Question 8:
Describe the choice of anesthetics you would prefer to use during induction and maintenance?

Answer:
Patients with MG have little respiratory reserve and therefore opioid or benzodiazepines are used cautiously as premedication. One may choose to completely depend on deep inhalational anesthesia with rapid volatile agents for intubation and maintenance. They have an advantage of rapid onset and quicker emergence at the end of surgery but may have a downside of inferior relaxation, hemodynamic instability, and high dose of volatile anesthetics compared to skeletal relaxants. Sevoflurane may be better choice owing to low blood gas coefficient, concentration-dependent inhibitory action on neurotransmission and causing less irritation to airways [42].

Total intravenous anesthesia (TIVA) can also be used. This technique is somewhat tolerated well by younger patients because of known hemodynamic fluctuations. Propofol can be used reliably as an induction agent along with remifentanil (ultra-short acting opioid) can be a reasonable option. Other agents helpful to blunt the sympathetic response are lidocaine and esmolol.

The decision to use muscle relaxants should be individualized. Rapid sequence intubation may be considered in patients with bulbar involvement or severe disease with high risks of aspiration.

MG patients have fewer acetylcholine receptors on the muscle end plate and are more resistant to depolarizing muscle relaxants. ED95 of succinylcholine for MG patients is 2.6 times that of non-MG patients and there is no associated hyperkalemic response. Recovery occurs as succinylcholine diffuses away from the neuromuscular junction, down a concentration gradient and metabolized by plasma cholinesterase. Prior treatment with anticholinergics such as pyridostigmine may prolong the effect of depolarizing muscle relaxant. Hence larger dose is needed to intubate, and the duration response appears to be unpredictable. Also, these patients are prone to develop Phase II block with repeated doses of succinyl choline.

Additionally, MG patients are also very sensitive to non-depolarizing muscle relaxants because of competitive inhibition for fewer AchR sites at NMJ. Therefore, reduced doses of non-depolarizing muscle relaxants are recommended. 1/5th–1/10th the calculated weight-based dose is enough to cause muscle relaxation effect. They should be administered in small incremental doses, preferably graded boluses titrated to the effect by the use of a TOF monitor. This sensitivity is seen even in post-thymectomy patients,

more in generalized disease than in ocular myasthenic [43, 44]. Mann et al. also demonstrated pre-induction T4/T1 to predict individual dose of atracurium in MG. The author concluded that patients with T4/T1 < 0.9 require smallest dose of atracurium while those with T4/T1 > 0.9 require doses similar to non-MG patients [45].

The other technique is utilizing combination of IV anesthetics, volatiles, and graded small boluses of muscle relaxants under TOF monitoring.

In our case, general anesthesia with thoracic epidural is a wise choice and starting epidural with graded boluses in turn helps reducing opioid requirement. For optimal relaxation, we decided to use sevoflurane and reduced doses of non-depolarizing muscle relaxants.

Question 9:
During intraoperative period, the patient develops bradyarrhythmias accompanying pre-mature atrial contractions; however, the blood pressure seems to be stable. What is the etiology of arrhythmias in MG patients and how would you treat?

Answer:
Arrhythmias and cardiomyopathy can occur in MG patients due to myocarditis. It may reveal as asymptomatic EKG changes to unstable ventricular tachycardias. Cardiac involvement suggests autoimmune target for both skeletal and cardiac muscles in MG. Anticholinesterases reduce the action potential duration and slow down sinus rate which may potentiate the myocardial depressant effect of anesthetics such as volatile agents. Anticholinergics, for example, atropine, usually reverses this effect. However, if not reversed immediately, one should always follow routine ACLS guidelines of arrhythmias.

Question 10:
The surgery is close to end, during the surgery the patient received intermittent boluses of rocuronium. How will you reverse this patient?

Answer:
However, the unpredicted response of muscle relaxants can land up into a dilemma of reversing or not reversing at the end of surgery because it will be difficult to individuate cholinergic crisis if patient lands up in such scenario. ACEI blocks the degradation of Ach and increases concentration of Ach at NMJ, causing muscle contraction. Patients who are already on ACEI, risk of overdose and hence cholinergic crisis might occur with the simultaneous use of ACEI reversal. Additionally, in anti-MuSK patients, there are reports of hypertensive reaction with the use of ACEI. Out of the available NMBA, the steroid-based agent rocuronium can be rapidly and efficiently reversed by sugammadex. It does not bind neuromuscular blocking drugs that do not have a steroid nucleus. Block produced by succinylcholine or by any of the benzylisoquinolines, such as atracurium, cisatracurium and mivacurium, is unaffected by sugammadex [46].

Sugammadex is capable of reversing any depth of neuromuscular blockade induced by steroidal neuromuscular blockers (such as rocuronium, and to a lesser extent pancuronium and vecuronium) by forming a 1:1 inactive complex and creating a concentration gradient for the neuromuscular blocker to move away from the neuromuscular junction further leading to restoration of normal neuromuscular function without interfering with cholinergic mechanisms, therefore continuation of pyridostigmine will not affect the efficacy of reversal. Other predictable and reliable signs of extubation may be helpful.

Recent literature also showed different recovery time among two different muscle groups with sugammadex—careful monitoring is indicated even after reversal [47].

As for any patient with a neurodegenerative disease, delayed emergence and an increased likelihood of respiratory complications must be anticipated after surgery. Our patient was reversed by sugammadex after successful signs of extubation were observed.

Question 11:
The patient was extubated and transferred to PACU. She states that she feels weak and is having trouble breathing in the PACU. What would be some appropriate treatment options?

Answer:
The likely cause for muscle weakness and hypoventilation in this patient is either a myasthenic crisis or a cholinergic crisis. Both can result in muscle weakness. MG patients can exhibit neuromuscular weakness several hours post-surgery necessitating intubation and therefore should be closely monitored in high definition units or ICU. Anticholinesterases medication should be reestablished as soon as possible after extubation. Common precipitating factors for myasthenic crisis include surgical stress, infections, sedation, and emotional stress [14]. Myasthenic crisis may be defined as respiratory failure or delayed extubation due to weakness of upper airways muscles (such as respiratory or bulbar) causing dysphagia, change in phonation, weak cough further leading to hypoventilation, aspiration, or obstruction. A myasthenic crisis should be treated with pyridostigmine. Approximately, 8–27% of patients experience myasthenic crisis.

Cholinergic crisis may be due to overdose of anticholinesterases exhibiting signs of cholinergic excess (bradycardia, salivation, lacrimation, urination, defecation, gastrointestinal distress, and emesis) and may also lead to severe muscle weakness. In a cholinergic crisis, the pupils are constricted, whereas in a myasthenic crisis they are dilated. Anticholinergics are used to treat mild disease. Moderate to severe disease is treated by anticholinergics and immunomodulating therapy including corticosteroids followed by azathioprine, cyclosporine, cyclophosphamide, and IVIG.

In a myasthenic crisis, a small dose of edrophonium improves muscle strength; in a cholinergic crisis, it does not improve muscle weakness. Any further doses of neostigmine should be used cautiously to avoid a cholinergic crisis. Differentiating these two scenarios is vital. Myasthenic crisis may involve prolonged respiratory support and urgent therapy with plasma exchange or IVIG. Additionally, immunomodulating therapy may be considered and a neurology consult should be obtained.

Other considerations may include recurarization, opioid-induced respiratory failure, and insufficient analgesia. Doxapram is a respiratory stimulant and naloxone may be helpful in reversing opioid-induced respiratory depression.

Question 12:
The patient continued to feel weak, lethargic and also complains of "insufficient muscle strength." ABG showed respiratory acidosis and decision was made to reintubate the patient and transfer further care to ICU. How will you manage post-extubation respiratory failure?

Answer:
Post-extubation respiratory failure management should include low threshold to intubate in immediate postoperative period. It is important to differentiate myasthenic and cholinergic crisis since the treatment strategy is different for both. The two conditions may be differentiated clinically with Tensilon test. Small dose (10 mg) of edrophonium is administered intravenously and the response is noted clinically. Improvement in muscle strength represents myasthenia crisis, whereas worsening of symptoms or no change indicates cholinergic crisis. After the establishment of myasthenic crisis is made in intubated patient, neurologist should be involved to rapidly initiate plasma exchange or IVIG therapy. Anticholinesterases can be temporarily withdrawn as it may complicate the ventilatory management and can be started when patient starts to exhibit clinical improvement. The reports on usefulness of non-invasive ventilation therapy are limited. Table 24.5 illustrates differences between myasthenia crisis and cholinergic crisis.

Question 13:
Discuss the predictors of extubation failure in ICU in this patient?

Answer:
Limited studies were done on predictors of extubation failure with patients having myasthenic crisis. Older age, pulmonary infections, lower PH, lower FVC, and atelectasis are known risk factors for increased risk of extubation failure in MG patients. In a study, atelectasis was found to be consistently present in all patients

Table 24.5 Differences between myasthenia crisis and cholinergic crisis

Myasthenic crisis	Cholinergic crisis
Exacerbation of myasthenic symptoms following precipitating factors or due to inadequate dose of anticholinesterases—manifested as increased muscle weakness, ptosis, bulbar weakness, impaired swallowing, and hypersecretions which may further lead to aspiration	Acute exacerbation following excessive anticholinesterases resulting in increased Ach, causing muscle weakness, flaccid paralysis, fasciculations, twitching, miosis, salivation, sweating, lacrimation Weakness occurs within 1 h of anticholinesterases
Respiratory distress is common feature	Respiratory distress is common feature
Improved muscle strength after IV anticholinesterases	Worsening of symptoms noticed after anticholinesterases
Treatment begins with airway protection, active suctioning, withholding anticholinesterase—ineffective for few initial days	Treatment begins with airway protection, withholding anticholinesterases, glycopyrrolate, or atropine

who had extubation failure [48]. General guidelines such as improved sustained respiratory muscle strength, FVC > 15 mL/kg, and MIP of −20 cm H_2O should be considered to determine the timing of extubation. Bedside PFTs are helpful in assessing the readiness of patient for extubation. Early tracheostomy facilitates better pulmonary toileting especially in patients with preoperative severe disease, and longer duration of intubation. Optimal pain relief with multimodal analgesics regimen especially in patients who underwent abdominal surgeries is also important.

Multiple Choice Questions

1. Which of the following is true regarding the etiology of MG?
   (a) Autoimmune disease affecting the neuromuscular system characterized by fluctuating muscle weakness commonly involving voluntary muscles, often the facial and eye muscles
   (b) Acute inflammatory demyelinating polyneuropathy affecting the peripheral nervous system
   (c) Neurological disorder caused by inflammation across bilateral segmental levels of the spinal cord
   (d) Progressive neurodegenerative disease that attacks the upper and lower motor neurons

   Answer: a

   MG is the most common neuromuscular-autoimmune entity caused by antibodies directed against postsynaptic acetylcholine receptors leading to compromised end plate potential, and hence the effective synaptic transmission. It is characterized by fluctuating degree of skeletal muscle weakness primarily involving facial, eye, respiratory, or limb muscles. The other four neuromuscular disorders that may present a confusing picture with MG clinically are illustrated in Table 24.1.
2. Which of the following preoperative pulmonary function test is most likely normal?
   (a) FEV1
   (b) FVC
   (c) FEV1/FVC (correct)
   (d) Peak inspiratory flow

   Answer: c

   MG leads to respiratory muscle weakness which may manifest as restrictive ventilatory impairment leading to decrease in all lung volume (*Refer* Table 24.3). FEV1 and FVC are equally reduced; however, the decline in FVC is more than that of FEV1, resulting in normal to high FEV1/FVC.
3. Which of the following is MOST likely to increase the patient's risk for needing postoperative ventilatory support?
   (a) Pyridostigmine dose of 180 mg/day
   (b) Age > 30 years
   (c) Disease duration of 2 years
   (d) Vital capacity of 2.5 L (answer)

   Answer: d

   Out of the four risk factors listed in Leventhal criteria, low preoperative vital capacity (often defined as <2.9 L) has been one of the factors most strongly associated with the need for postoperative mechanical ventilation, whereas the predictive ability of factors like disease duration (c) or pyridostig-

mine dosage (a) has been inconsistent across studies [22].

4. Which of the following statement about regional anesthesia of pain control in MG patient is true?
   (a) Epidural or other regional techniques are contraindicated in this patient because high dose local anesthetics decrease sensitivity of post-junctional membrane to acetyl choline.
   (b) Regional techniques such as peripheral nerve blocks and neuraxial are not contraindicated, albeit helpful as they decrease the systemic use of opioids.
   (c) Neuraxial anesthesia is proven to cause uncontrollable bleeding in MG patients when compared to general population.
   (d) None is correct.

   Answer: b

   Regional anesthetic technique including neuraxial and peripheral nerve blocks are not contraindicated, in fact they are safe and confer many benefits including intra- as well as postoperative pain control with minimal or no opioid use [25, 26]. MG has never been shown to cause an increased sensitivity to local anesthetics [27]. It offers advantages by minimizing opioids—the risk of respiratory depression, and secondly better analgesia with improvement of respiratory mechanics.

5. Out of the following risk factors, which one was found to be consistently associated and had increased likelihood of extubation failure and reintubation:
   (a) Elderly age
   (b) Atelectasis
   (c) Pulmonary infection
   (d) Acidosis

   Answer: b

   General guidelines such as improved sustained respiratory muscle strength, FVC > 15 mL/kg, and MIP of −20 cm H_2O should be considered to determine the timing of extubation. In an observational study published in JAMA, atelectasis was found to be the strongest predictor of reintubation [48]. Noninvasive ventilation post extubation and aggressive pulmonary therapy may be helpful.

References

1. Keesey JC. Clinical evaluation and management of myasthenia gravis. Muscle Nerve. 2004;29(4):484–505.
2. Srivastava A, Kalita J, Misra UK. A comparative study of single fiber electromyography and repetitive nerve stimulation in consecutive patients with myasthenia gravis. Electromyogr Clin Neurophysiol. 2007;47(2):93–6.
3. Yuki N, Hartung HP. Guillain-Barre syndrome. N Engl J Med. 2012;366(24):2294–304.
4. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barre syndrome. Ann Neurol. 1990;27(Suppl):S21–4.
5. Krishnan C, Kaplin AI, Pardo CA, et al. Demyelinating disorders: update on transverse myelitis. Curr Neurol Neurosci Rep. 2006;6(3):236–43.
6. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology. 2002;59(4):499–505.
7. Beh SC, Greenberg BM, Frohman T, et al. Transverse myelitis. Neurol Clin. 2013;31(1):79–138.
8. Rowland LP. What's in a name? Amyotrophic lateral sclerosis, motor neuron disease, and allelic heterogeneity. Ann Neurol. 1998;43(6):691–4.
9. Rowland LP. Progressive muscular atrophy and other lower motor neuron syndromes of adults. Muscle Nerve. 2010;41(2):161–5.
10. Osserman KE, Kornfeld P, Cohen E, et al. Studies in myasthenia gravis: review of two hundred eighty-two cases at the Mount Sinai Hospital, New York City. AMA Arch Intern Med. 1958;102(1):72–81.
11. Gilhus NE, Owe JF, Hoff JM, et al. Myasthenia gravis: a review of available treatment approaches. Autoimmune Dis. 2011;2011:847393.
12. Dretchen KL, Morgenroth VH 3rd, Standaert FG, et al. Azathioprine: effects on neuromuscular transmission. Anesthesiology. 1976;45(6):604–9.
13. Ahuja S, Cohen B, Hinkelbein J, et al. Practical anesthetic considerations in patients undergoing tracheobronchial surgeries: a clinical review of current literature. J Thorac Dis. 2016;8(11):3431–41.
14. Wendell LC, Levine JM. Myasthenic crisis. Neurohospitalist. 2011;1(1):16–22.
15. Choi KH, Nam TS, Lee SH, et al. Preoperative pulmonary function is strongly related to myasthenic crisis after thymectomy. Neurol India. 2014;62(2):164–8.
16. https://www.ncbi.nlm.nih.gov/pubmed/25470186. PMID 25470186.
17. Lin Y-P, Iqbal U, Nguyen P-A, et al. The Concomitant Association of Thyroid Disorders and Myasthenia Gravis. Transl Neurosci. 2017;8:27–30.

18. Grasso N, Celestre C, Borrata F, et al. An unexpected difficult intubation in a patient with myasthenia gravis undergoing video-assisted transcervical thymectomy. BMJ Case Rep. 2013;2013:bcr2013010135.
19. Leventhal SR, Orkin FK, Hirsh RA. Prediction of the need for postoperative mechanical ventilation in myasthenia gravis. Anesthesiology. 1980;53(1):26–30.
20. Grant RP, Jenkins LC. Prediction of the need for postoperative mechanical ventilation in myasthenia gravis: thymectomy compared to other surgical procedures. Can Anaesth Soc J. 1982;29(2):112–6.
21. Thomas CE, Mayer SA, Gungor Y, et al. Myasthenic crisis: clinical features, mortality, complications, and risk factors for prolonged intubation. Neurology. 1997;48(5):1253–60.
22. Chigurupati K, Gadhinglajkar S, Sreedhar R, et al. Criteria for postoperative mechanical ventilation after thymectomy in patients with myasthenia gravis: a retrospective analysis. J Cardiothorac Vasc Anesth. 2018;32(1):325–30.
23. Usmani A, Kwan L, Wahib-Khalil D, et al. Excellent response to therapeutic plasma exchange in myasthenia gravis patients irrespective of antibody status. J Clin Apher. 2019;34(4):416–22.
24. Baraka A, Taha S, Yazbeck V, et al. Vecuronium block in the myasthenic patient. Influence of anticholinesterase therapy. Anaesthesia. 1993;48(7): 588–90.
25. Romero A, Joshi GP. Neuromuscular disease and anesthesia. Muscle Nerve. 2013;48(3):451–60.
26. Ferretti F, Crestani S, Rodriguez NJ, et al. [Can one use high thoracic epidural analgesia in postoperative intensive care of the myasthenia patient following trans-sternal thymectomy?]. Schweiz Med Wochenschr. 1987;117(12):438–41.
27. Mundada SD, Shah B, Atram S. Emergency cesarian section in a patient of myasthenia gravis: is neuraxial anesthesia safe? Saudi J Anaesth. 2012;6(4):430–1.
28. Abel M, Eisenkraft JB. Anesthetic implications of myasthenia gravis. Mt Sinai J Med. 2002;69(1–2):31–7.
29. Sinha A, Ahmad K, Harrop-Griffiths W. The use of a vertical infraclavicular brachial plexus block in a patient with myasthenia gravis: effects on lung function. Anaesthesia. 2001;56(2):165–8.
30. Hunter JM, McGrath CD. Monitoring of neuromuscular block. Contin Edu Anaesth Crit Care Pain. 2006;6(1):7–12.
31. Takahashi K, Niiya T, Takada Y, et al. Severity of myasthenia gravis influences the relationship between train-of-four ratio and twitch tension and run-down of rat endplate potentials. Anesthesiology. 2016;124(2):369–77.
32. Choi EM, Shim JK, Choi YS, et al. Persistent train-of-four fade in myasthenia gravis patients after sevoflurane anaesthesia. Br J Anaesth. 2008;100(5):724–5.
33. Pittinger CB, Eryasa Y, Adamson R. Antibiotic-induced paralysis. Anesth Analg. 1970;49(3):487–501.
34. Hokkanen E. The aggravating effect of some antibiotics on the neuromuscular blockade in myasthenia gravis. Acta Neurol Scand. 1964;40(4):346–52.
35. Cadisch R, Streit E, Hartmann K. [Exacerbation of pseudoparalytic myasthenia gravis following azithromycin (Zithromax)]. Schweiz Med Wochenschr. 1996;126(8):308–10.
36. Gunduz A, Turedi S, Kalkan A, et al. Levofloxacin induced myasthenia crisis. Emerg Med J. 2006;23(8):662.
37. Albrecht RF 2nd, Lanier WL. Potentiation of succinylcholine-induced phase II block by vancomycin. Anesth Analg. 1993;77(6):1300–2.
38. So EL, Penry JK. Adverse effects of phenytoin on peripheral nerves and neuromuscular junction: a review. Epilepsia. 1981;22(4):467–73.
39. Bikhazi GB, Leung I, Flores C, et al. Potentiation of neuromuscular blocking agents by calcium channel blockers in rats. Anesth Analg. 1988;67(1):1–8.
40. Rath J, Mauritz M, Zulehner G, et al. Iodinated contrast agents in patients with myasthenia gravis: a retrospective cohort study. J Neurol. 2017;264(6):1209–17.
41. Matsuo S, Rao DB, Chaudry I, et al. Interaction of muscle relaxants and local anesthetics at the neuromuscular junction. Anesth Analg. 1978;57(5):580–7.
42. Nitahara K, Sugi Y, Higa K, et al. Neuromuscular effects of sevoflurane in myasthenia gravis patients. Br J Anaesth. 2007;98(3):337–41.
43. Itoh H, Shibata K, Nitta S. Sensitivity to vecuronium in seropositive and seronegative patients with myasthenia gravis. Anesth Analg. 2002;95(1):109–13, table of contents.
44. Itoh H, Shibata K, Nitta S. Difference in sensitivity to vecuronium between patients with ocular and generalized myasthenia gravis. Br J Anaesth. 2001;87(6):885–9.
45. Mann R, Blobner M, Jelen-Esselborn S, et al. Preanesthetic train-of-four fade predicts the Atracurium requirement of myasthenia gravis patients. Anesthesiology. 2000;93(2):346–50.
46. Sungur Ulke Z, Yavru A, Camci E, et al. Rocuronium and sugammadex in patients with myasthenia gravis undergoing thymectomy. Acta Anaesthesiol Scand. 2013;57(6):745–8.
47. Iwasaki H, Takahoko K, Otomo S, et al. Monitoring of neuromuscular blockade in one muscle group alone may not reflect recovery of total muscle function in patients with ocular myasthenia gravis. Can J Anaesth. 2013;60(12):1222–7.
48. Seneviratne J, Mandrekar J, Wijdicks EFM, et al. Predictors of extubation failure in Myasthenic crisis. Arch Neurol. 2008;65(7):929–33.

25 Management of Patient with Parkinson's Disease (DBS)

Sandra Machado

Stem Case Terminology

A 78-year-old male, 72 kg, with the diagnosis of medically intractable Parkinson's disease (PD). PMH significant for multiple hospitalizations for pneumonia, autonomic dysfunction, and depression. Presents with "pill-rolling" tremor, muscular rigidity, postural instability, and bradykinesia. He is currently taking levodopa/carbidopa and selegiline. VS: BP 135/68 lying flat and 105/42 standing up, HR 90, RR 18, $satO_2$ 95%. Labs within normal range.

Question 1:
Which are the nuclei that constitute basal ganglia?

Answer:
Basal ganglia is formed by a complex circuitry that includes neurons of the caudate nucleus, putamen, subthalamic nucleus (STN), globus pallidus, and substantia nigra (SN).

Question 2:
What is the pathophysiology of PD?

Answer:
The most pronounced abnormality in PD is the loss of the nigrostriatal dopaminergic neurons originating from the SN pars compacta of the midbrain, resulting in dopamine depletion from basal ganglia [1]. As a result, there is a reduction in firing inhibition of extrapyramidal motor neurons and unopposed stimulation by acetylcholine. The mechanism for cell death is unknown. But it is speculated that mitochondrial dysfunction, oxidative stress, excitotoxins, and immune system may play a role [2].

Question 3:
Which are the main drugs used in the management of PD?

Answer:
The drugs used more often in the treatment of PD are levodopa/carbidopa, anticholinergic agents, dopamine receptor agonists, amantadine, and selegiline. The main goal of the therapy is to improve quality of life and to slow the progression of the disease.

Question 4:
Why carbidopa is usually associated with levodopa? What is the half-life of levodopa?

Answer:
Levodopa undergoes decarboxylation to produce dopamine. Carbidopa is a decarboxylase inhibitor. When associated with levodopa, it blocks this process, reducing peripheral side effects of

S. Machado (✉)
Department of Anesthesiology and Critical Care Medicine, Cleveland Clinic, Cleveland, OH, USA
e-mail: machads@ccf.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_25

dopamine such as nausea, vomiting, and postural hypotension [3].

Levodopa half-life is about 30–60 min.

The patient presents with a stomach flu and has persistent nausea and vomiting for about 3 days. He is unable to ingest his scheduled medications. The patient's wife had some leftover metoclopramide in her cabinet and decided to give it to her husband.

The family has noticed that he is now agitated, has more muscle rigidity, and is febrile (temp 40 °C).

Question 5:
What is your differential diagnosis?

Answer:
Acute exacerbation of the PD symptoms related to noncompliance to his medical treatment, serotonin syndrome (SS), or neuroleptic malignant syndrome (NMS).

SS is a potentially life-threatening clinical spectrum that presents with mental status changes, autonomic instability, and neuromuscular abnormalities [4]. It is usually seen with inadvertent interactions between drugs. Specifically in this case, the patient routinely takes carbidopa-levodopa that indirectly causes release of serotonin and selegiline (MAOi) that inhibits serotonin metabolism. Additionally, he was given metoclopramide that impairs reuptake from the synaptic cleft into the presynaptic neuron. The combination of the medication may have precipitated the serotonin toxicity [5]. NMS has a similar clinical presentation of mental status change, neuromuscular symptoms, fever, and autonomic changes. A detailed history and physical examination can easily help to establish the diagnosis. SS has an onset and resolution within 24 h, and the main neuromuscular finding is hyperactivity such as tremor and clonus. Nevertheless, NMS has a longer onset and resolution (days to weeks), and it usually presents with bradyreflexia and muscular rigidity.

The patient improved from acute decompensation after adequate treatment.

His neurologist believes that there is an indication for surgical treatment considering the progression of the disease. Functional neurosurgery is consulted and offers deep brain stimulation (DBS) surgery and patient agrees to proceed.

The patient presents in the preoperative area for elective stereotactic implantation of the DBS leads after optimization and clearance by internal medicine. The neurology and neurosurgery teams have decided for implantation in the subthalamic area, and the surgeon's preference is for implantation guided by awake intraoperative electrophysiological mapping including microelectrode recording (MER) and macrostimulation with the DBS lead. You are the physician assigned to provide perioperative care to this patient.

25.1 Preoperative

Question 6:
Which are the key features that the anesthesiologist should focus when evaluating this patient?

Answer:
The anesthesiologist should go through a detailed assessment of patients with PD. It is particularly important to know the duration and severity of the disease and potential multisystemic involvement. A few organs of interest are cardiovascular, respiratory, and gastrointestinal.

Additionally, the anesthesiologist should understand potential drug interactions of the antiparkinsonian medications and discuss with the surgeon the need to hold it for adequate intraoperative mapping.

Question 7:
Would you consider additional tests before surgery?

Answer:
CBC and CMP should be part of the preoperative evaluation to rule out anemia, infection, dehydration, abnormal glucose metabolism (selegiline), and hypoalbuminemia. This patient has a history of multiple hospitalizations due to aspiration pneumonia, thus a CXR is recommended [2]. Additionally, an EKG and echocardiogram should be considered as the patient has a history

of autonomic dysfunction and possible inability to assess the functional capacity.

Question 8:
Is aspiration prophylaxis recommended?

Answer:
Patients with PD have an increased risk of aspiration pneumonia due to an inability to adequately clear secretion, gastric stasis, and upper airway muscle weakness. Hence, preoperative aspiration prophylaxis should be considered [6].

25.2 Intraoperative

Question 9:
What is DBS?

Answer:
DBS is an efficacious surgical treatment for medication-refractory hypokinetic and hyperkinetic movement disorders which involves delivery of electrical pulses to specific nuclei of the brain. The main objective is to modulate the function of such structures in order to achieve a reversible, adjustable, and therapeutic or clinically beneficial effect [7]. Permanently implanted DBS devices have three components: the DBS lead, which is inserted into the brain and extends to the outside of the skull; the implantable pulse generator, typically located in the infraclavicular area; and an extension cable that connects the two components (Fig. 25.1).

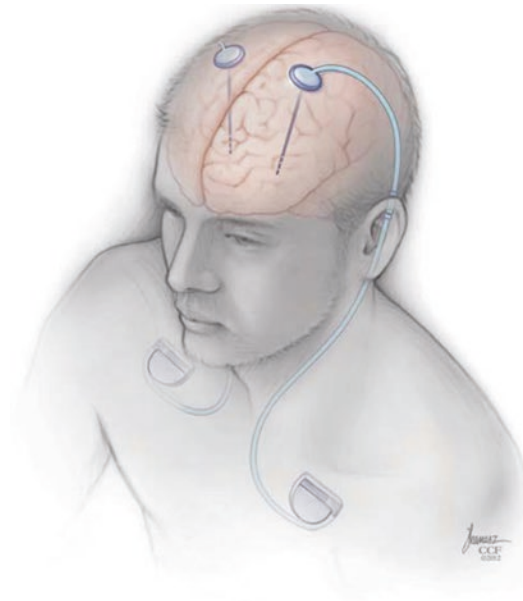


Fig. 25.1 DBS devices have three components: DBS lead, implantable pulse generator, and extension cable

Question 10:
Which are the current indications for DBS?

Answer:
DBS is an established surgical modality in the treatment of idiopathic PD, essential tremor, and primary dystonia.

Question 11:
What are the mechanisms of action of DBS?

Answer:
The mechanisms of action of DBS are still under investigation, and there are several hypothesis. DBS activates neurons from the targeted nucleus and fiber pathways to modulate the basal ganglia and thalamocortical fibers. Consequently, it regularizes pathologic activity and oscillations of this network, resulting in an improvement of the symptoms of the disease [8–10].

Question 12:
Is this procedure staged?

Answer:
Patients with PD may receive bilateral, staged, or unilateral implants. It is a common practice to stage the procedure in two parts: (a) stereotactic lead implantation of the DBS leads and (b) internalization of the pulse generator. The last part is usually performed a few days or weeks after brain electrode placement in an attempt to minimize the risk associated with a prolonged procedure in patients that are commonly elderly and with multiple comorbidities. Additionally, the edema related to the surgical trauma around the electrodes may cause a temporary improvement of the symptoms compromising the testing for efficacy of the stimulation and side effects [11].

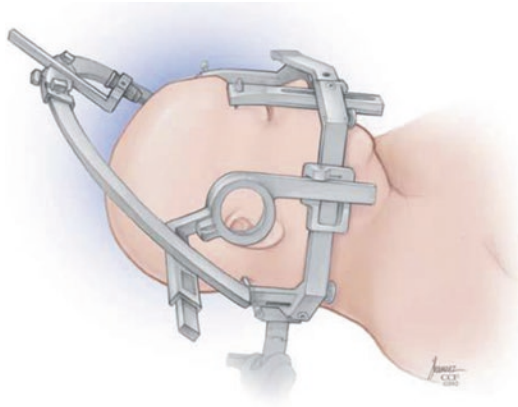


Fig. 25.2 Patient positioned with the stereotactic frame attached to the bed

Question 13:
How the patient is usually positioned for lead implantation guided by awake electrophysiology?

Answer:
Most commonly the patient is positioned supine or in semi-sitting position with the stereotactic frame attached to the bed (Fig. 25.2). The frame is used to increase the accuracy via a coordinate system acquired with a preoperative CT scan.

Question 14:
How are you going to monitor this patient?

Answer:
Noninvasive blood pressure, five-lead electrocardiogram, pulse oximeter, end-tidal CO_2, skin temperature probe, urinary catheter, and neuromonitoring are the standard monitors. Invasive blood pressure should be considered in patients with uncontrolled hypertension or severe cardiorespiratory comorbidities. The anesthesiologists should also foresee the potential for significant hemodynamic instability in patients with severe autonomic dysfunction.

Question 15:
What is awake electrophysiology? How will it impact the anesthetic technique?

Answer:
Microelectrode recording (MER) is a neuromonitoring technique to facilitate the localization of the nuclei in the brain through the recognition of characteristic electrical activity of neuronal groups. It involves the insertion of high-impedance electrodes 10–15 mm above the targeted structure that are slowly advanced toward the nuclei while neuronal signals are recorded. This technique is used in association with macrostimulation testing during the procedure in order to verify that the lead is inserted in an adequate location. The last is performed through a neurophysiologist assessment for potential clinical improvement of tremor and other cardinal motor symptoms as well as side effects while the targeted area is stimulated with different parameters.

There are multiple studies trying to determine the best anesthetic technique with the least effect on MER. The majority of anesthetics have some impact on neuromonitoring. It has been reported that propofol affects the background neuronal discharges and patterns during recording [12]. Additionally, there is a variation of the neuronal effect depending on the disease and the target nuclei. Propofol may have an impact on macrostimulation testing, considering that it can provoke dyskinesia [13, 14]. Dexmedetomidine is an alpha 2 agonist that is commonly used due to its analgesic effect, minimal respiratory depression in addition to being easily titratable. The main disadvantage of this drug is the possible suppression of MER in higher doses [15] and potential hemodynamic instability (hypotension and bradycardia). Overall, opioids are thought to have minimal effects in MER and are usually safely used.

Having said that, the main goal of the anesthesia is to provide comfort and analgesia during the initial part of the DBS while been able to easily wake up the patient for the neurological assessment. The most common approach is deep sedation alternating with awake portions for neuromonitoring. Propofol and dexmedetomidine are routinely used, particularly because they are easily titratable and have little and known impact on the neurocognitive testing once the patient is awake.

Question 16:
Patient is extremely anxious. Are you going to premedicate with midazolam?

Answer:
There should be a cautious use of anxiolytics such as benzodiazepines due to the potential of oversedation or paradoxical agitation.

Question 17:
Which are the main concerns when deciding on the anesthetic technique? What is asleep-awake-asleep technique? Which are the pros and cons of MAC/deep sedation vs. general anesthesia for the first stage of DBS?

Answer:
The anesthesiologist should consider a few aspects when deciding on the anesthetic technique:

1. The need for neuromonitoring and the impact of the anesthetic drugs
2. Comorbidities such as chronic pain and respiratory and cardiovascular disorders
3. Inability to stay still and cooperate such as children or patients with severe involuntary movements

In our experience, most of the DBS procedures for PD are performed with the asleep-awake-asleep technique. In this approach, the patient is under moderate/deep sedation from the initial portion of the surgery such as positioning, local infiltration of the skin, burr hole, opening of the meninges, and cannulae insertion. Sedation should be withheld for at least 15 min prior to MER so the patient is ready to cooperate with neurological assessment. The benefit of sedation with easily titratable agents such as propofol and/or dexmedetomidine is that they have a predictable pharmacokinetic profile facilitating the process of intraoperative emergence. As a result, the patient is able to provide the most reliable and robust data to assist the electrode placement. The main disadvantages of this technique are limited access to manipulate the airway and risk associated with a patient's unexpected inability to cooperate when awake. It is not uncommon for PD patients to present with intraoperative delirium [16] or with severe involuntary movements when off their medications for PD, compromising the quality of neuromonitoring.

General anesthesia is a more tolerable and comfortable technique for patients, expanding the number of candidates that can be treated. However, it interferes in the MER and prevents most of the clinical evaluation and side effects of macrostimulation testing [17].

Intraoperative MRI can be used to confirm placement of implanted electrode under general anesthesia, replacing awake monitoring in select patients [18, 19].

Question 18:
Which are the main anatomical targets in the surgical treatment of DBS? How are these targets localized?

Answer:
The most common targets of DBS include the ventralis intermedius nucleus (Vim) for essential tremor and the STN [8] or the globus pallidus (GPi) for PD.

Frame-based technique is the most common approach to DBS surgery [20]. The frame is used as reference for the entire procedure. After its placement, computed tomography or MRI is then performed, so that the images are co-registered with the fiducial points of the stereotactic frame. The calculated coordinates to the specific target are then transferred to the stereotactic frame and arc. This system will guide the leads' entry points [21]. Once the electrode is about 10–15 mm above the targeted area, it is advanced in submillimeter increments along the planned trajectory while MER and macrostimulation testing are used to help confirm the location provided by the coordinates.

The surgeon requests tight BP control (systolic BP < 130 mmHg).

Question 19:
Why is it important? Are beta blockers a good option?

Answer:
Adequate blood pressure control is one of the main pillars in the anesthetic management of this population. Hypertension might increase the chance of intraoperative hemorrhage. It has been

speculated that the intraoperative use of beta blockers could interfere with the macrostimulation testing, but there is not enough data to support it.

25.3 Postoperative

The patient is nauseous in PACU.

Question 20:
Which anti-emetic medications should be avoided?

Answer:
Droperidol and metoclopramide should be avoided as they could exacerbate PD symptoms [22].

You are called to the bedside in PACU as the patient has a loud stridor and difficulty breathing. He is A/O x3, BP 146/82, HR 110, $satO_2$ 89%, and RR 40.

Question 21:
What you think is going on? Why?

Answer:
There is a high percentage of PD patients who present with some degree of upper airway obstruction diagnosed by spirometry [23]. Upper airway obstruction has been described in up to one third of patients with PD [24].

The complete occlusion is believed to be a result of rigidity and hypokinesia, affecting the intrinsic laryngeal muscles and probably most of the muscles of upper airway [25]. Furthermore, the airway dysfunction is an important contributor for frequent respiratory infections/aspiration pneumonia, which are commonly diagnosed in patients with PD.

Patients undergoing general anesthesia with endotracheal tube should be closely observed after extubation for possible laryngospasm and respiratory failure [26].

The patient recovers from the procedure, and the stimulation parameters are optimized and programmed.

The patient is now scheduled for the second stage of the procedure.

Question 22:
What is the second stage of DBS?

Answer:
After the leads are placed, the patient undergoes the second stage of the procedure. In this step, the pulse generator is implanted, typically in the chest, and connected to the brain leads by tunneling extension cables through the scalp and subcutaneously on the side of the neck [21].

Question 23:
What is your anesthetic technique?

Answer:
The standard anesthetic technique for second stage of DBS is general anesthesia.

Question 24:
Which are the main potential complications of DBS?

Answer:
Potential complications of DBS may be related to the surgery, hardware, or stimulation. Surgical complications include intracranial and intracerebral hemorrhage, infection, misplacement of the DBS leads, or suboptimal placement of the leads. The incidence of hemorrhage ranges between 0.5 and 5% of DBS procedures [27], and it is one of the most feared complications. The main hardware complications include migration of the leads, erosion of the subcutaneous portions of the hardware, and DBS lead failure. Stimulation-related adverse effects are reversible with programing and/or drug adjustments.

The patient has a successful placement of DBS electrode and pulse generator with better control of his symptoms. He is discharged home on postoperative day 2.

Question 25:
Six months later, he is brought to the ER for abdominal pain. After an inconclusive CT scan, the surgeon orders an MRI to better assess the abdomen, but he decides to check if there is a contraindication before he orders it. What do you say?

Answer:
There are multiple variables that will determine if the DBS system is compatible with MRI. The best approach is to alert the patient for the safety issue and to contact the neurostimulation manufacturer and the patient's physician to learn if MRI is safe with that specific device.

The surgeon recommends emergent surgery for free air in the abdomen.

Question 26:
Which are the perioperative considerations for patients with implanted non-cardiac electrical devices?

Answer:
Ideally, patients with implantable neurological devices should be checked preoperatively. In emergent surgical procedures, all the surgical staff should be aware of the device and the potential impact of the electromagnetic interference such as:

1. Turning the device on/off
2. Resetting the IPG to new parameters
3. Brain tissue damage
4. Permanent damage of the device

The use of bipolar cautery should be favored. In the event that monopolar needs to be used, Srejic et al. [28] recommend the following:

1. Turn IEMD off, turn voltage to 0
2. Place the grounding pad as far as possible from the leads and generator
3. Avoid the use of full-length grounding pads. Use a nonconductive surface or bed.

Multiple Choice Questions

1. The following are cardinal manifestations of PD except:
   (a) Bradykinesia
   (b) Postural instability
   (c) Hyperreflexia
   (d) Tremor
   (e) Rigidity
   Answer: c
2. Which of the following is not a medication commonly used in the treatment of PD:
   (a) Dopamine
   (b) Selegiline
   (c) Bromocriptine
   (d) Trihexyphenidyl
   (e) Amantadine
   Answer: a
3. Which of the following is not a common target for DBS:
   (a) Ventralis intermedius nucleus (Vim)
   (b) Subthalamic nucleus (STN)
   (c) Globus pallidus (GPi)
   (d) Nucleus accumbens
   (e) Nucleus ambiguus
   Answer: e
4. Which one is the most feared complication of DBS?
   (a) Bleeding
   (b) Infection
   (c) Electrode misplacement
   (d) Electrode migration
   Answer: a

References

1. Hornykiewicz O. The discovery of dopamine deficiency in the Parkinsonian brain. J Neural Transm Suppl. 2006;70:9–15.
2. Nicholson G, Pereira AC, Hall GM. Parkinson's disease and anaesthesia. Br J Anaesth. 2002;89(6):904–16.
3. Ngai SH. Parkinsonism, levodopa, and anesthesia. Anesthesiology. 1972;37(3):344–51.
4. Birmes P, et al. Serotonin syndrome: a brief review. CMAJ. 2003;168(11):1439–42.
5. Isbister GK, Buckley NA. The pathophysiology of serotonin toxicity in animals and humans: implications for diagnosis and treatment. Clin Neuropharmacol. 2005;28(5):205–14.
6. Shaikh SI, Himanshu V. Parkinson's disease and anaesthesia. Indian J Anaesth. 2011;55(3):228–34.
7. Oluigbo CO, Salma A, Rezai AR. Deep brain stimulation for neurological disorders. IEEE Rev Biomed Eng. 2012;5:88–99.
8. Krack P, et al. Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 2003;349(20):1925–34.
9. Williams NR, Foote KD, Okun MS. STN vs. GPi deep brain stimulation: translating the rematch into clinical practice. Mov Disord Clin Pract. 2014;1(1):24–35.

10. Miocinovic S, et al. History, applications, and mechanisms of deep brain stimulation. JAMA Neurol. 2013;70(2):163–71.
11. Rezai AR, et al. Deep brain stimulation for Parkinson's disease: surgical issues. Mov Disord. 2006;21(Suppl 14):S197–218.
12. Raz A, et al. Propofol decreases neuronal population spiking activity in the subthalamic nucleus of Parkinsonian patients. Anesth Analg. 2010;111(5):1285–9.
13. Krauss JK, et al. Propofol-induced dyskinesias in Parkinson's disease. Anesth Analg. 1996;83(2):420–2.
14. Venkatraghavan L, Manninen P. Anesthesia for deep brain stimulation. Curr Opin Anaesthesiol. 2011;24(5):495–9.
15. Elias WJ, et al. Dexmedetomidine and arousal affect subthalamic neurons. Mov Disord. 2008;23(9): 1317–20.
16. Lange M, et al. Anesthesiologic regimen and intraoperative delirium in deep brain stimulation surgery for Parkinson's disease. J Neurol Sci. 2015;355(1–2):168–73.
17. Anderson BJ, Marks PV, Futter ME. Propofol--contrasting effects in movement disorders. Br J Neurosurg. 1994;8(3):387–8.
18. Coubes P, et al. Deep brain stimulation for dystonia. Surgical technique. Stereotact Funct Neurosurg. 2002;78(3–4):183–91.
19. Venkatraghavan L, Luciano M, Manninen P. Review article: anesthetic management of patients undergoing deep brain stimulator insertion. Anesth Analg. 2010;110(4):1138–45.
20. Machado A, et al. Deep brain stimulation for Parkinson's disease: surgical technique and perioperative management. Mov Disord. 2006;21(Suppl 14):S247–58.
21. Machado AG, Deogaonkar M, Cooper S. Deep brain stimulation for movement disorders: patient selection and technical options. Cleve Clin J Med. 2012;79(Suppl 2):S19–24.
22. Erickson KM, Cole DJ. Anesthetic considerations for awake craniotomy for epilepsy and functional neurosurgery. Anesthesiol Clin. 2012;30(2):241–68.
23. Canning CG, et al. Parkinson's disease: an investigation of exercise capacity, respiratory function, and gait. Arch Phys Med Rehabil. 1997;78(2):199–207.
24. Neu HC, et al. Obstructive respiratory dysfunction in Parkinsonian patients. Am Rev Respir Dis. 1967;95(1):33–47.
25. Trotti LM, Bliwise DL. No increased risk of obstructive sleep apnea in Parkinson's disease. Mov Disord. 2010;25(13):2246–9.
26. Easdown LJ, Tessler MJ, Minuk J. Upper airway involvement in Parkinson's disease resulting in postoperative respiratory failure. Can J Anaesth. 1995;42(4):344–7.
27. Zrinzo L, et al. Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. J Neurosurg. 2012;116(1):84–94.
28. Srejic U, Larson P, Bickler PE. Little black boxes: noncardiac implantable electronic medical devices and their anesthetic and surgical implications. Anesth Analg. 2017;125(1):124–38.

Management in a Patient with Stroke

26

Vasudha Singhal

Stem Case Terminology

A 72-year-old male presented to the emergency department (ED) with a history of acute onset right-sided weakness and inability to speak since the past 1 h. He is a known hypertensive and diabetic, and smokes 1 pack of cigarettes on a daily basis. He is on metoprolol, ramipril, rosuvastatin, ecosprin, and oral hypoglycemics for his medical condition. On physical examination, the patient is awake but confused. The power in his right upper and lower limbs is 0/5 while on the left side is 4+/5. He has global aphasia and is unable to comprehend.

Question 1:
What Is the Differential Diagnosis of the Acute Neurological Dysfunction in This Patient?

Answer:
The acute onset of focal neurological symptoms (hemiparesis and aphasia, in this case), attributable to a defined vascular territory, with hypertension, diabetes, and smoking in the background, indicate to the possibility of an **acute stroke**. But prior to making a clinical diagnosis of an acute stroke, it should be ascertained whether the process leading to the symptoms is vascular, or a stroke-like mimic [1].

The common **stroke mimics** that need exclusion are:

1. Hypoglycemia
2. Seizures
3. Complicated migraine
4. Hypertensive encephalopathy
5. Wernicke's encephalopathy
6. Intoxication
7. Brain tumor
8. CNS abscess
9. Traumatic brain injury
10. Psychogenic

A detailed history with a thorough neurological examination is the key to exclude stroke mimics. The patient's past history, especially the presence of systemic diseases, family history, temporal course and progression of the focal symptoms and findings, and accompanying symptoms such as headache, vomiting, and depressed mentation, all point to a definitive diagnosis.

- A diabetic patient with a low glucose level and decreased level of consciousness usually has hypoglycemia.
- A patient with a witnessed seizure activity and a known history, is usually in a postictal phase, which explains his depressed mentation.

V. Singhal (✉)
Department of Neuroanesthesiology and Critical Care, Medanta, The Medicity, Gurgaon, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_26

- Presence of significant hypertension, a history of migraines, alcohol abuse, patient taking drugs like lithium, necessitate exclusion of mimics like hypertensive encephalopathy, migraine with aura, Wernicke's encephalopathy and intoxication, respectively.
- Gradual progression of symptoms with seizure at onset may be seen in brain tumors.
- Those with CNS abscess may have a history of fever, with endocarditis or an implant in situ.
- The presence of inconsistent examination findings, with neurological findings in a non-vascular distribution, and a lack of objective cranial nerve deficits, may be seen in a psychogenic illness.

Question 2:
Discuss the Causes and Risk Factors of Acute Stroke

Answer:
Acute stroke is characterized by an acute neurological dysfunction, attributable either to focal ischemia (**ischemic stroke**) or a focal collection of blood in the brain parenchyma or ventricles (**hemorrhagic stroke**). About 80% of all strokes are ischemic, which in turn, can be either thrombotic (arterial occlusion by atherosclerotic plaques) or embolic (mostly cardiogenic emboli).

The common risk factors associated with strokes include:

1. Demographics—older age/male gender/African-American race have a higher predisposition for stroke
2. Positive family history
3. Prior history of stroke
4. Smoking
5. Hypertension
6. Diabetes mellitus
7. Cardiovascular disease, including heart failure, atrial fibrillation, carotid stenosis
8. Dyslipidemia
9. Hyperhomocysteinemia
10. Obesity & physical inactivity
11. Alcohol abuse
12. Estrogen therapy
13. Illicit drug use
14. Hypercoagulable states

Question 3:
Why Does a Patient Presenting with Symptoms of Stroke Need Emergency Triage and Evaluation?

Answer:
Acute ischemic stroke is invariably caused by the critical reduction in the blood supply of a cerebral vascular territory due to arterial occlusion or stenosis. Due to its high metabolic rate and complete dependence on aerobic metabolism, the brain tissue is particularly vulnerable to ischemia, and the cells in the brain begin to die within minutes of the compromise in oxygen supply. An average patient loses 1.9 million neurons every minute a large vessel stroke is left untreated. Every hour delay in treatment results in a loss of as many neurons as would occur with 3.6 years of normal aging! [2] It is therefore commonly said that "time lost is brain lost" or simply, "**time is brain**."

Stroke is considered a neurological emergency, and its evaluation and treatment takes immediate priority and triaging, in order to salvage the brain tissue which is at risk due to vessel occlusion, but not irreversibly damaged (typically known as the penumbra). The goal of treatment in stroke is early arterial recanalization, either by the dissolution of the occluding thrombus (by means of intravenous thrombolytic therapy), or mechanical retrieval of the clot (endovascular treatment). A typical time frame of ≤60 minutes is commonly followed as the "door to needle" (DTN) time, wherein a patient with suspected stroke is expected to get a non-contrast computed tomography (NCCT) head and its evaluation (to exclude hemorrhage), followed by intravenous thrombolysis, preferably within an hour of reaching the ED.

Question 4:
How Do You Approach a Patient with Signs and Symptoms Suggestive of Stroke?

Answer:
A potential stroke patient is treated like a medical emergency, with immediate stabilization of the

airway, breathing, and circulation (ABC). This is followed by a quick history and assessment of neurological deficits. Activation of the in-hospital rapid response system, or **stroke code**, is done if symptoms are suggestive of stroke, so as to expedite diagnostic and therapeutic interventions.

History: The most important point in the patient's history is the time of symptom onset, or the time when the patient was last seen normal or symptom-free. In patients with a "wake-up" stroke, the onset time is usually unknown, and leading questions like the time when the patient was last ambulatory to the bathroom, may help in identifying the approximate timelines. Establishing the onset time helps in decision-making for definitive therapy, such as intravenous thrombolysis or endovascular treatment.

Further history taking should aim at recognizing the eligibility for the planned therapeutic interventions. These include the comorbidity status of the patient—presence of hypertension, diabetes, cardiac disease, history of anticoagulation or antiplatelet therapy, recent surgery or trauma, seizures, pregnancy, etc.

Neurological examination: A thorough neurological assessment is indicated to quantify the degree of neurological deficits, identify the affected vascular territory, select appropriate interventions, and aid in prognostication. Use of formal and standardized stroke scales such as the NIHSS (National Institute of Health Stroke Scale), evaluating the level of consciousness, response to commands, motor palsy, sensory deficits, aphasia, limb ataxia, etc., help in this quantification [3]. Stroke mimics can also be excluded through a careful neurological examination.

Diagnostic tests: The immediate diagnostic test that should be done in all patients suspected of an acute stroke is a NCCT head to rule out parenchymal hemorrhage, thereby excluding patients not fit to receive iv thrombolysis. A quick blood glucose test helps to rule out hypoglycemia, one of the commonest stroke mimics, and in fact, is the only laboratory test necessary prior to initiating intravenous thrombolysis for an ischemic stroke. The door to imaging (DTC, or door to CT) time is aimed at ≤25 min, and its interpretation in ≤45 min, in order to start fibrinolytic therapy as early as feasible. All other laboratory investigations proceed simultaneously, and blood samples are sent for a complete blood count, renal function tests with serum electrolytes, coagulation profile, liver function tests and cardiac enzymes, along with obtaining a baseline ECG. However, fibrinolytic therapy is not delayed awaiting results of these tests. In women of child-bearing age, a pregnancy test is advisable, although pregnancy is no longer considered a contraindication to intravenous thrombolysis [4].

The incidence of unsuspected coagulopathy or thrombocytopenia is very low in the general population. The results of PT (prothrombin time), aPTT (activated partial thromboplastin time), or platelet count should therefore, not delay intravenous thrombolysis in a patient with symptoms of stroke, unless the patient has a bleeding disorder, has been on warfarin or heparin, or the anticoagulation use is uncertain.

Question 5:
What-all Brain Imaging Is Indicated in the Evaluation of Stroke to Guide Therapeutic Interventions?

Answer:
Decision regarding acute management of stroke with fibrinolytic drugs can be made by an **NCCT** (non-contrast CT) head, which is the most cost effective imaging modality that helps not only to exclude intracranial hemorrhage (ICH), but also to distinguish the nonvascular causes of neurological dysfunction, such as brain tumor, from stroke. Though NCCT is relatively insensitive in detecting acute cortical or subcortical infarctions, it may identify early, subtle ischemic changes, like loss of gray-white matter differentiation, seen as lenticular obscuration (loss of distinction in the nuclei of basal ganglia) and insular ribbon sign (blending of insular cortex gray and white matter densities). Large vessel occlusion may be seen as the hyperdense MCA (middle cerebral

artery) sign on NCCT, and is a strong predictor of poor neurological outcome.

The extent and severity of acute CT hypoattenuation or the presence of the hyperdense MCA sign are no longer used as a criteria to withhold intravenous thrombolysis in patients who otherwise qualify [5, 6].

MRI brain may not be widely favored in the acute setting, not only because it is time consuming and requires the patient to lie motionless for a long duration, but also it is costly, has a limited availability and cannot be performed in the presence of cardiac pacemakers or metal implants. The DWI (diffusion weighted image) sequence of MRI however, is highly sensitive and specific in identifying hyperacute infarcts, especially in the brainstem and posterior fossa. Gradient echo sequences of MRI may help in detecting acute hemorrhage and prior microbleeds, which otherwise may not be apparent in the normal MRI sequences.

Vascular imaging is an important aspect in the evaluation of stroke patients—firstly, to detect large vessel occlusion and collateral flow status for planning endovascular therapy, and secondly, to establish the mechanism of stroke (vessel occlusion or stenosis) for subsequent preventive care. The most rapid, noninvasive imaging modality to assess both extra- and intracranial vasculature is CTA (CT Angiography). CTA-SI (CT angiography-source imaging) is extremely sensitive in detecting ischemic regions. Intracranial MRA (MR Angiography) may be performed in combination with MRI brain in acute stroke for therapeutic decision-making. The TOF (time of flight) MRA sequence typically helps in identifying proximal large vessel occlusions, including extracranial carotid stenosis. Digital subtraction angiography (DSA) however, remains the gold standard for the detection of arterial stenosis, both extracranial as well as intracranial.

Brain perfusion imaging provides information about regional cerebral hemodynamics (cerebral blood flow, cerebral blood volume, and mean transit time), and combined with the parenchymal imaging, helps in delineating the ischemic penumbra. CTP (CT Perfusion) or perfusion-weighted MRI are now a part of multimodal imaging protocols, that help in identifying the core ischemia and the potentially salvageable penumbra to guide therapy in acute stroke, more specifically the endovascular therapy.

It must always be remembered that multimodal imaging, including CTA/CTP or MRI/diffusion-perfusion mismatch should not delay administration of iv thrombolysis. In a typical scenario, a patient with symptoms suggestive of acute stroke is shifted for NCCT head, and iv thrombolysis started immediately after excluding ICH on the CT, in the radiology suite itself. Further imaging proceeds simultaneously and the patient is evaluated for the feasibility of endovascular treatment on the basis of vascular and perfusion studies.

Question 6:
Describe the Guidelines for the Management of Blood Pressure in Patients with Ischemic Stroke

Answer:
Acute hypertensive response in stroke is not treated too aggressively, as it helps by improving cerebral perfusion to the vulnerable ischemic region in the brain, in face of an impaired cerebral autoregulation. But at the same time, too high a blood pressure raises concerns about hemorrhagic transformation in the infarct and cerebral edema. Guidelines therefore recommend reducing systolic blood pressure (SBP) to <185 mm Hg and diastolic blood pressure (DBP) to <110 mm Hg before initiating reperfusion therapies, and maintaining it <180/105 mm Hg for 24 h post thrombolysis. Labetalol and nicardipine are reasonable choices of antihypertensive medications for treatment. Hydralazine and enalaprilat may also be considered. Intravenous sodium nitroprusside is used in refractory cases where DBP exceeds 140 mm Hg despite standard therapy.

Patients with marked hypertension who are not otherwise candidates for fibrinolysis, should receive antihypertensive medication if the SBP >220 mm Hg or the DBP is >120 mm Hg. A rational goal is to lower the BP by ~15% in the first 24 h after stroke onset in a well-controlled manner.

Presence of arterial hypotension in stroke patients is not common, and may suggest a cardiac cause, such as arrhythmia, acute coronary event, aortic dissection, or shock. The underlying cause should be immediately addressed, hypovolemia corrected with intravenous fluids, and vasopressors initiated in refractory cases to maintain systemic perfusion and support organ function.

Question 7:
What Are the Indications, Dosing, and Contraindications of Intravenous Fibrinolytic Therapy?

Answer:
Intravenous fibrinolytic therapy is the mainstay of treatment in acute ischemic stroke, and should be initiated as early as feasible in all eligible patients. Thrombolytic drugs, also called clot buster drugs, lyse the intraluminal thrombi in the cerebral circulation by activating the fibrinolytic system, thereby recanalizing the occluded artery and reperfusing the ischemic penumbra, resulting in recovery of stroke symptoms. The efficacy of thrombolytic drugs is dependent on the age of the clot—older clots are more compacted and thereby difficult to dissolve.

The thrombolytic drug licensed for use in stroke is intravenous alteplase (or recombinant tissue plasminogen activator, r-tPA). It has a short half-life of around 5 min, and hence is administered as an iv bolus, followed by an infusion. The newer third generation fibrinolytic—tenecteplase has a longer half-life and can be administered as an iv bolus.

All patients presenting with the onset of symptoms of stroke within the last **3 h, irrespective of age and severity of symptoms**, should be offered treatment with iv tPA, after excluding major contraindications (Table 26.1). An informed patient consent is necessary prior to fibrinolytic therapy. For an incompetent patient, proxy consent from a legally authorized representative is obtained. In an emergency, where the patient is not competent, nor is there any authorized representative available, it is both ethically as well as legally permissible to proceed with thrombolysis.

Table 26.1 Contraindications to intravenous thrombolysis

1.	Unclear time of symptom onset
2.	Acute intracranial hemorrhage (ICH) or a history of ICH
3.	Frank hypodensity on NCCT head
4.	Symptoms suggestive of subarachnoid hemorrhage
5.	Prior ischemic stroke in the past 3 months
6.	Recent severe head trauma (within 3 months)
7.	Intracranial or intraspinal surgery in the past 3 months
8.	Gastrointestinal (GI) malignancy or recent GI bleed in the past 3 weeks
9.	Thrombocytopenia (platelet count <100,000/mm^3) or coagulopathy (PT >15 s, INR >1.7, aPTT >40 s)
10.	Patients on therapeutic doses of low molecular weight heparin (LMWH) or direct thrombin/factor Xa inhibitors, and patients on warfarin with INR > 1.7
11.	Infective endocarditis
12.	Aortic arch dissection
13.	Presence of an intracranial lesion –
	• Intra-axial neoplasm
	• Arteriovenous malformation
	• Giant, unruptured aneurysm
	• Intracranial arterial dissection
14.	Arterial puncture at a noncompressible site within the last 7 days

Alteplase is administered in a dose of 0.9 mg/kg, with a maximum dose of 90 mg, over 60 min. The initial 10% of the dose is given as an iv bolus over 1 min. The newer drug **tenecteplase**, is administered as a **single iv bolus of 0.4 mg/kg**, and has been found to be associated with a higher incidence of reperfusion in patients with a large vessel occlusion [8].

Intravenous alteplase is also recommended for selected patients who present within **3–4.5 h of symptom onset** [9]. Although age > 80 years, oral anticoagulant intake irrespective of INR, a combined history of diabetes and stroke, and very severe strokes (NIHSS>25), were excluded from the patient selection group earlier due to an increased risk of ICH, these are no longer considered contraindications to iv thrombolytic use in the 3–4.5 h time window [7]. Alteplase appears safe in patients taking warfarin and with an INR <1.7, presenting in the 3–4.5 h window [10, 11]. The benefit of iv alteplase in patients

with very severe stroke (NIHSS >25) however, remains uncertain.

After administration of iv tPA, all patients are admitted to an intensive care or stroke unit for neuromonitoring, for atleast 24 h. Careful control of BP to <180/105 mmHg is ensured by frequent measurements and use of antihypertensive medications as necessary. Placement of all invasive lines, including nasogastric tube, urinary catheter, arterial line, etc. are deferred for the first 24 h. Serial neurological assessments (GCS, pupillary size and reaction, and limb power) and vitals (pulse, BP, temperature, and respiratory rate) are performed every 15 min after initiation of r-tPA for 2 h, then half hourly for 6 h, and then every hour until 24 h. Any signs of acute neurological deterioration, or development of a new headache, nausea, vomiting and acute rise in BP, prompt discontinuation of tPA infusion (if ongoing), and an urgent NCCT head to exclude intracranial bleed. During administration of tPA, care should be exercised for any anaphylactic reactions—orolingual angioedema may be seen in <1% patients receiving iv tPA, especially those on angiotensin converting enzyme (ACE) inhibitors prestroke. It is a standard practice to get a follow-up NCCT head 24 h post thrombolysis, and start oral antiplatelets only after excluding a parenchymal bleed.

Question 8:
Discuss the Relative Exclusion Criteria for the Administration of Intravenous Thrombolysis

Answer:
Apart from the listed contraindications (Table 26.1), iv alteplase should be given after weighing the treatment risks against the potential therapeutic benefits in most conditions listed below:

- Prior antiplatelet drug monotherapy or combination therapy
- End-stage renal disease on dialysis with a normal aPTT
- Mild stroke with disabling symptoms (such as aphasia, monoparesis)
- Age > 80 years
- Patients on oral anticoagulants with INR <1.7
- Pre-existing disability (mRS score ≥ 2) & pre-existing dementia
- Seizure at onset
- Lumbar puncture in the last 7 days
- Recent major trauma not involving the head in the last 14 days
- Recent major surgery in the preceding 14 days
- Menstruating women/patients with recent or active history of menorrhagia without clinically significant anemia or hypotension
- Extracranial cervical dissection
- Small or moderate sized (<10 mm) unruptured and unsecured intracranial aneurysm
- Small number of chronic microbleeds [1–10] demonstrable on MRI
- Extra-axial intracranial neoplasm
- Recent myocardial infarction (MI) in the last 3 months
- Patients with acute pericariditis/left atrial or ventricular thrombus/cardiac myxoma/papillary fibroelastoma—treatment may be reasonable only if the stroke is a major stroke producing severe disability
- Procedural strokes—during cardiac or cerebral angiographic procedures
- Systemic malignancy if life expectancy reasonable.
- Pregnancy
- History of diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions—risk of visual loss to be weighed against benefits
- Sickle cell disease
- Illicit drug use
- Stroke mimics

In stroke patients with concurrent acute MI, iv alteplase is administered at the dose appropriate for cerebral ischemia (0.9 mg/kg). This is followed by percutaneous coronary angioplasty and stenting if required.

Question 9:
What Are the Complications of Intravenous Thrombolytics and |How Do You Manage These Complications, if They Arise?

Answer:
Complications related to intravenous r-tPA therapy include [12]:

1. Symptomatic ICH
2. Major systemic hemorrhage
3. Angioedema

Acute symptomatic intracranial hemorrhage (sICH) is the most feared complication of intravenous thrombolysis—the risk varies from 2 to 7%, but the mortality may be as high as 50%. It is defined as a CT- or MRI-documented hemorrhage post-thrombolytic treatment, associated with neurological deterioration in the patient. Age, male sex, obesity, uncontrolled hypertension, diabetes, combination antiplatelet therapy, increased stroke severity, large areas of early ischemic changes, atrial fibrillation, and congestive heart failure—all predispose to the development of sICH [13, 14]. Since most hemorrhages occur in already infarcted tissue, neurological deterioration may not occur at the onset of hemorrhage, and new symptoms are typically detected only after an increase in intracranial pressure or mass effect develops. Therefore, a low threshold for repeat imaging may be considered in patients with high NIHSS scores [15].

The general principles of treating patients with post-thrombolytic hemorrhage include:

– Cardiovascular and respiratory support when needed
– Blood pressure management
– Monitoring for neurological deterioration
– Prevention of hematoma expansion
– Treatment of elevated intracranial pressure and other complications like seizures

Hematoma expansion is a major predictor of death and disability in this group of patients. Therefore, aggressive reversal of coagulopathy is indicated with cryoprecipitate (10 Units over 10–30 min, or more if the fibrinogen levels are low). Fresh frozen plasma (FFP), platelet transfusions, prothrombin complex concentrates (PCC), Vitamin K, recombinant factor VIIa, and antifibrinolytics such as tranexamic acid (1 g iv over 10 min) or ε-aminocaproic acid (4–5 g over 1 h, followed by 1 g IV until bleeding is controlled) may be given. Strict blood pressure control may be reasonable to prevent hematoma expansion. Neurosurgical decompression may be considered in selected patients with sICH for whom surgery may improve outcome despite the ischemic injury.

Major systemic hemorrhage is a rare complication after thrombolysis if appropriate exclusion criteria for the administration of iv tPA are followed. Serious systemic hemorrhage occurred in ~1.6% patients in earlier trials [16]. Appropriate resuscitation with blood transfusions and/or surgical correction may be needed in cases of serious systemic hemorrhage.

Orolingual angioedema after iv alteplase is reported in ~1.3–5.1%, and may be unilateral or bilateral. It is usually mild, but may be serious compromising the airway in a few. The risk of angioedema is increased with the concomitant use of angiotensin converting enzyme inhibitors (ACE-I), and in frontal and insular strokes. Standard treatment includes airway control (if the oropharynx, larynx, and floor of the mouth are involved), corticosteroids, antihistamines, and subcutaneous epinephrine. Icatibant, a selective bradykinin β_2 receptor antagonist (30 mg subcutaneous), and plasma-derived C1 esterase inhibitor (20 IU/kg) has been successfully used in hereditary angioedema and ACE-I related angioedema [17–19].

Question 10:
Discuss the Options for Endovascular Treatment of Acute Ischemic Stroke. Also Describe the Preferred Anesthesia Technique for Endovascular Procedures

Answer:
Endovascular reperfusion therapy includes *intra-arterial fibrinolysis* and *mechanical thrombectomy*, and are considered in patients with large, proximal arterial occlusions and in those who are ineligible for intravenous tPA. Patients eligible for iv tPA should receive iv alteplase even if endovascular therapy is being considered. What should also be remembered is that the disability

outcome at 90 days after ischemic stroke is directly associated with the time from symptom onset to the arterial puncture—therefore, any cause for delay to mechanical thrombectomy, including observing for a clinical response to iv tPA, should be avoided [20].

Three classes of mechanical thrombectomy devices are available—clot retrievers (Merci™), aspiration devices (Penumbra™), and stent retrievers (Solitaire™, Trevo™). Five randomized controlled trials of endovascular treatment of acute ischemic stroke with primarily stent retrievers were carried out from 2010 to 2015 (MR CLEAN [21], ESCAPE [22], SWIFT PRIME [23], EXTEND IA [24], and REVASCAT [25]), which exclusively demonstrated improved results for both recanalization rates and outcome in acute ischemic stroke. This led to a new set of recommendations in 2015 [26] advocating the use of endovascular therapy with stent retrievers within 6 h of symptom onset. The eligibility criteria for mechanical thrombectomy includes:

1. Prestroke mRS (modified Rankin Score) 0–1
2. Large vessel occlusion—ICA (internal carotid artery) or proximal MCA (M1 segment of MCA) occlusion
3. Age ≥ 18 years
4. NIHSS score ≥ 6
5. ASPECTS (Alberta Stroke Program Early CT score [27]) of ≥6
6. Groin puncture initiated within 6 h of symptom onset

Mechanical thrombectomy for occlusion of M2/M3 segments of MCA, anterior cerebral artery (ACA), vertebral artery, basilar artery, or posterior cerebral artery (PCA) may be reasonable within 6 h of symptom onset, although the benefits are uncertain [28]. It may also be used in patients with prestroke mRS score > 1, ASPECTS <6, or NIHSS score < 6, but with uncertain benefit.

The DAWN and DEFUSE-3 trials [29, 30] extended the time window for mechanical thrombectomy in large anterior circulation vessel occlusion to 6–24 h in patients who had a mismatch between the severity of the clinical deficit and the infarct volume. This is a major breakthrough for wake up and late presenting strokes, in whom reperfusion therapy was not an option earlier.

The technical goal of mechanical thrombectomy should not only be recanalization, but to achieve reperfusion in the infarcted tissue. The assessment tool of choice for post-endovascular reperfusion is the mTICI (modified Thrombolysis in Cerebral Infarction) score [31, 32], and a grade of 2b/3 angiographic result is reflective of a good functional outcome. A reperfusion to TICI 2b/3 should be achieved as early as possible within the therapeutic window.

Choice of Anesthesia: Either conscious sedation or general anesthesia (GA) may be used as the anesthetic technique during endovascular thrombectomy, as neither has been proven to be superior to the other [33–35]. Conscious sedation allows for neurologic assessment throughout the procedure, and prevents delays associated with anesthesia induction. GA, on the other hand, may reduce the risk of aspiration and eliminate patient movement, thereby making the procedure safer and more technically feasible. Either of the two techniques may be used so long as there is strict control of BP (avoiding large falls in MAP) and systems in place to ensure minimal delays. It is reasonable to select the anesthesia technique based on the patient's risk factors, and technical performance of the procedure. Maintaining a systolic BP between 140–180 mm Hg during the procedure is useful in promoting and keeping collateral flow adequate. A drop in MAP <70 mm Hg or > 40% from the baseline should be avoided during revascularization [36]. Post intervention, following a successful reperfusion, a systolic BP < 140 mm Hg is recommended in the first 24 hours to prevent reperfusion injury [29].

Question 11:
When Should Oral Antiplatelet Therapy Be Started in Patients Presenting with Acute Ischemic Stroke

Answer:
Antiplatelet therapy with aspirin should be started within 24–48 hours of symptom onset in

stroke, either orally or via nasogastric tube (if the patient is unable to swallow). It has been shown to reduce the risk of early recurrent ischemic stroke without a major risk of early hemorrhagic complications [37]. For patients who have received iv thrombolysis, aspirin is delayed until 24 hours and is administered after ruling out ICH on a follow-up NCCT on the first day. The benefits of aspirin in acute stroke are drawn from trials that tested a dose of aspirin between 160 mg and 330 mg daily [38, 39]. Aspirin, however, should not be considered a substitute for iv alteplase or mechanical thrombectomy in acute stroke, if the patient is otherwise eligible. In patients presenting with minor stroke (NIHSS score ≤ 3) or transient ischemic attacks, dual antiplatelet therapy with aspirin and clopidogrel should be started within 24 h and continued for atleast 21 days, to prevent early secondary stroke [40].

Urgent anticoagulation with low molecular weight heparin (LMWH) to prevent early recurrent stroke or neurological deterioration, is not recommended [41, 42]. Its use is also uncertain in patients with a nonocclusive, extracranial intraluminal thrombus causing stroke.

Question 12:
What Are the General Supportive Care Measures That Should Be Given to All Stroke Patients After Admission to the Hospital?

Answer:
Post-acute reperfusion therapy with either thrombolytics or endovascular treatment, all patients with stroke should preferably be admitted to a specialized stroke care unit with adequate rehabilitation services. The general supportive care in ischemic stroke patients includes:

- *Airway support*—Ventilatory assistance may be needed in cases of depressed mentation or bulbar palsy causing airway compromise. Supplemental oxygen may be given if the oxygen saturation is below 94%, which is of no benefit otherwise.
- *Adequate blood pressure control* (discussed previously)—For patients who are neurologically stable and have a BP of >140/90 mm Hg, antihypertensive therapy should be started during hospitalization, to improve long-term control.
- *Temperature control*—Hyperthermia (temperature > 38 °C) should be treated aggressively to prevent morbidity. Therapeutic hypothermia for neuroprotection has no role.
- *Glucose control*—Both hyperglycemia (blood sugar >200 mg/dl) and hypoglycemia (< 60 mg/dl) should be treated, maintaining target blood sugar levels of 140–180 mg/dl.
- *Dysphagia screening*—Swallowing assessment is an important component of post-stroke care, as dysphagia is seen in ~ 37–78% of all stroke patients, and may predispose to aspiration pneumonia with poor outcomes. Screening stroke patients before allowing them orally, is therefore reasonable to identify patients at higher risk for adverse outcomes [43, 44].
- *Nutrition*—Enteral diet should be started as early as possible, and latest within 7 days of an acute stroke admission. Feeding via nasogastric tube in the early phase seems to be a reasonable option in stroke patients suspected to have dysphagia. Oral hygiene protocols should be strictly adhered to for preventing aspiration pneumonia.
- *Deep vein thrombosis (DVT) prophylaxis*—Intermittent pneumatic compression devices should be used in addition to standard care (aspirin and hydration) to improve outcome and reduce the risk of thromboembolism in immobile patients with stroke [45]. The benefit of prophylactic dose of heparin (unfractionated or low molecular weight) is not well established. Elastic compression stockings are not favored due to an increased rate of skin complications.
- *Inpatient rehabilitation*—
  - Regular skin assessment to check for pressure ulcers—eliminate skin friction, avoid excessive moisture, maintain adequate hydration and nutrition, use appropriate support surfaces
  - Early mobilization maneuvers such as regular turning, out of bed sitting, assisted walking, etc.

– Routine placement of indwelling catheters is not indicated for the risk of urinary tract infections

Question 13:
What Causes Early Neurological Deterioration (END) in Patients with Acute Ischemic Stroke?

Answer:
Early neurological deterioration refers to the clinical worsening of a patient in the first 72 h after an acute ischemic stroke. 13–37% of all stroke patients deteriorate within the acute phase [46]. Initial stroke severity, non cardioembolic strokes, hyperglycemia, hypo- or hypertension, presence of a large vessel occlusion, extensive lesions involving >one-third of MCA on NCCT, atrial fibrillation, and high serum urea—all are considered predictors of END. The causes may include:

1. *Progressive or recurrent stroke*—failure of collateral development in a large vessel occlusion, progression of thrombosis with consequential increase in ischemic area, or early re-occlusion of a recanalized artery may lead to clinical deterioration in a stroke patient. Recurrent embolism from a cardiac source may cause recurrent stroke, resulting in END. Prompt initiation of antithrombotic therapy may help in reducing the risk of recurrent stroke.
2. *Hemorrhagic transformation in ischemic stroke*—incidence may be higher in patients treated with intravenous fibrinolytics.
3. *Cerebral edema*—raised intracranial pressure (ICP), more commonly seen with large hemispheric or cerebellar infarcts, may cause signs of brain herniation, warranting surgical decompression as a life saving measure.

   New or further impairment of consciousness, cerebral ptosis, and changes in pupillary size signify deterioration in supratentorial strokes. Swollen cerebellar infarcts manifest as early loss of corneal reflexes and the development of miosis, along with depressed level of consciousness due to brain stem compression. Close neuromonitoring and complex medical care to control the ICP is warranted. Airway control and mechanical ventilation with brief moderate hypocarbia (pCO_2 target 30–34 mm Hg), hemodynamic support, adequate fluids, maintaining adequate glucose levels and preventing hyperthermia, is indicated in patients with cerebral edema. Osmotic therapy may be used for patients with clinical deterioration from cerebral swelling. However, steroids are not indicated for cerebral edema complicating stroke [47].
4. *Seizures*—commonly seen in large cortical infarcts, result in neurological worsening in ~5% of ischemic stroke patients. Nonconvulsive seizures may present a diagnostic challenge, and can be confirmed with electroencephalography (EEG). Patients with documented seizures are treated with antiepileptic drugs. Prophylactic use of antiseizure drugs in ischemic stroke is however, not recommended.

Question 14:
Discuss the Role of Neurosurgical Decompression in Acute Ischemic Stroke

Answer:
The benefits of surgical intervention have been repeatedly proven in patients who deteriorate neurologically after ***cerebellar infarction***. In patients who develop symptoms of obstructive hydrocephalus from a cerebellar stroke, emergency ventriculostomy (external ventricular drainage, or EVD) is a reasonable first step in the surgical management. In cases of significant edema or mass effect, conservative CSF (cerebrospinal fluid) drainage or subsequent decompression may be needed to prevent upward brain herniation. Decompressive suboccipital craniectomy with dural expansion is indicated in cerebellar infarcts causing brainstem compression despite maximal medical therapy or ventriculostomy [48, 49].

In large territorial supratentorial infarctions, timely surgical decompression to relieve severe intracranial hypertension has been shown to reduce mortality [50]. In patients ≤60 years with malignant hemispheric strokes, decompressive craniectomy with dural expansion reduces mor-

tality by ~50%, with most patients achieving either moderate disability (55%) or independence by 12 months (18%). In patients >60 years however, the functional outcomes seem to be worse, with 11% of surgical survivors achieving moderate disability, and none achieving independence at 12 months follow-up. But taking into account the significant mortalilty benefit, decompressive craniectomy should be offered in this patient population as well [51–53].

To summarize, careful patient selection for surgical decompression, in conjunction with a comprehensive neurocritical care and rehabilitation, and due consideration to the family/caretaker preferences for long-term care, is important.

Multiple Choice Questions

1. A patient comes to the triage with a history of weakness in the right upper and lower limbs, and a difficulty in speaking since the past 8 h. Which imaging modality would you choose first to guide treatment?
   (a) MRI brain
   (b) CT angiography head and neck vessels
   (c) NCCT head
   (d) MR perfusion studies

   Answer: c

   Although the patient presents after 8 h of symptom onset, and an MRI brain or vascular imaging would give us more information on the patient's eligibility for endovascular therapy, NCCT head would still be the first imaging to be done in order to rule out stroke mimics, most importantly ICH.
2. A 35-year-old female arrives to the ED with complaints of left-sided weakness, inability to speak adequately, and gaze paresis since 4 h. She is a follow-up case of double valve replacement (mitral/aortic) on warfarin. Her INR on the point of care machine is found to be 1.6. What treatment option would you offer to this patient?
   (a) No therapeutic intervention, only general supportive care
   (b) Intravenous thrombolysis
   (c) Mechanical thrombectomy using a stent retriever if large vessel occlusion on advanced imaging
   (d) Intravenous thrombolysis followed by mechanical thrombectomy if eligible

   Answer: d

   The patient has presented within 4 h (<4.5 h time window) and the INR is <1.7 on warfarin—it would be reasonable to proceed with intravenous thrombolysis, and at the same time, proceed onto advanced imaging to look for eligibility for mechanical thrombectomy.
3. A 65-year-old hypertensive, diabetic patient woke up with symptoms of right hemiparesis and aphasia. He was last known well the previous night by his caretaker. His NCCT head shows no ICH. The NIHSS score is 10. Advanced imaging shows a left M1 MCA occlusion on CTA, with an infarct volume of ~25 ml on CTP. Which therapeutic option do you think is the best?
   (a) No intervention as the symptom onset time is unknown
   (b) Intravenous thrombolysis
   (c) Mechanical thrombectomy
   (d) Intravenous thrombolysis followed by mechanical thrombectomy

   Answer: c

   Since the symptom onset time is unknown in this patient with a wake-up stroke, intravenous thrombolysis is not an option. According to the recent DAWN trial, such patients may be offered mechanical thrombectomy with stent retrievers, if the CTA-CTP studies show a mismatch between clinical deficit (NIHSS >10) and infarct (large vessel occlusion with an infarct volume < 30 ml)
4. Which of the following measures are recommended for DVT prophylaxis in patients with acute stroke?
   (a) Graduated compression stockings
   (b) Intermittent pneumatic compression devices
   (c) Low molecular weight heparins
   (d) Aspirin

   Answer: b

   Intermittent pneumatic compression (IPC) devices are recommended for DVT prophylaxis in acute stroke. The benefit of low dose heparin is not well established.

5. A patient diagnosed with an acute ischemic stroke of the right ICA is under observation in the stroke unit. On the second day of symptom onset, he deteriorates neurologically. Which of the following is the least possible cause of neurological worsening in this patient?
   (a) Recurrent stroke
   (b) Cerebral edema
   (c) Seizures
   (d) Meningoencephalitis

   Answer: d

   Early neurological worsening in acute ischemic stroke may be caused by progression of stroke, stroke recurrence, hemorrhagic transformation, cerebral edema, and seizures. Meningoencephalitis is not a cause for END in stroke.

References

1. Jauch EC, Saver JL, Adams HP Jr, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early Management of Patients with Acute Ischemic Stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44(3):870–947.
2. Saver JL. Time is brain—quantified. Stroke. 2006;37(1):263–6.
3. National Institute of Health, National Institute of Neurological Disorders and Stroke. Stroke Scale. https://www.ninds.nih.gov/sites/default/files/NIH_Stroke_Scale_Booklet.pdf
4. Demchuk AM. Yes, intravenous thrombolysis should be administered in pregnancy when other clinical and imaging factors are favorable. Stroke. 2013;44:864–5.
5. Charidimou A, Pasi M, Fiorelli M, Shams S, von Kummer R, Pantoni L, Rost N. Leukoaraiosis, cerebral hemorrhage, and outcome after intravenous thrombolysis for acute ischemic stroke: a meta-analysis (v1). Stroke. 2016;47:2364–72.
6. Qureshi AI, Ezzeddine MA, Nasar A, Suri MF, Kirmani JF, Janjua N, Divani AA. Is IV tissue plasminogen activator beneficial in patients with hyperdense artery sign? Neurology. 2006;66:1171–4.
7. Demaerschalk BM, Kleindorfer DO, Adeoye OM, Demchuk AM, Fugate JE, Grotta JC, Khalessi AA, et al. On behalf of the American Heart Association stroke council and council on epidemiology and prevention. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2016;47:581–641.
8. Campbell BCV, Mitchell PJ, Churilov L, et al. Tenectaplase versus alteplase before thrombectomy for ischemic stroke. N Engl J Med. 2018;378:1573–82.
9. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, ECASS Investigators, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359:1317–29.
10. Cronin CA, Shah N, Morovati T, Hermann LD, Sheth KN. No increased risk of symptomatic intracerebral hemorrhage after thrombolysis in patients with European cooperative acute stroke Study (ECASS) exclusion criteria. Stroke. 2012;43:1684–6.
11. Cronin CA, Sheth KN, Zhao X, Messe SR, Olson DM, Hernandez AF, Bhatt DL, Schwamm LH, Smith EE. Adherence to third European cooperative acute stroke Study 3- to 4.5-hour exclusions and association with outcome: data from get with the guidelines-stroke. Stroke. 2014;45:2745–9.
12. Miller DJ, Simpson JR, Silver B. Safety of thrombolysis in acute ischemic stroke: a review of complications, risk factors, and newer technologies. Neurohospitalist. 2011;1(3):138–47.
13. Wahlgren N, Ahmed N, Eriksson N, et al. Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials: safe implementation of thrombolysis in stroke-MOnitoring STudy (SITS-MOST). Stroke. 2008;39(12):3316–22.
14. Cucchiara B, Kasner SE, Tanne D, et al. Factors associated with intracerebral hemorrhage after thrombolytic therapy for ischemic stroke: pooled analysis of placebo data from the stroke-acute ischemic NXY treatment (SAINT) I and SAINT II trials. Stroke. 2009;40(9):3067–72.
15. Yaghi S, Willey JZ, Cucchiara B, Goldstein JN, Gonzales NR, Khatri P, et al. Treatment and outcome of hemorrhagic transformation after intravenous alteplase in acute ischemic stroke. : A scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2017;48(12):e343–61.
16. Intracerebral hemorrhage after intravenous t-PA therapy for ischemic stroke. The NINDS t-PA stroke Study group. Stroke. 1997;28(11):2109–18.
17. O'Carroll CB, Aguilar MI. Management of post-thrombolysis hemorrhagic and orolingual angioedema complications. Neurohospitalist. 2015;5:133–41.
18. Myslimi F, Caparros F, Dequatre-Ponchelle N, Moulin S, Gautier S, Girardie P, Cordonnier C, Bordet R, Leys D. Orolingual angioedema during or after thrombolysis for cerebral ischemia. Stroke. 2016;47:1825–30.
19. Pahs L, Droege C, Kneale H, Pancioli A. A novel approach to the treatment of orolingual angioedema after tissue plasminogen activator administration. Ann Emerg Med. 2016;68:345–8.
20. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, HERMES Collaborators, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. JAMA. 2016;316:1279–88.

21. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, MR CLEAN Investigators, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2015;372:11–20.
22. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, ESCAPE Trial Investigators, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372:1019–30.
23. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, SWIFT PRIME Investigators, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med. 2015;372:2285–95.
24. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, EXTEND-IA Investigators, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015;372:1009–18.
25. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, REVASCAT Trial Investigators, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med. 2015;372:2296–306.
26. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, et al. American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early Management of Patients with Acute Ischemic Stroke Regarding Endovascular Treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2015;46(10):3020–35.
27. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study group. Alberta stroke Programme early CT score. Lancet. 2000;355(9216):1670–4.
28. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, HERMES Collaborators, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387:1723–31.
29. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med. 2018;378(1):11–21.
30. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med. 2018;378(8):708–18.
31. Higashida RT, Furlan AJ, Roberts H, et al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke. 2003;34(8):e109–37.
32. Zaidat OO, Yoo AJ, Khatri P, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. Stroke. 2013;44(9):2650–63.
33. Löwhagen Hendén P, Rentzos A, Karlsson JE, Rosengren L, Leiram B, Sundeman H, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: the AnStroke trial (anesthesia during stroke). Stroke. 2017;48:1601–7.
34. Schönenberger S, Uhlmann L, Hacke W, Schieber S, Mundiyanapurath S, Purrucker JC, et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. JAMA. 2016;316:1986–96.
35. Simonsen C, Yoo A, Sorensen L, Juul N, Johnsen SP, Andersen G, et al. Effect of generalized anesthesia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke: a randomized clinical trial. JAMA Neurol. 2018;75:470–7.
36. Vitt JR, Trillanes M, Hemphill JC 3rd. Management of Blood Pressure during and after Recanalization Therapy for acute ischemic stroke. Front Neurol. 2019;10:138.
37. Sandercock PA, Counsell C, Tseng MC, Cecconi E. Oral antiplatelet therapy for acute ischaemic stroke. Cochrane Database Syst Rev. 2014:CD000029.
38. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke: international stroke trial collaborative group. Lancet 1997;349:1569–1581.
39. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke: CAST (Chinese Acute Stroke Trial) Collaborative Group. Lancet. 1997;349:1641–1649.
40. Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, CHANCE Investigators, et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med. 2013;369:11–9.
41. Whiteley WN, Adams HP Jr, Bath PM, Berge E, Sandset PM, Dennis M, Murray GD, Wong KS, Sandercock PA. Targeted use of heparin, heparinoids, or low-molecular-weight heparin to improve outcome after acute ischaemic stroke: an individual patient data meta-analysis of randomised controlled trials. Lancet Neurol. 2013;12:539–45.
42. Sandercock PA, Counsell C, Kane EJ. Anticoagulants for acute ischaemic stroke. Cochrane Database Syst Rev. 2015:CD000024.
43. Miles A, Zeng IS, McLauchlan H, Huckabee ML. Cough reflex testing in dysphagia following stroke: a randomized controlled trial. J Clin Med Res. 2013;5:222–33.
44. Joundi RA, Martino R, Saposnik G, Giannakeas V, Fang J, Kapral MK. Predictors and outcomes of dysphagia screening after acute ischemic stroke. Stroke. 2017;48:900–6.
45. Dennis M, Caso V, Kappelle LJ, Pavlovic A, Sandercock P. European stroke organisation (ESO) guidelines for prophylaxis for venous thromboembolism in immobile patients with acute ischaemic stroke. Eur Stroke J. 2016;1:6–19.

46. Thanvi B, Treadwell S, Robinson T. Early neurological deterioration in acute ischaemic stroke: predictors, mechanisms and management. Postgrad Med J. 2008;84(994):412–7.
47. Wijdicks EFM, Sheth KN, Carter BS, Greer DM, Kasner SE, Kimberley WT, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American stroke association. Stroke. 2014;45:1222–38.
48. Agarwalla PK, Stapleton CJ, Ogilvy CS. Craniectomy in acute ischemic stroke. Neurosurgery. 2014;74(suppl 1):S151–62.
49. Mostofi K. Neurosurgical management of massive cerebellar infarct outcome in 53 patients. Surg Neurol Int. 2013;4:28.
50. Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, DECIMAL, DESTINY, and HAMLET Investigators, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. Lancet Neurol. 2007;6:215–22.
51. Maciel CB, Sheth KN. Malignant MCA stroke: an update on surgical decompression and future directions. Curr Atheroscler Rep. 2015;17:40.
52. Yang MH, Lin HY, Fu J, Roodrajeetsing G, Shi SL, Xiao SW. Decompressive hemicraniectomy in patients with malignant middle cerebral artery infarction: a systematic review and meta-analysis. Surgeon. 2015;13:230–40.
53. Alexander P, Heels-Ansdell D, Siemieniuk R, Bhatnagar N, Chang Y, Fei Y, Zhang Y, McLeod S, Prasad K, Guyatt G. Hemicraniectomy versus medical treatment with large MCA infarct: a review and meta-analysis. BMJ Open. 2016;6:e014390.

Part III

Neuroradiology

27 Management of Patient Undergoing Embolization: Aneurysm/AVMs

Deepali Garg and Mariel Manlapaz

Stem Case Terminology

A 42-year-old female is brought to the emergency department (ED) by paramedics. She was watching television at her house when she had sudden onset of headache and nausea followed by loss of consciousness. On her arrival in ED, she was drowsy but obeying commands, no other neurologic deficits. Pupils were equal and reactive. On chest auscultation, B/L basal rales were heard. Her vital signs were BP—212/108 mmHg, pulse—48/min, SpO_2—94% with O_2 6 L by facemask, temperature—36.8 °F. EKG showed T wave inversion with ST segment depression. A computed tomography (CT) scan showed subarachanoid hemorrhage (SAH) in the right sylvian fissure with a right frontotemporal intraparenchymal clot. An angiogram was performed and showed right middle cerebral artery (MCA) aneurysm. Blood investigations showed Na—130 mmol/L, K—3.2 mmol/L, glucose—238 mg/dL, Hb—13 g/dL, WBC—18×10^9/L, platelets—300,000/μL. Toxicology screen was positive for cocaine. Patient had a smoking history of 20 pack-years. There was no other significant medical history.

D. Garg · M. Manlapaz (✉)
Department of General Anesthesia, Cleveland Clinic, Cleveland, OH, USA
e-mail: manlapm@ccf.org

Question 1:
When evaluating a patient with SAH, what are the common classifications used? How do these grading correlate with patient's outcome?

Answer:
Hunt and Hess [1], World Federation of Neurological Surgeons [2], and modified Fischer grade [3] are used to standardize clinical assessment in patients with SAH. Knowledge and understanding of these grading scales are required for effective communication between physicians, assessment of the severity of the underlying pathophysiological abnormalities, and rational planning of the perioperative anesthetic management.

In general, the higher the clinical grade, the more likely are cerebral vasospasm, elevated intracranial pressure (ICP), impaired cerebral autoregulation, impaired vascular CO_2 reactivity, cardiac arrhythmias and dysfunction [4], hypovolemia, and hyponatremia [5]. Patients with Hess and Hunt grade I and II are likely to have normal ICP and preserved cerebrovascular reactivity. In contrast, patients with Hess and Hunt grade III and IV are likely to have increased ICP and impaired cerebrovascular reactivity; hyperventilation is thus unlikely to result in reliable cerebral vasoconstriction.

The Fisher scale was proposed to predict cerebral vasospasm after SAH. The scale assigns a grade based on the pattern of blood visualized on initial CT scanning.

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_27

World Federation of Neurological Surgeons scale			Hunt and Hess scale		Modified Fischer scale		
Grade	Glasgow coma scale	Neurologic examination	Grade	Neurologic examination	Scale	Subarachnoid hemorrhage	Intraventricular hemorrhage
1	15	No motor deficit	1	Asymptomatic or minimal headache and slight nuchal rigidity	0	Absent	Absent
2	13–14	No motor deficit	2	Moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy	1	Thin	Absent
3	13–14	Motor deficit	3	Drowsy, confusion, or mild focal deficit	2	Thin	Present
4	7–12	With or without motor deficit	4	Stupor, moderate to severe hemiparesis	3	Thick	Absent
5	3–6	With or without motor deficit	5	Comatose, motor posturing or no motor response	4	Thick	Present

Question 2:
What is the role of transmural pressure (TMP) and cerebral perfusion pressure (CPP) in this case?

Answer:
There are two major forces in effect that need to be considered when caring for a patient with a cerebral aneurysm at risk:

(a) TMP is the pressure across the aneurysmal dome and is a strong determinant of aneurysm rupture. TMP is defined as the difference between mean arterial pressure (MAP) and the ICP. To decrease the likelihood of rupture, drastic changes in TMP should be avoided.
(b) CPP is also defined as the difference between MAP and ICP. The higher the CPP, more is the perfusion present for the brain, guarding against ischemia.

TMP and CPP are mathematically defined by the same variables. Thus, as one seeks to perfuse the brain, the risk of rupture is increased. As one seeks to reduce the risk of rupture, the risk of underperfusing the brain is increased. Knowing the patient's baseline pressure and corresponding neurologic status can serve as a starting point. However, the choice of blood pressure target must be tailored to unique patient scenario and the risk of rupture versus hypoperfusion.

Question 3:
What are the cardiac manifestations of SAH? What cardiac abnormalities that occur in SAH interfere with patient outcome?

Answer:
Cardiac dysfunction is a well-known complication of SAH and can range from minor ECG changes to severe stress cardiomyopathy. EKG changes can be seen in 40–100% of patients with aneurysmal SAH, and they include T-wave inversions, ST segment depression, prolonged QTc interval, and dysrhythmias such as atrial fibrillation and flutter, ventricular tachycardia, and ventricular fibrillation [6]. Prolonged QTc was found to be an independent predictor of poor survival during follow-up after ICH [7].

The incidence of left ventricular dysfunction in the first week after SAH ranges from 9 to 30% and can range from regional wall motion abnormalities not correlating with coronary artery territo-

ries or severe systolic left ventricular dysfunction with an ejection fraction of less than 30% [8, 9]. Detectable cardiac troponin I (cTI) release occurs in 20–40% of patients, but these elevations are usually small, with the vast majority below the diagnostic threshold for myocardial infarction [10]. However, elevated cTI can have detrimental effect on in-hospital morbidity and long-term outcome. Naidech et al. investigated the effect of raised cTI in 253 patients with SAH and concluded that peak cTI level was associated with echocardiographic left ventricular dysfunction, pulmonary edema, hypotension requiring pressors, delayed cerebral ischemia from vasospasm and death or poor functional outcome at discharge [11].

Cardiac dysfunction seen in SAH patients is believed to be neurally mediated and is related to the catecholamine surge. Catecholamine surge during aneurysm rupture results in direct myocardial injury, leading to decreased inotropy and an increase in cardiac preload due to venous constriction, as well as increased cardiac afterload due to peripheral arterial constriction [12]. Consequently, stroke volume diminishes, which cannot be compensated by reflex tachycardia, resulting in decreased cardiac output and neurocardiogenic shock. In the most severe form of cardiac injury after SAH, myocardial enzyme release is associated with a syndrome of neurogenic stunned myocardium characterized by reversible left ventricular systolic dysfunction, cardiogenic shock, and pulmonary edema. Due to loss of myocardial compliance, the cardiac silhouette on a ventriculogram and chest radiograph has the characteristic shape of a Japanese octopus fishing pot (tako-tsubo), getting its name Takotsubo cardiomyopathy [13]. Neurogenic cardiomyopathy in SAH is associated with higher mortality and worse long-term outcomes.

Question 4:
What is the significance of smoking history in this patient? What could be the possible reasons for B/L basilar rales?

Answer:
Cigarette smoking is a well-known risk factor for the development and rupture of cerebral aneurysms. An estimated 29% of the attributable risk of aneurysmal SAH is due to smoking, and smoking cessation decreases the risk of SAH [14]. Dasenbrock et al. evaluated the association of smoking with outcomes after SAH and concluded that smoking was associated with increased odds of delayed cerebral ischemia, a younger age of rupture, and increased number of comorbidities, highlighting the negative impact of smoking in patients with cerebral aneurysms.

However, the exact mechanism by which smoking promotes cerebral aneurysm formation remains largely unknown though several mechanisms are postulated such as cigarette atherosclerosis, hemodynamic stress, and endothelial dysfunction leading to aneurysm wall weakening and rupture, release of inflammatory mediators, chronic inflammation causing vessel wall remodeling, and damage [15].

The patient had B/L basilar rales on chest auscultation which could indicate pulmonary edema. Neurogenic pulmonary edema (NPE) is an increase in interstitial and alveolar lung fluid occurring as a direct consequence of acute central nervous system injury and is observed in 8–28% of patients with SAH. Several mechanisms are postulated for NPE. Increased intracranial pressure occurring after SAH causes intense sympathetic activation leading to pulmonary as well as systemic vasoconstriction. According to the "blast theory," proposed by Theodore and Robin, severe transient rise of pulmonary capillary pressure increases pulmonary vascular permeability, leading to an interstitial and alveolar pulmonary edema. Also increased systemic pressure causes decreased left ventricular compliance and increased left atrial pressures, thereby causing increased pulmonary capillary pressure resulting in pulmonary edema. However, NPE might also occur independent from hemodynamic mechanisms. Some of the postulated mechanisms are modulation of the endothelial permeability in pulmonary microvessels by adrenergic receptors, pulmonary microembolization secondary to intravascular thrombosis and platelet aggregation, and pulmonary lymphatic obstruction due to sympathetic activation.

Question 5:
The patient is noted to have electrolyte disturbances. Is it related to patient's intracranial

pathology? If yes, what are the probable etiologies for this derangement?

Answer:
Hyponatremia is the most common, clinically significant electrolyte abnormality seen in patients with aneurysmal subarachnoid hemorrhage and has prevalence ranging from 30 to 56% [16]. According to the latest recommendations, hyponatremia should be further investigated and treated when the serum Na level is less than 131 mmol/L. [17] Hyponatremia following SAH is most commonly associated with syndrome of inappropriate antidiuretic hormone secretion (SIADH). Other associated causes include acute cortisol insufficiency, cerebral salt wasting syndrome (CSW), excessive fluid therapy, and/or diuretic therapy**.** SIADH is categorized as the most frequent cause of hyponatremia among patients with aneurysmal SAH [18]. In SIADH, excessive secretion of antidiuretic hormone is caused by the stimulation of the hypothalamus with various traumatic or ischemic factors, resulting in the enhancement of water reabsorption in the distal convoluted tubule of the kidney, causing fluid retention and dilutional hyponatremia. It is characterized by hyponatremia in the setting of an inappropriately concentrated urine, increased urine Na^+ concentration and evidence of normal or slightly increased intravascular volume. Whereas CSW syndrome is caused by increased circulating brain natriuretic peptide level causing urinary sodium excretion, as well as reductions of extracellular fluid and circulating blood volume, eventually resulting in hyponatremia [19].

It is important to note that in both CSW and SIADH, the laboratory findings are similar: low serum sodium (<134 mEq/mL), low serum osmolality (<274 mmol/L), high urine sodium (>20 mmol/L), and high urine osmolality (>100 mmol/L). The only differentiating finding is the patient's intravascular volume status; CSW is a hypovolemic state, while patients with SIADH are euvolemic or even hypervolemic. It is of utmost importance to correctly differentiate these two syndromes because the treatment is opposite and an incorrect diagnosis with improper treatment can lead to detrimental effects in patients with SAH [20].

CSW is treated with fluid administration and sometimes a continuous infusion of hypertonic saline (1.5–3%) and fludrocortisone if diuresis and natriuresis impede the maintenance of adequate volume status. However, patients with SIADH are treated with fluid restriction and sometimes diuresis with loop diuretics. Serum sodium as well as the volume status must be followed closely.

Question 6:
What is the significance of placing extraventricular drain (EVD) in these patients? How can EVD help in our anesthesia management?

Answer:
EVD is placed in the emergent management of hydrocephalus and ICP after SAH. It helps in the treatment as well as monitoring of raised ICP. The rate of acute hydrocephalus in aneurysmal SAH requiring EVD has been estimated at 20% [21]. However, placing an EVD in patients who are going to undergo endovascular therapy (EVT) of aneurysm can be challenging, and a difficult decision as EVD placement before EVT may increase risk of rebleeding while placing it after may delay normalizing increased ICP. [22] EVT for aneurysms has seen significant growth in the past few years after international subarachnoid aneurysm trial (ISAT) trial [23] as well as introduction of stents; however, this necessitates additional administration of antiplatelet agents. There are no standard protocols of anticoagulation with heparin and/or antiplatelet drugs in the guidelines [24]. The influence of anticoagulation and the management of EVD insertion (before or after endovascular treatment) on ventriculostomy-related hemorrhage is unclear. Scheller et al. investigated the rate of ventriculostomy-related hemorrhage after endovascular treatment vs. clipping and concluded that ventriculostomy-related hemorrhage is an underestimated complication after endovascular treatment and can lead to revision surgeries and bacterial infections and may have a negative impact on long-term outcome. The probability of occurrence is increased when anticoagulation is performed by heparin in combination with antiplatelet drugs as compared

to heparin alone. They also suggested the use of lumbar drainage as an alternative for the treatment of acute hydrocephalus in patients with Hunt and Hess grade 1–3 [25]. Contrary to these findings, Lim et al. studied the placement of EVD before and after EVT in patients with aneurysmal SAH and reported that placing EVD before EVT did not increase the rate of rebleeding or EVD-related hemorrhagic complications. Thus, concluding that performing EVD before EVT may be beneficial to normalize increased ICP and may improve clinical outcomes at discharge, especially in patients with rebleeding [26].

Question 7:
How does one decide between endovascular coiling and open clipping of aneurysm? What are the advantages and disadvantages of endovascular aneurysm coiling?

Answer:
With the publication of the ISAT, which compared endovascular coiling to surgical clipping after SAH, the treatment of an unsecured aneurysm has shifted from surgical clipping to mostly endovascular coiling [27]. ISAT showed that patients in the endovascular coiling group had significantly higher odds of survival free of disability 1 year after SAH and a lower risk of epilepsy when compared to the surgical clipping group. Even 10 years after SAH, patients who underwent endovascular coiling had better outcomes [28]. In contrast, the risk of rebleeding and incomplete occlusion of the aneurysm was lower with surgical clipping. Lanzino et al. did a meta-analysis of all published prospective studies and concluded that the odds of poor outcome are higher after surgical treatment than after endovascular treatment, despite a higher early risk of rebleeding from the target aneurysm after coil embolization [29]. Furthermore, subgroup analyses from these clinical trials indicated that the risks of seizures, delayed cerebral ischemia, ischemic lesions on MR imaging, and in-hospital complications are lower after coil embolization than after surgical clip ligation.

These observations provide convincing evidence that endovascular coil embolization should be strongly considered as the preferred treatment technique for a ruptured aneurysm amenable to either therapeutic technique. However, follow-up angiograms are necessary, as the recurrence rate of aneurysms is higher when they are treated with endovascular coiling [28].

However, some patients might be better candidates for surgical clip ligation. Very small aneurysms are often challenging to treat with an endovascular approach [30]. Similarly, many MCA aneurysms have an unfavorable geometry for primary coiling, and they are often better treated with surgical clipping [31]. Moreover, very young patients with ruptured anterior circulation aneurysms (especially those who may be noncompliant with follow-up imaging) may also be better candidates for surgical treatment rather than endovascular coil embolization due to increased rate of recurrence [32]. Despite the evidence from randomized clinical trials, the decision on what is the best treatment for a ruptured aneurysm in a given patient should be individualized by taking into consideration aneurysm-related and patient-specific factors. Finally, based on the available literature, the current consensus is that if there is equipoise between clipping and coiling, one should favor the endovascular options.

Question 8:
What additional concerns we have regarding radiation in a neuroendovascular suite?

Answer:
Personnel working in the neuroendovascular suite have the risk of exposure to ionizing radiation. Biologic effects resulting from radiation exposure are traditionally divided into stochastic effects and deterministic effects [33]. Deterministic effects create cell death at the tissue level resulting in defects, in particular lens opacities, skin injuries, and infertility. Deterministic effects occur predictably when the dose exceeds a certain threshold and severity of the effect varies with radiation dose. Whereas, stochastic injuries are due to genetic transformation which can

occur due to point mutations, chromosomal translocations, or gene fusions. The likelihood of stochastic effects increases with the total radiation energy absorbed, but their severity is independent of total dose. Stochastic effects are cumulative and have a long latency period [33]. Recent data indicate that radiation-induced cataracts are a stochastic effect rather than deterministic [34].

Various sources of radiation include direct radiation from the X-ray tube, leakage of radiation through the collimators and protective shielding, and scatter radiation that is reflected from the patient and the surrounding area [35]. For the anesthesiologist, the two most important factors in reducing radiation exposure are distance and shielding. Ionizing radiation follows the inverse square law, i.e., the amount of exposure decreases proportionally to the square of the distance from the source of the radiation [36]. International commission on radiological protection (ICRP) has lowered its recommended maximum yearly total body effective dose equivalent from 50 mSv/year to 20 mSv/year for personnel exposed to radiation [37]. Injections of drugs or alterations in pump settings draw the anesthesiologist toward the intravenous tubing and, thus, toward the patient's head; closer to the source of scatter radiation; and closer to the front edge of the protective shield. Also, switching the anesthesia ventilator off temporarily, to create apneic movement-free periods, would do the same; therefore, activity near the head of the patient should be kept to a minimum during fluoroscopy, and the use of extension tubing is required for infusion and monitoring lines. Appropriate radiation shielding is crucial. Standard lead aprons or transparent leaded acrylic shields, both with 0.5-mm lead-equivalent protection, reduce fluoroscopy levels of radiation by more than 98% each [38]. All personnel working in the room should wear protective lead aprons and thyroid shields throughout the procedure. Clear lead screens can be used to reduce exposure further. Anastasian et al. analyzed the radiation exposure to the face of the anesthesiologist during interventional neuroradiology procedures and found that exposure to the anesthesiologist's face was sixfold greater than that during angiography and threefold greater than that of the radiologist. They concluded that anesthesiologists who spend significant time in neurointerventional radiology suites should wear protective eyewear [38].

Question 9:
Surgeon decides to go ahead with coiling of aneurysm. Describe the considerations to achieve induction of anesthesia for coiling. What anesthetic agents can be used for maintenance phase of anesthesia?

Answer:
Anesthetic considerations when providing anesthesia to patients undergoing INR procedures include maintenance of patient immobility and physiological stability, manipulating systemic and regional cerebral blood flow, managing anticoagulation, treating sudden unexpected complications during the procedure, medical management of critically ill patients during transport to and from radiology suites, and smooth and rapid recovery from anesthesia to facilitate neurological examination.

Preoperative assessment: Detailed patient evaluation and understanding of the underlying neuropathology are essential. In addition to the normal preanesthetic evaluation, a patient undergoing a neuroradiology procedure requires a careful neurological examination to identify any deficits present. Baseline arterial pressure and cardiovascular reserve should be evaluated, as should renal insufficiency. As anticoagulation is employed during most procedures, evaluation of coagulation is important. Patients with arthritis of neck, back, or other joints will have difficulty in lying supine for prolonged time under sedation or local anesthesia.

Anesthesia technique: The anesthesia machine is best located opposite the surgeon and toward the patient's feet. This position keeps it out of the way, and imaging equipment can move freely around the patient's head. Endovascular treatment of cerebral aneurysm can be performed under sedation or general anesthesia; however,

general anesthesia is the preferred technique by most anesthesiologists.

Sedation: Primary goals of the technique employing conscious sedation include alleviating pain or discomfort, anxiolysis, and patient immobility. Endovascular treatment is not very painful, and hence, achieving analgesia is not very difficult. However, pain may be associated with the injection of contrast material into the cerebral arteries or distension and traction of cerebral arteries [39]. The procedure can be long, leading to discomfort for the patient by having to lie still for long periods. Hence, if being done under sedation, it is important to ensure that the patient is in a comfortable position before commencing conscious sedation. Short-acting agents such as fentanyl, midazolam, and propofol are used, so that sedation is readily titratable. This allows the evaluation of the patient's neurological status during the procedure.

General anesthesia: Most anesthesiologists prefer general anesthesia as opposed to sedation as this provides an immobile patient with improved image quality, patient comfort, better control of the respiratory and hemodynamic profile, and ability to manage raised ICP. Also, under general anesthesia, an emergency complication such as hemorrhage may be treated more quickly, for example, by ventriculostomy or by deepening anesthesia for cerebral protection. The disadvantages are the inability to perform neurological assessment intraoperatively and the consequences of endotracheal intubation and extubation producing hypertension, coughing, or straining which can lead to raised ICP.

Monitoring: Monitoring includes ECG, pulse oximetry, inspired and expired gas analysis, intra-arterial blood pressure, and temperature monitoring. Due to the ambient temperature of neuroradiology suite and the duration of the procedure, active warming devices can be used to prevent hypothermia in these patients. Even though hypothermia has been used as a method of neuroprotection for many decades, there is no conclusive human data to support the use of hypothermia as being neuroprotective in the clinical setting of SAH [40]. Hyperthermia, on the other hand, can augment brain injury and hence should be avoided. Hence, normothermia should be maintained during endovascular repair. A urinary catheter is inserted as a large volume of contrast and flush may be used.

Induction: The goal during induction of anesthesia for endovascular repair of cerebral aneurysm is to reduce the risk of aneurysm rupture by minimizing any acute changes in TMP while simultaneously maintaining an adequate CPP. The incidence of aneurysmal rupture during induction of anesthesia has been reported to be around 2% [41].

Maintenance: The aims of maintenance of anesthesia include maintaining a stable BP, ablate the response to painful stimuli, and avoid any further increases in ICP. This can be achieved using a volatile or total intravenous anesthesia (TIVA) anesthesia. A TIVA-based technique using propofol, remifentanil, muscle relaxation, and endotracheal intubation may be used. The effects of propofol on cerebral physiology have been well studied, and it is shown to decrease both CBF and CMRO2 in a parallel and dose-related manner [42].Remifentanil offers stable and easily controllable hemodynamics and particularly rapid postoperative recovery [43]. The advantages of TIVA-based technique include reduction in both CBF and CMRO2 in parallel, avoidance of inhalational agents, and faster recovery. Inhalational agents can be used as well, the change in CBF secondary to a change in arterial CO_2 tension is preserved at 1 MAC (minimal alveolar concentration) end-tidal sevoflurane anesthesia and "coupling" of CBF and CMRO2 is maintained [44]. Isoflurane and desflurane in less than 1 MAC concentrations have also been used safely. Nitrous oxide is preferably avoided, as there is risk of enlargement of micro air bubbles during injection of contrast or irrigation fluid. A combination of low dose of propofol and remifentanil infusions supplemented with sevoflurane can also be used to maintain anesthesia. This combination of low doses of i.v. agents and vapor mini-

mizes individual drugs' side-effects and allows "fine tuning" of the depth of anesthesia by varying vapor concentration [45].

Maintenance of cardiovascular stability is sometimes difficult as noxious stimulation during coiling is usually minimal. In patients with SAH, avoidance of hypotension is vital, as cerebral autoregulation is impaired. The BP may need to be supported with fluids and vasopressors. On the other hand, essential or reactive hypertension may require treatment to prevent rebleeding or cerebral edema. There is no skull decompression during endovascular treatment; therefore, an increase in transmural pressure, which may cause aneurysm rupture, must be avoided, especially at endotracheal intubation and extubation.

Ventilation of the lungs should be adjusted to achieve low normocapnia ($PaCO_2$ 30–34 mmHg) [46]. This is appropriate in an attempt to direct flow away from normal brain and toward a lesion that is intended to receive the occlusive device or material. It may also help reduce the raised ICP associated with SAH. Hyperventilation also improves the quality of the vascular image, as vasoconstriction allows contrast to fill the arterial lumen to the edges so that a clearer picture is obtained [47].

Anticoagulation: Careful management of coagulation is required to prevent thromboembolic complications during and after the procedure. In general, after a baseline activated clotting time (ACT) is obtained, i.v. heparin (70 IU/kg) is given to prolong ACT by two to three times. ACT is monitored at least every hour and if required additional dose of heparin is given [39].

Question 10:
What materials are used for endovascular aneurysm treatment? How does our perioperative management differ?

Answer:
Endovascular techniques have brought a paradigm shift in the management of intracranial aneurysms. Various different techniques exist for the treatment of aneurysms, and newer materials are rapidly developing to make the procedures safer and more efficacious.

Coil embolizaiton: The Guglielmi electrolytically detachable coil system was introduced in the early 1990s. They are platinum coils, inserted into the lumen of the aneurysm, causing a local thrombus formation around the coils, thereby obliterating the aneurysmal sac [48].

Complications of endovascular coiling include thromboembolism and intraprocedural aneurysm rupture. Both of these complications are more common in the setting of SAH than for unruptured aneurysms [49, 50]. Thromboembolism occurred in 12.5% of endovascularly treated aneurysms in one series. Aneurysm size >10 mm and neck size >4 mm were risk factors for this complication [49].

While of unproven benefit, some combination of heparin and/or antiplatelet therapy is used in most centers to minimize sequelae. In one large series, 9.3% of patients experienced a thromboembolic event during coiling despite use of heparin and aspirin [51]. Rescue treatment with abciximab appeared safe and effective; no patients experienced a bleeding complication and 29 of 42 patients did not suffer a clinical or radiologic infarction. In one series, GIIB/IIIa inhibitors, such as abciximab, appeared to be safer for this indication than thrombolytic agents [52].

Newer techniques: Endovascular therapy for cerebral aneurysms is evolving and continues to have significant advances in technology like improved microcatheter design, new coil design including bioactive and expansile hydrogel coils, remodeling the neck of the aneurysm using balloon catheters (a nondetachable balloon catheter is deployed across the aneurysm neck and balloon inflated when coils are deployed in the aneurysm, thus preventing prolapse into the parent vessel and allow tighter packing), availability of stent-assisted coil embolization (a self-expandable stent is deployed across the aneurysm and then the microcatheter is manipulated through the stent mesh into the aneurysm remnant and coils deployed sequentially occluding the remnant), flow diverters and disruptors, and

new embolic material including liquids offer promise that aneurysms previously considered not amenable to therapy will be treatable in the future [53].

Insertion of stent requires pre-procedural administration of antiplatelet agents like aspirin and Plavix, which might lead to increased bleeding risk during insertion of invasive lines like central venous catheter or arterial line. Intraoperative decision to use a stent or flow diverter in patients who are not preloaded on antiplatelet agents might require insertion of a nasogastric tube for the administration of these medications. In patients with aneurysmal subarachnoid hemorrhage (Hunt and Hess Grade 3 and above), who need flow divertors, a decision to insert an EVD is often made before starting them on perioperative antiplatelet agents, to reduce the hemorrhage risk of EVD insertion in the postoperative period [54].

Question 11:
What is the role of neurophysiologic monitoring in endovascular coiling of aneurysm?

Answer:
Neurophysiological monitoring (NPM) can directly assess the functional state of specific cerebral regions and provide an indirect measure of regional ischemia produced in the cerebral circulation. EVT of aneurysms can alter regional cerebral blood flow (rCBF) and cause ischemic complications. In addition, EVT may result in thromboembolic complications or may partially impede blood flow in the parent vessel. As these therapeutic maneuvers are often performed in the patients under general anesthesia, therefore, a technique to detect and monitor significant changes in rCBF at the time of endovascular treatment of aneurysms may provide useful information.

The type of NPM is determined by the location of the aneurysm and its associated vascular territory and can include somatosensory evoked potential (SSEP), motor evoked potential (MEP), electroencephalography (EEG), and brainstem auditory evoked potential (BAEP). SSEPs that use median and posterior tibial nerve stimulation are useful in assessing the functional state of the middle and anterior cerebral artery territories by detecting impairment along the respective somatosensory pathways. BAEP monitoring detects functional changes along the auditory brain stem pathways. This is most often caused by a brain stem insult, which could result from vertebrobasilar ischemia; however, ischemia in the cerebellum or posterior cerebral artery territories could still be missed. EEG provides a more global assessment of cerebral ischemia but cannot be used to monitor the posterior fossa. It may be used to detect ischemia in the posterior cerebral artery territory, but its sensitivity is limited because only a limited number of electrodes can be placed on the patient's head as more electrodes would obscure optimal working projections for endovascular treatment [55]. MEP monitoring can give valuable information regarding descending tracts as SSEP can only be used to monitor ascending tracts. As single signals can be evaluated in MEP, the time interval necessary for the detection of an impending neurological deficit is shortened. Also, MEP monitoring can be performed in patients with moderate to severe neurological deficits [56]. The limitations of NPM include relative insensitivity in detecting ischemic changes in certain vascular territories such as posterior cerebral artery territory. Also, anesthetic agents can cause confounding effects which mimics cerebral ischemia. Obtaining good quality signals might be difficult in the radiology suite, and performing NPM necessitates the presence of a technician and/or neurophysiologist throughout the procedure [57].

Question 12:
Surgeon is trying to navigate the coil, you suddenly notice patient's BP rises to 240/120 mmHg, HR 42/min. You inform this to the surgeon who also notices extravasation of contrast material. What do you think happened and how can it be managed surgically? What is the role of anesthesiologist in this scenario?

Answer:
The clinical picture suggests an aneurysm rupture. Hemorrhagic complications like aneurysm rupture and perforation or dissection of major blood vessels may manifest with severe hemody-

namic alterations like abrupt hypertension, widened pulse pressure, bradycardia, tachycardia, and arrhythmias. Aneurysms may rupture during micro-catheter negotiation, coil delivery, or blood pressure surges while guide wire or catheters can induce perforation/dissection of the feeding artery. The anesthetic management centers on blood pressure control as a means of maintaining adequate cerebral perfusion pressure (CPP) and stabilizing the transmural pressure gradient (TMPG). Any sudden increase or decrease in TMPG should be avoided as that can worsen the vascular leak.

Treatment unique to aneurysm rupture during endovascular coiling includes consideration of the need for urgent reversal of anticoagulation. Immediate reversal of heparin may be required (1 mg protamine for each 100 units of heparin given) [58]. Extraventricular drainage (EVD) might be needed urgently for acute management of hydrocephalus [59]. Surgeon can try rapid packing of the ruptured aneurysm with additional coils. If it fails, emergency craniotomy for hematoma evacuation and aneurysm clipping might be needed.

Management of hypertension is a difficult issue in patients with SAH. Aggressive treatment of surges of BP predisposes to a risk of ischemia in areas with loss of autoregulation; [60] hence, it seems best to reserve antihypertensive therapy for patients with extreme elevations of BP. A common practice is to maintain BP at the same level as prior to the bleeding [59]. Other measures that can be taken to control raised ICP include hyperventilation, administration of osmotically active agents like hypertonic saline or mannitol, initiation of burst suppression, and elevation of the head as feasible. Finally, the availability of type and cross-matched blood should be confirmed.

In the event of aneurysm rupture, clear communication with the surgeon is key, as is systematic approach to hemodynamic control and volume resuscitation.

Question 13:
If surgeon suspects a cerebral infarction due to vessel occlusion, what measures can you take as an anesthesiologist to minimize risk of ischemia?

Answer:
Cerebral infarction can occur due to vascular occlusion which may be caused by coil misplacement or fracture, thromboembolism, catheters, or vasospasm. This needs to be managed emergently to ensure adequate blood supply to the ischemic area of the brain. In the event of thromboembolic occlusion, the arterial pressure should be raised to increase collateral blood flow and prevent ischemic complications. Angiographically visible thrombus may be treated by mechanical lysis using a guide wire or local infusion of saline. Thrombolytic agents like intra-arterial tissue plasminogen activator and antiplatelet agents such as abciximab, aGPIIb/IIIa inhibitor have been shown to achieve recanalization [61, 62]. Misplaced or malpositioned coils are removed by endovascular retrieval; however, rarely craniotomy may be needed.

Vasospasm reduces CBF, causing cerebral ischemia and subsequent delayed ischemic neurodeficits (DIND). It usually manifests locally at the site of the bleeding, and therefore, symptoms are usually related to the territory of the bleeding; however, severe diffuse spasm can be seen in patients with severe SAH. Treatment of vasospasm can be medical (induced hypertension), pharmacological, or by angioplasty.

Triple H therapy (hypertension, hypervolemia, and hemodilution) was previously recommended for the management of SAH; however, the current volume status goal is euvolemia. Hypertension is the only component that is shown to improve CBF independently. Hypervolemia with consequent hemodilution also increases CBF but at the expense of blood oxygen content and by extension cerebral oxygen delivery [63].

Intra-arterial papaverine infusion results in clinical improvement in 25–50% of patients with vasospasm [64]. However, papaverine has a transient effect up to 24 h and is associated with side effects, including monocular blindness, mydriasis, seizures, transient increase in ICP, hypertension, tachycardia, and paradoxical worsening of vasospasm [65]. Intra-arterial calcium channel blocker like nimodipine results in reduction of angiographic vasospasm and increase in cerebral perfusion as detected by perfusion CT

after 24 h. Hypotension can occur as a side effect after the initial bolus; however, it is temporary and could be easily treated by adjusting the vasoactive medication [66].

Angioplasty is most effective when done early, within 2 h of symptomatic ischemia, to prevent the transformation of an ischemic infarct to a hemorrhagic infarct. It is effective in 98–100% of patients and results in clinical improvement in 70–80% [67]. Complications include vessel rupture (2–5%) and rebleed from an unprotected aneurysm (5%) [68]. The procedure is often limited by the size of the vessel involved and is usually not done beyond A1 and M1 segments.

Question 14:
After the aneurysm is secured, what will be your hemodynamic goals for this patient? What factors will you take into consideration before deciding whether to extubate the patient or not?

Answer:
Blood pressure control will depend on whether the aneurysm has been completely occluded or not. If completely occluded, there is more liberation for systolic blood pressure to rise, mainly to preemptively manage the risk of vasospasm.

If possible, all patients should be emerged from anesthesia, so that a neurologic examination can be performed. A rapid emergence in order to facilitate a neurologic examination is helpful and continued neurologic examinations on a frequent basis should be utilized in the immediate postoperative period. However, emergence from anesthesia may be impeded by factors that include preoperative neurological condition, intraoperative events like aneurysmal rupture, hemodynamic instability, and prolonged surgical time. In addition, extubation should be based on patient's ability for airway protection.

Question 15:
On postoperative day 6, the patient became drowsy and stopped responding to verbal commands. On clinical examination, he was noted to have left-sided hemiparesis. What could be the possible cause of this neurologic deterioration? How can you investigate this further and what will be the treatment options?

Answer:
The patient is showing signs and symptoms of delayed cerebral ischemia, commonly caused by cerebral vasospasm. It is the delayed narrowing of large capacitance arteries at the base of the brain after SAH, which is often associated with radiographic or CBF evidence of diminished perfusion in the distal territory of the affected artery. After aneurysmal SAH, angiographic vasospasm is seen in 30–70% of patients, with a typical onset 3–5 days after the hemorrhage, maximal narrowing at 5–14 days, and a gradual resolution over 2–4 weeks [69].

Often, the development of a new focal deficit, unexplained by hydrocephalus or rebleeding, is the first objective sign of symptomatic vasospasm. In addition, unexplained increases in MAP may occur as cerebral arterial autoregulation attempts to improve cerebral circulation to prevent ischemia.

The risk for delayed cerebral ischemia increases with SAH thickness and intraventricular hemorrhage, as demonstrated by the modified Fisher scale. Additional risk factors include poor clinical grade, loss of consciousness at ictus, cigarette smoking, cocaine use, SIRS, hyperglycemia, hydrocephalus, and non-convulsive seizures [70].

The mechanism for the development of DCI includes large-vessel narrowing with subsequent low flow, early brain injury triggering glial activation, endothelial dysfunction, inflammatory pathways, microcirculatory dysfunction with loss of autoregulation, cortical spreading depolarization, and microthrombosis [71].

The combination of neurologic examination and imaging studies can enhance the early detection and proper management. Clinical examination in awake patients who can follow commands is the most reliable way to detect and diagnose DCI. Monitoring is usually multimodal and can include ICP monitoring, continuous EEG, transcranial Doppler (TCD) monitoring, cerebral blood flow monitoring, brain tissue oxygen tension, jugular venous oximetry, and cerebral

microdialysis. Vascular imaging modalities like digital subtraction angiography (DSA), CT angiography (CTA), and CT perfusion (CTP) imaging are also used when indicated [72]. DSA is the gold standard and offers the possibility of endovascular treatment. CTA is often applied for vasospasm screening before DSA, given its high degree of specificity and lack of invasiveness. Perfusion imaging allows for the evaluation of the functional consequences of both large-vessel and small-vessel vasospasm.

TCD provides a noninvasive, safe bedside modality for dynamic assessment and monitoring of vasospasm. It has a high sensitivity and negative predictive value for predicting vasospasm with high accuracy, thus making it ideal for monitoring; [73] however, it is highly dependent on the operator and cranial bone window. Absolute values of TCD readings can be misleading in the setting of systemic hemodynamic variations but the Lindegaard ratios (ratio of the velocity in the brain vessel of choice to the velocity in the ipsilateral extracranial internal carotid artery) have been shown to be helpful in following trends [74].

The treatment of DCI is complex, and these patients should be cared for in specialized, high-volume centers to maximize good outcome. Use of vasopressors to augment blood pressure is the cornerstone of therapy for DCI. Norepinephrine, dopamine, phenylephrine, and vasopressin-induced hypertension all have been demonstrated to significantly improve CBF and/or cerebral oxygenation, resulting in clinical improvement of the neurological deficit [75]. A starting systolic target ranging between 160 and 180 mmHg is usually selected, depending on the patient's baseline blood pressure. Once therapy is instituted, absence of response in 30 min should trigger an escalation of the BP target. Most centers use a maximal target range of around 120 mmHg for CPP, 140 mmHg for MAP, and 220 mmHg for SBP [75]. Regarding fluid management, current guidelines suggest that isotonic fluids should be used judiciously to correct hypovolemia, with the ultimate goal of maintaining a euvolemic state while avoiding fluid overload [76]. Calcium channel blocker like nimodipine is used for DCI prophylaxis and has class I evidence for decreasing the risk of poor functional outcome; however, it does not decrease the frequency of angiographic vasospasm [77]. Possible mechanisms of action include reduction of angiographic vasospasm, increase in fibrinolytic activity, neuroprotection, and inhibition of cortical spreading ischemia.

When confronted with medically refractory DCI, endovascular therapy should be the next step. Endovascular therapy can be subdivided into mechanical dilation and intra-arterial infusion of vasodilators. Percutaneous transluminal balloon angioplasty (PTCA) is based on mechanical stretching and dilation of vasospastic arteries; however, this technique is limited to proximal vessels. Intra-arterial vasodilators such as papaverine, nicardipine, verapamil, nimodipine, milrinone, amrinone, and fasudil have several advantages over PTCA like better distal penetration, a more diffuse effect, and a better safety profile. Disadvantages include recurrent vasospasm due to the short-lasting effect of these agents, increased ICP secondary to vasodilation, and potential hypotension due to systemic effects [75].

Cardiac output augmentation using inotropes is shown to improve brain perfusion after SAH. Milrinone, a selective inhibitor of the phosphodiesterase III isoenzyme, provides more effective inotropy than dobutamine in the setting of neurogenic stunned myocardium, which is associated with beta-receptor desensitization [78].

References

Question 1

1. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. J Neurosurg. 1968;28(1):14–20.
2. Drake CG. Report of world Federation of Neurological Surgeons Committee on a universal subarachnoid hemorrhage grading scale. J Neurosurg. 1988;68:985–6.
3. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery. 1980;6(1):1–9.

4. Davies K, Gelb AW, Manninen PH, Boughner DR, Bisnaire D. Cardiac function in aneurysmal subarachnoid haemorrhage: a study of electrocardiographic and echocardiographic abnormalities. BJA: British Journal of Anaesthesia. 1991;67(1):58–63.
5. Diringer MN, Lim JS, Kirsch JR, Hanley DF. Suprasellar and intraventricular blood predict elevated plasma atrial natriuretic factor in subarachnoid hemorrhage. Stroke. 1991;22(5):577–81.

Question 3

6. Sakr YL, Ghosn I, Vincent JL. Cardiac manifestations after subarachnoid hemorrhage: a systematic review of the literature. Prog Cardiovasc Dis. 2002;45(1):67–80.
7. Hjalmarsson C, Bergfeldt L, Bokemark L, Manhem K, Andersson B. Electrocardiographic abnormalities and elevated cTNT at admission for intracerebral hemorrhage: predictors for survival? Ann Noninvasive Electrocardiol. 2013;18(5):441–9.
8. Banki N, Kopelnik A, Tung P, Lawton MT, Gress D, Drew B, Dae M, Foster E, Parmley W, Zaroff J. Prospective analysis of prevalence, distribution, and rate of recovery of left ventricular systolic dysfunction in patients with subarachnoid hemorrhage. J Neurosurg. 2006;105(1):15–20.
9. Pollick C, Cujec B, Parker S, Tator C. Left ventricular wall motion abnormalities in subarachnoid hemorrhage: an echocardiographic study. J Am Coll Cardiol. 1988;12(3):600–5.
10. Bulsara KR, McGirt MJ, Liao L, Villavicencio AT, Borel C, Alexander MJ, Friedman AH. Use of the peak troponin value to differentiate myo- cardial infarction from reversible neurogenic left ventricular dysfunction associatedwith aneurysmal subarachnoid hemorrhage. J Neurosurg. 2003;98:524–8.
11. Naidech AM, Kreiter KT, Janjua N, Ostapkovich ND, Parra A, Commichau C, Fitzsimmons BF, Connolly ES, Mayer SA. Cardiac troponin elevation, cardiovascular morbidity, and outcome after subarachnoid hemorrhage. Circulation. 2005;112(18):2851–6.
12. Bassil R, Kaddouh F, Greer DM, Muehlschlegel S. Neurogenic shock. In: Layon AJ, Gabrielli A, Yu M, Wood KE, editors. Civetta, Taylor, and Kirby'scritical care medicine. 5th ed. Philadelphia, PA: Wolters Kluwer. p. 2017.
13. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, Cammann VL, Sarcon A, Geyer V, Neumann CA, Seifert B. Clinical features and outcomes of Takotsubo (stress) cardiomyopathy. N Engl J Med. 2015;373(10):929–38.

Question 4

14. Dasenbrock HH, Rudy RF, Lai PM, Smith TR, Frerichs KU, Gormley WB, Aziz-Sultan MA. Du R. cigarette smoking and outcomes after aneurysmal subarachnoid hemorrhage: a nationwide analysis. J Neurosurg. 2018;129(2):446–57.
15. Chalouhi N, Ali MS, Starke RM, Jabbour PM, Tjoumakaris SI, Gonzalez LF, Rosenwasser RH, Koch WJ, Dumont AS. Cigarette smoke and inflammation: role in cerebral aneurysm formation and rupture. Mediat Inflamm. 2012;2012:1.

Question 5

16. Marupudi N, Mittal S. Diagnosis and management of hyponatremia in patients with aneurysmal subarachnoid hemorrhage. J Clin Med. 2015;4(4):756–67.
17. Rahman M, Friedman WA. Hyponatremia in neurosurgical patients: clinical guidelines development. Neurosurgery. 2009;65(5):925–36.
18. Kao L, Al-Lawati Z, Vavao J, Steinberg GK, Katznelson L. Prevalence and clinical demographics of cerebral salt wasting in patients with aneurysmal subarachnoid hemorrhage. Pituitary. 2009;12(4):347.
19. Palmer BF. Hyponatremia in patients with central nervous system disease: SIADH versus CSW. Trends in Endocrinology & Metabolism. 2003;14(4):182–7.
20. Muehlschlegel S. Subarachnoid hemorrhage. CONTINUUM: Lifelong Learning in Neurology. 2018;24(6):1623–57.

Question 6

21. Gijn JV, Hijdra A, Wijdicks EF, Vermeulen M, Crevel HV. Acute hydrocephalus after aneurysmal subarachnoid hemorrhage. J Neurosurg. 1985;63(3):355–62.
22. Lim YC, Shim YS, Oh SY, Kim MJ, Park KY, Chung J. External ventricular drainage before endovascular treatment in patients with aneurysmal subarachnoid hemorrhage in acute period: its relation to hemorrhagic complications. Neurointervention. 2019;14:35.
23. Molyneux AJ, Kerr RS, Yu LM, Clarke M, Sneade M, Yarnold JA, International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet. 2005;366:809–17.
24. Connolly ES Jr, Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, American Heart Association Stroke Council, Council on Cardiovascular Radiology and Intervention, Council on Cardiovascular Nursing, Council on Cardiovascular Surgery and Anesthesia, Council on Clinical Cardiology, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012;43:1711–37.

25. Scheller C, Strauss C, Prell J, Simmermacher S, Brandt S. Increased rate of ventriculostomy-related hemorrhage following endovascular treatment of ruptured aneurysms compared to clipping. Acta Neurochir. 2018;160(3):545–50.
26. Lim YC, Shim YS, Oh SY, Kim MJ, Park KY, Chung J. External ventricular drainage before endovascular treatment in patients with aneurysmal subarachnoid hemorrhage in acute period: its relation to hemorrhagic complications. Neurointervention. 2019;14:35.

Question 7

27. Molyneux A, Kerr R. International subarachnoid aneurysm trial (ISAT) collaborative group. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomized trial. J Stroke Cerebrovasc Dis. 2002;11(6):304–14.
28. Molyneux AJ, Birks J, Clarke A, Sneade M, Kerr RS. The durability of endovascular coiling versus neurosurgical clipping of ruptured cerebral aneurysms: 18 year follow-up of the UK cohort of the international subarachnoid aneurysm trial (ISAT). Lancet. 2015;385(9969):691–7.
29. Lanzino G, Murad MH, d'Urso PI, Rabinstein AA. Coil embolization versus clipping for ruptured intracranial aneurysms: a meta-analysis of prospective controlled published studies. Am J Neuroradiol. 2013;34(9):1764–8.
30. Brinjikji W, Lanzino G, Cloft HJ, Rabinstein A, Kallmes DF. Endovascular treatment of very small (3 mm or smaller) intracranial aneurysms: report of a consecutive series and a meta-analysis. Stroke. 2010;41(1):116–21.
31. Lanzino G, Fraser K, Kanaan Y, et al. Treatment of ruptured intracranial aneurysms since the international subarachnoid aneurysm trial: practice utilizing clip ligation and coil embolization as individual or complementary therapies. J Neurosurg. 2006;104:344–9.
32. Mitchell P, Kerr R, Mendelow AD, et al. Could late rebleeding overturn the superiority of cranial aneurysm coil embolization over clip ligation seen in the international subarachnoid aneurysm trial? J Neurosurg. 2008;108:437–42.

Question 8

33. Dagal A. Radiation safety for anesthesiologists. Current Opinion in Anesthesiology. 2011;24(4): 445–50.
34. Klein LW, Miller DL, Balter S, Laskey W, Haines D, Norbash A, Mauro MA, Goldstein JA. Members of the joint inter-society task force on occupational hazards in the interventional laboratory. Occupational health hazards in the interventional laboratory: time for a safer environment. Catheter Cardiovasc Interv. 2009;73(3):432–8.
35. Varma MK, Price K, Jayakrishnan V, Manickam B, Kessell G. Anaesthetic considerations for interventional neuroradiology. Br J Anaesth. 2007;99(1):75–85.
36. Hall EJ. Glossary, radiobiology for the radiologist. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2000. p. 521–52.
37. Recommendations of the International Commission on Radiological Protection. Elmsford, NY: Pergamon Press, 1991; 21: 1–25. ICRP publication 60.
38. Anastasian ZH, Strozyk D, Meyers PM, Wang S, Berman MF. Radiation exposure of the anesthesiologist in the neurointerventional suite. Anesthesiology. 2011;114(3):512–20.

Question 9

39. Hashimoto T, Gupta DK, Young WL. Interventional neuroradiology- anesthetic considerations. Anesthesiol Clin A. 2002;20:347–59.
40. Todd MM. Intraoperative hypothermia for aneurysm surgery trial (IHAST) Investigators: Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med. 2005;352:135–45.
41. Tsementzis SA, Hitchcock ER. Outcome from" rescue clipping" of ruptured intracranial aneurysms during induction anaesthesia and endotracheal intubation. J Neurol Neurosurg Psychiatry. 1985;48(2):160–3.
42. Vandesteene A, Trempont V, Engelman E, Deloof T, Focroul M, Schoutens A, De Rood M. Effect of propofol on cerebral blood flow and metabolism in man. Anaesthesia. 1988;43:42–3.
43. Warner DS. Experience with remifentanil in neurosurgical patients. Anesth Analg. 1999;89(4S):33.
44. Moss E. Editorial II: Volatile anaesthetic agents in neurosurgery.
45. Lakhani S, Guha A, Nahser HC. Anaesthesia for endovascular management of cerebral aneurysms. Eur J Anaesthesiol. 2006;23(11):902–13.
46. Jones M, Leslie K, Mitchell P. Anaesthesia for endovascular treatment of cerebral aneurysms. J Clin Neurosci. 2004;11(5):468–70.
47. Turner J. Anaesthesia for neuroradiology. Textbook of Neuroaanesthesia and critical care. London: Greenwich Medical Media; 2000.

Question 10

48. Guglielmi G, Viñuela F, Sepetka I, Macellari V. Electrothrombosis of saccular aneurysms via endovascular approach: part 1: electrochemical basis, technique. and experimental results Journal of neurosurgery. 1991;75(1):1–7.

49. Pierot L, Wakhloo AK. Endovascular treatment of intracranial aneurysms: current status. Stroke. 2013;44(7):2046–54.
50. Sturiale CL, Brinjikji W, Murad MH, Lanzino G. Endovascular treatment of intracranial aneurysms in elderly patients: a systematic review and meta-analysis. Stroke. 2013;44(7):1897–902.
51. Ries T, Siemonsen S, Grzyska U, Zeumer H, Fiehler J. Abciximab is a safe rescue therapy in thromboembolic events complicating cerebral aneurysm coil embolization: single center experience in 42 cases and review of the literature. Stroke. 2009;40(5):1750–7.
52. Brinjikji W, McDonald JS, Kallmes DF, Cloft HJ. Rescue treatment of thromboembolic complications during endovascular treatment of cerebral aneurysms. Stroke. 2013;44(5):1343–7.
53. Pierot L, Cognard C, Anxionnat R, Ricolfi F, Investigators C. Ruptured intracranial aneurysms: factors affecting the rate and outcome of endovascular treatment complications in a series of 782 patients (CLARITY study). Radiology. 2010;256(3):916–23.
54. Lin N, Brouillard AM, Keigher KM, Lopes DK, Binning MJ, Liebman KM, et al. Utilization of pipeline embolization device for treatment of ruptured intracranial aneurysms: US multicenter experience. Journal of NeuroInterventional Surgery. 2015;7(11):808–15.

Question 11

55. Liu AY, Lopez JR, Do HM, Steinberg GK, Cockroft K, Marks MP. Neurophysiological monitoring in the endovascular therapy of aneurysms. Am J Neuroradiol. 2003;24(8):1520–7.
56. Zentner J, Schumacher M, Bien S. Motor evoked potentials duringinterventional neuroradiology. Neuroradiology. 1988;30:252–5.
57. Lakhani S, Guha A, Nahser HC. Anaesthesia for endovascular management of cerebral aneurysms. Eur J Anaesthesiol. 2006;23(11):902–13.

Question 12

58. Varma MK, Price K, Jayakrishnan V, Manickam B, Kessell G. Anaesthetic considerations for interventional neuroradiology. Br J Anaesth. 2007;99(1):75–85.
59. Schulenburg E, Matta B. Anaesthesia for interventional neuroradiology. Curr Opin Anaesthesiol. 2011;24:426–32.
60. Torner JC, Nibbelink DW, Burmeister LF. Statistical comparisons of end results of a randomised treatment study. Aneurysmal subarachnoid hemorrhage: report of the Cooperatice study. Baltimore: Urban&Schwarzenberg; 1981. p. 249–76.

Question 13

61. Hähnel S, Schellinger PD, Gutschalk A, et al. Local intra-arterialfibrinolysis of thromboemboli occurring during neuroendovascularprocedures with recombinant tissue plasminogen activator. Stroke. 2003;34:1723–8.
62. Fiorella D, Albuquerque FC, Han P, McDougall CG. Strategies forthe management of intraprocedural thromboembolic complicationswith Abciximab (ReoPro). Neurosurgery. 2004;54:1089–98.
63. Hoefnagel AL, Rajan S, Martin A, Mahendra V, Knutson AK, Uejima JL, Kositratna G, Weller M, Yang H, Ahuja S, Bailey C. Cognitive aids for the diagnosis and treatment of Neuroanesthetic emergencies: consensus guidelines on behalf of the Society for Neuroscience in anesthesiology and critical care (SNACC) education committee. J Neurosurg Anesthesiol. 2019;31(1):7–17.
64. Liu JK, Tenner MS, Gottfried ON, et al. Efficacy of multipleintraarterial papaverine infusions for improvement in cerebral circulationtime in patients with recurrent cerebral vasospasm. J Neurosurg. 2004;100:414–21.
65. Clyde BL, Firlik AD, Kaufmann AM, Spearman MP, Yonas H. Paradoxical aggravation of vasospasm with papaverine infusionfollowing aneurysmal subarachnoid haemorrhage. case report J Neurosurg. 1996;84:690–5.
66. Hänggi D, Turowski B, Beseoglu K, Yong M, Steiger HJ. Intra-arterial nimodipine for severe cerebral vasospasm after aneurysmal subarachnoid hemorrhage: influence on clinical course and cerebral perfusion. Am J Neuroradiol. 2008;29(6):1053–60.
67. Varma MK, Price K, Jayakrishnan V, Manickam B, Kessell G. Anaesthetic considerations for interventional neuroradiology. Br J Anaesth. 2007;99(1):75–85.
68. Brothers MF, Holgate RC. Intracranial angioplasty for treatment of vasospasm after subarachnoid hemorrhage: technique and modifications to improve branch access. Am J Neuroradiol. 1990;11(2):239–47.

Question 15

69. Heros RC, Zervas NT, Varsos V. Cerebral vasospasm after subarachnoidhemorrhage: an update. Ann Neurol. 1983;14:599–608.
70. Macdonald RL. Delayed neurological deterioration after subarachnoid haemorrhage. Nat Rev Neurol. 2014;10(1):44–58. https://doi.org/10.1038/nrneurol.2013.246.

71. Budohoski KP, Guilfoyle M, Helmy A, Huuskonen T, Czosnyka M, Kirollos R, Menon DK, Pickard JD, Kirkpatrick PJ. The pathophysiology and treatment of delayed cerebral ischaemia following subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry. 2014;85(12):1343–53.
72. Muehlschlegel S. Subarachnoid hemorrhage. CONTINUUM: Lifelong Learning in Neurology. 2018;24(6):1623–57.
73. Suarez JI, Qureshi AI, Yahia AB, et al. Symptomatic vasospasm diagnosis after subarachnoid hemorrhage: evaluation of transcranial Doppler ultrasound and cerebral angiography as related to compromised vascular distribution. Crit Care Med. 2002;30(6):1348–55.
74. Lindegaard KF, Nornes H, Bakke SJ, Sorteberg W, Nakstad P. Cerebral vasospasm diagnosis by means of angiography and blood velocity measurements. Acta Neurochir. 1989;100(1–2):12–24.
75. Francoeur CL, Mayer SA. Management of delayed cerebral ischemia after subarachnoid hemorrhage. Crit Care. 2016;20(1):277.
76. Diringer MN, Bleck TP, Hemphill JC, Menon D, Shutter L, Vespa P, Bruder N, Connolly ES, Citerio G, Gress D, Hänggi D. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical care Society's multidisciplinary consensus conference. Neurocrit Care. 2011;15(2):211.
77. Mees SM, Rinkel GJ, Feigin VL, Algra A, Van den Bergh WM, Vermeulen M, Van Gijn J. Calcium antagonists for aneurysmal subarachnoid hemorrhage. Stroke. 2008;39(2):514–5.
78. Naidech A, Du Y, Kreiter KT, Parra A, Fitzsimmons BF, Lavine SD, Connolly ES, Mayer SA, Commichau C. Dobutamine versus milrinone after subarachnoid hemorrhage. Neurosurgery. 2005;56(1):21–7.

28 Management of Patient Undergoing Carotid Stenting

Shilpa Rao

Stem Case Terminology

A 70-year-old female patient is referred to the preoperative clinic for symptoms of intermittent right-sided weakness since 3–4 months; in addition, she also complains of intermittent blurry vision which resolves spontaneously. Significant past medical history includes placement of a drug-eluting stent (DES) for stenosis of her left main coronary artery 1 year ago. The patient has been complianing with her dual antiplatelet therapy. Other past medical history includes hypertension on amlodipine, hyperlipidemia, and type 2 diabetes mellitus on insulin.

Physical examination: Alert, awake, and oriented, BMI 30 kg/m^2.

Airway assessment: Mallampati-2, Thyromental distance >3 fingerbreadths.

Normal C-spine range of movement, normal dentition.

Preoperative laboratory work includes:

Complete blood count: normal limits.

Basic metabolic panel: within normal limits except for serum creatinine 2.1 mg/dL.

Blood glucose: 170 mg/dL.

Type and screen is available.

Preoperative carotid ultrasound reveals >75% stenosis of the left internal carotid artery and > 50% stenosis of the right internal carotid artery.

She i;s now scheduled for the placement of a carotid stent.

Question 1:

Do you require any further preoperative testing of this patient prior to proceeding for surgery? Why?

Answer:

A detailed preoperative history, including assessment of functional capacity of this patient, is important and vital as part of preoperative risk stratification. The questions are focused on her level of activity without shortness of breath, prior episodes of cardiac symptoms if any, glucose control, etc. Assessment of metabolic equivalents (METS) gives valuable information regarding the patient's functional status.

This patient may require further cardiac testing due to her associated history of DES placement and the intermediate surgical risk factor. Optimization of preoperative cardiac risk factors is important prior to proceeding with carotid artery surgery due to increased incidence of perioperative adverse cardiac events. Below is the risk stratification for noncardiac surgical procedures.

Cardiac Risk∗ Stratification for Noncardiac Surgical Procedures [1]

S. Rao (✉)
Division of Neuroanesthesiology, Department of Anesthesiology, Yale School of Medicine, Yale New Haven Hospital, New Haven, CT, USA
e-mail: shilpa.rao@yale.edu

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_28

High risk (reported cardiac risk > 5%).

Emergent major operations, particularly in older patients.

Aortic and other major vascular surgeries.

Peripheral vascular surgery.

Anticipated prolonged surgical procedures associated with large fluid shifts, blood loss, or both.

Intermediate risk (reported cardiac risk > 1% but < 5%).

Carotid endarterectomy.

Head and neck surgery.

Intraperitoneal and intrathoracic surgery.

Orthopedic surgery.

Prostate surgery.

Low risk (reported cardiac risk < 1%).

Endoscopic procedures.

Superficial procedure.

Cataract surgery.

Breast surgery.

The Revised Cardiac Risk Index (RCRI) is a widely used index to assess the risk of major cardiac complications in patients undergoing noncardiac surgery [2].

Independent Predictors of Major Cardiac Complications

1. High-risk type of surgery (e.g., vascular surgery, open intraperitoneal or intrathoracic procedures).
2. History of ischemic heart disease.
3. History of heart failure.
4. History of cerebrovascular disease.
5. Diabetes mellitus requiring treatment with insulin.
6. Preoperative serum creatinine >2.0 mg/dL.

The risk of major cardiac complications (cardiac death, nonfatal myocardial infarction (MI), nonfatal cardiac arrest, postoperative cardiogenic pulmonary edema, complete heart block) varied according to the number of risk factors. The following combined rates of nonfatal MI, nonfatal cardiac arrest, and cardiac death were seen in various studies [3].

- No risk factors—0.4%.
- One risk factor—1%.
- Two risk factors—2.4%.
- Three or more risk factors—5.4%.

If the patient belongs to the intermediate-risk group, he or she should be managed aggressively with lipid-lowering agents and tight BP control. The class I recommendations are to continue perioperative beta blockers in patients who are already on beta blockers preoperatively. Much debate is ongoing concerning the use of noninvasive stress testing in this patient subgroup. In any case, there is little evidence supporting the use of revascularization before noncardiac surgery. The role of preoperative PCI in reducing untoward perioperative cardiac complications is uncertain given the available data. Performing PCI before noncardiac surgery should be limited to:

1. Patients with left main coronary artery disease whose comorbidities preclude coronary artery bypass surgery without undue risk.
2. Patients with unstable coronary artery disease who would be appropriate candidates for emergency or urgent revascularization [4].

Based on the above data, this patient may require a preoperative 12-lead ECG (if symptomatic) and/or a noninvasive stress ECHO to assess her cardiac function prior to proceeding with surgery.

Question 2:

What are the indications of carotid artery surgery?

Answer:

Indications for Carotid artery surgery include any patient with symptomatic carotid artery stenosis in whom the surgery will improve the natural history of the disease as compared to medical management.

Indications of Carotid Endarterectomy: Carotid endarterectomy (CEA) should be considered for any patient with carotid artery stenosis in whom surgery will improve the natural history of the disease to a greater degree than the corresponding medical treatment would [5]. In symptomatic low-risk patients with surgical morbidity and mortality (stroke and death) of less than 6%, proven indications for CEA include the following:

- One or more transient ischemic attacks (TIAs) in the preceding 6 months and carotid artery stenosis exceeding 50% [6].

  The 2014 American Heart Association (AHA)/American Stroke Association (ASA) guidelines for the prevention of stroke in patients with stroke or TIA contained the following new or updated recommendations relevant to CEA [7].

  Carotid angioplasty and stenting (CAS) is indicated as an alternative to CEA for symptomatic patients at medium or low risk for complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by >70% by noninvasive imaging or > 50% by catheter-based imaging or noninvasive imaging with corroboration and the anticipated rate of peri-procedural stroke or death is <6% (class IIa; evidence level B).

  It is reasonable to consider the patient's age in choosing between CAS and CEA; for patients older than about 70 years, CEA may be associated with improved outcome compared to CAS, particularly when the arterial anatomy does not favor endovascular intervention; for younger patients, CAS is equivalent to CEA in terms of risk for periprocedural complications and long-term risk for ipsilateral stroke (class IIa; evidence level B).

  CAS and CEA in the above settings should be performed by operators with established periprocedural stroke and mortality rates of <6% for symptomatic patients (class I; evidence level B).
- Routine, long-term follow-up imaging of the extracranial carotid circulation with carotid duplex ultrasonography is not recommended (class III; evidence level B).

  There are relatively few contraindications for CEA, which include any associated acute life-threatening illness/condition which poses an imminent threat to life, or any other immediate condition which requires prioritization in terms of surgery.

  Carotid artery stenting is typically performed in an angiography suite. These patients are "preloaded" with dual antiplatelet therapy (aspirin and clopidogrel, grade 1B evidence) prior to surgery [8].

Question 3:
What are the anesthetic techniques available for this type of surgery?

Answer:
An awake patient under monitored anesthesia care (MAC) is considered the gold standard to assess intact neurological status during the intraoperative and perioperative period. This is accomplished by

- Adequate preoperative preparation by discussing with the patient about staying awake during the surgery, with ability to follow simple commands (e.g., squeezing a ball by the tested hand).
- Ensuring adequate anxiolysis and analgesia to ensure patient comfort. This may be ensured by titrated boluses of Inj. midazolam 1–2 mg, and Inj. fentanyl 50–100 μg at a time.
- Additional infusions of Inj. dexmedetomidine at 0.3–0.5 μg/kg/h titrated to effect are effective in maintaining spontaneous ventilation as well as sedation throughout.
- Standard ASA monitors are required at all times.
- Femoral access/vascular access obtained under local anesthesia.
- Backup general anesthesia equipment and resuscitation equipment immediately available at all times.
- A trained anesthesia provider at all times.

However, not all patients are amenable/may tolerate this technique. Patients with high preoperative anxiety state and potential difficult airway obese patients with risk factors for sleep apnea may not tolerate sedation without airway obstruction. Hence a careful preoperative assessment is important prior to proceeding.

General anesthesia with endotracheal tube is preferred in patients who are not good candidates for MAC. The major advantage of general anes-

thesia is the ability to control the patient's airway and ensure absolute immobility during the intraoperative period. The risks associated with general anesthesia include hemodynamic instability during induction, laryngoscopy, intubation, and emergence, as well as reliance on indirect monitors of neurological function, i.e., neuromonitoring techniques which will be discussed later in this chapter.

Most available evidence suggests that the choice of anesthetic technique has no significant impact on major adverse primary outcomes (e.g., death and stroke) after CEA. However, the length of stay in the intensive care unit and hospital and certain adverse outcomes (e.g., hemodynamic instability, delirium) may be reduced in patients receiving local/regional anesthesia compared with general anesthesia, and some centers have reported a lower incidence of perioperative MI when local/regional anesthesia is selected [9, 10].

The GALA trial by Gough et al. in 2008 was a multicenter, randomized controlled trial which enrolled 3500 patients undergoing CEA from 90 centers between 2001 and 2007. They compared general anesthetic versus local anesthesia technique for these patients. They concluded that there was no major difference in 30-day mortality in either groups and that the choice of anesthetic does not affect the perioperative outcome [11].

Question 4:
This patient is not consenting for MAC technique. You decide to proceed to general anesthesia. How would you induce anesthesia in this patient?

Answer:
A non-consenting patient precludes the use of MAC type of anesthesia. Standard ASA monitors need to be used at all times. The period of induction and laryngoscopy/intubation is associated with significant hemodynamic changes which need to be minimized as much as possible. Any induction agent (e.g., Inj. propofol 2 mg/kg or Inj. etomidate 0.2 mg/kg) can be used. Hypotension needs to be avoided at all costs due to decreased cerebral perfusion and possibility of causing ischemic stroke. This can be achieved by slow titrated injections of the induction agent and associated use of vasopressors if needed (e.g., Inj. phenylephrine 50–100 μg bolus). The sympathetic response to laryngoscopy and intubation can be minimized by additional narcotics such as Inj. fentanyl 50–100 μg or Inj. lidocaine 50–100 mg, or beta blockers such as Inj. esmolol 30 mg, Inj. labetalol 5–10 mg in increments, titrated to effect.

Question 5:
What additional lines would you like to place in this patient and why?

Answer:
Large bore intravenous access is of paramount importance in any carotid artery surgery. It is preferable to dedicate one intravenous line for infusions and the second line for bolus/transfusions if necessary. An arterial catheter is required for continuous hemodynamic monitoring during the intraoperative period, as well as for laboratory draws. These may be continued in the postoperative period as well.

A central venous catheter is usually not required unless the patient has poor peripheral venous access/long-term vasoactive infusions are planned.

Question 6:
You secure the airway and obtain the required vascular access. Surgery commences. What are the available neuromonitoring techniques you can use?

Answer:
Neuromonitoring is required for intraoperative assessment of neurological function under general anesthesia. There are various available techniques as described below [11].

Neurological monitor	Description	Advantages	Disadvantages
Awake testing	Using simple tasks for the patient to perform to assess the signs for cerebral ischemia	Direct monitoring of neurological function	As stated above for performing CEA under regional anesthesia
Transcranial Doppler	A Doppler probe is placed on the petrous temporal bone allowing measurement of middle cerebral artery flow	Monitors both flow and emboli, used during intra- and postoperative period	• Operator-dependent • Placement is near the surgical site • Acoustic window not found in 10–20% of patients
Stump pressure	The stump pressure distal to the carotid clamp reflects the perfusion pressure around the circle of Willis	Specific measure of cerebral ischemia	
EEG	EEG is affected by cerebral ischemia Raw and processed (spectral array) data can be used		• Measurement only reflects cortical and not deeper structures • Difficult to interpret • GA can alter the signal • Cannot identify emboli
Somatosensory evoked potentials	EEG is recorded after a stimulus, thus reflects the cortex and deeper structure activity	Maybe useful if the baseline EEG is abnormal	• GA can alter the signal. • Thought to be no more sensitive or specific compared to EEG • Cannot identify emboli
Near-infrared spectroscopy (NIRS)	NIRS measures arterial venous and capillary oxygenation producing a regional cerebral oxygenation (rSO_2) value	High negative predictive value for cerebral ischemia	• Poor positive predictive value • Frontal lobe sensors • Interference from non-cerebral blood flow and light • Cannot identify emboli

Inhalational agents and certain infusions (e.g., propofol infusion) affect the EEG signals and may interfere with accurate monitoring. Hence, if EEG monitoring is being used, a suggested technique is to maintain an intravenous infusion of Inj. dexmedetomidine 0.3–0.7 μg/kg/h, along with <0.5 MAC of sevoflurane and avoiding boluses of Inj. propofol or benzodiazepines, to facilitate EEG monitoring. The use of each of the above monitors or a combination of the above is operator and facility-dependent. When selecting an anesthetic technique, one should take into consideration their effect on monitoring (e.g., inhalational anesthetics increase latency and decrease the amplitude of SSEP in high concentrations. Propofol infusion titrated to burst suppression will essentially abolish EEG signals. Dexmedetomidine generally has minimal effect on EEG monitoring).

Question 7:
Surgery proceeds uneventfully and the surgeon is now preparing for placement of carotid artery stent. What are the expected hemodynamic changes during this timeframe and how would you treat it?

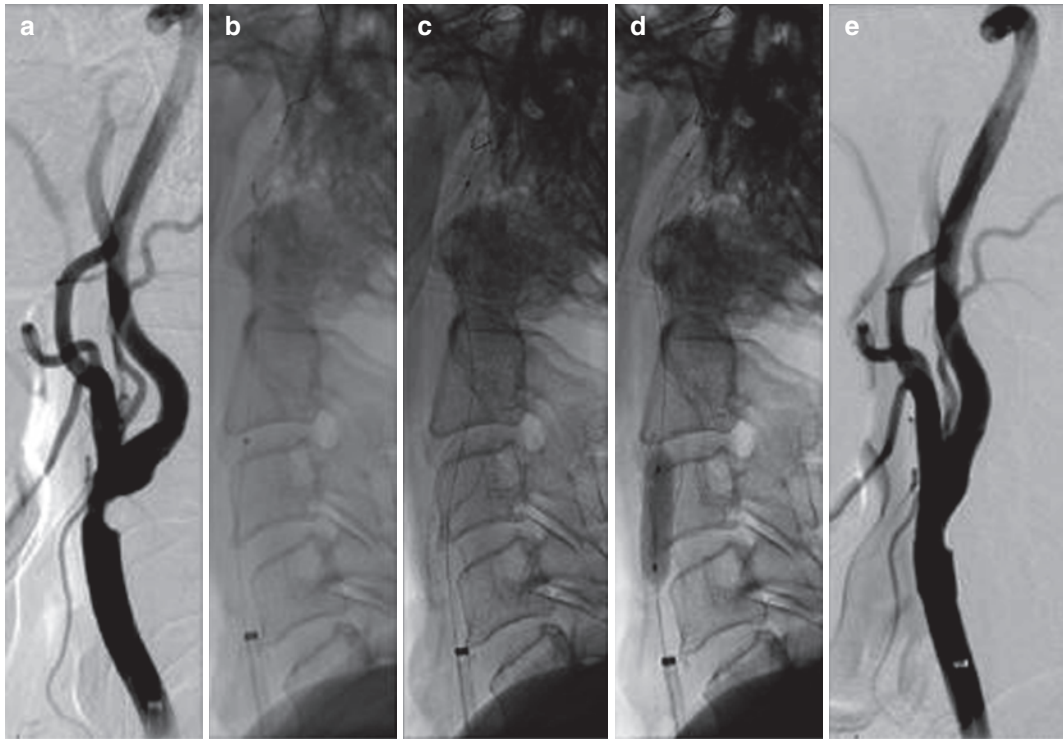
Answer:
Surgical manipulation/dilation of the carotid artery can potentially trigger the carotid sinus baroreceptor reflex. These receptors are stretch receptors, monitoring the changes of blood pressure through the distension of the vessel wall. They are innervated by branches of IX and X cranial nerves. Increased stretch is perceived as increased blood pressure, which activates the feedback circuit, involving the medullary nuclei such as nucleus tractus solitarii and caudal ventrolateral medulla. The afferent impulses activated by arterial BP pass by the NTS, CVLM, and RVLM, reach sympathetic preganglionic neurons leading to a decrease in sympathetic activity as well as an increase in parasympathetic activity, and complete the feedback circuit of the carotid baroreflex. This results in bradycardia, decreased cardiac contractility, and decreased peripheral vascular resistance [12]. These baroreflex mechanisms play a significant role in the short-term regulation of blood pressure.

Anticipation of such an occurrence is important, as well as adequate preparation is the key. The surgical stimulus needs to be stopped immediately, and this usually results in abolition of the reflex. Additional medications which can be used include Inj. glycopyrrolate 0.2 mg, Inj. atropine 0.2–0.4 mg, and Inj. epinephrine if required in unresolved situations. Rarely, transcutaneous pacing with/without Inj. epinephrine infusion may also be required if medical management fails.

Question 8:
You treat the reflex appropriately and the surgery proceeds. However, neuromonitoring specialist informs that there is a mild diffuse slowing in the cerebral cortex. What is the differential diagnosis and how would you approach this situation?

Answer:
Any change in the neuromonitoring signals during the intraoperative period is critical and may indicate early/ongoing decreased cerebral perfusion. Immediate recognition and treatment are important to prevent cerebral ischemia and neurological deficits. Multiple factors can contribute to the diffuse slowing in the quality of EEG signals. These include anesthetic factors such as excessive anesthetic depth/hypothermia/excessive hyperventilation/hypotension. These factors can be immediately recognized and treated appropriately.

The most concerning factor, however, is stroke. Stroke is the second most common cause of death following CEA. Stroke rates associated with CEA in large randomized trials are generally <3% for asymptomatic patients and < 5% for symptomatic patients [13, 14]. The treatment involves ensuring adequate anesthetic depth and normothermia and possibly placing a shunt if the patient is not tolerating balloon occlusion of the carotid artery. In addition, hypotension should be aggressively treated as appropriate during the occlusion period to aid perfusion. One of the methods to treat this hypotension involves a fluid bolus if due to dehydration, and/or adding an infusion of Inj. phenylephrine titrated to effect, treating with bolus of Inj. ephedrine 5–10 mg titrated to effect. The goal is to maintain the patient's blood pressure at or above the baseline.



Imaging demonstrating successful placement of carotid stent. (**a**) Lateral angiogram demonstrating a greater than 50% carotid stenosis. (**b**) Deployment of distal embolic protection device above the stenosis. (**c**) Stent deployment. (**d**) Post-stent balloon angioplasty. (**e**) Final result. (Photo Courtesy: Dr. Charles Matouk, Associate Professor of Neurosurgery; Chief, Neurovascular Surgery; Director, Neurovascular/Endovascular Fellowship, Yale School of Medicine, New Haven, CT)

Question 9:
What are the other potential intraoperative complications and how would you approach treating them?

Answer:
Apart from those mentioned above, there can be a few other potential intraoperative complications during placement of a carotid stent.

- Major blood loss: due to vascular injury.
- Carotid artery dissection: from the guidewire/during the stent placement.
- Myocardial ischemia: in major randomized trials, the periprocedural incidence of myocardial infarction with CAS has ranged from 1 to 4%. Risk factors for myocardial infarction included older age, coronary heart

disease, peripheral artery disease, and carotid restenosis [15–17].
- Hematoma at the site of vascular access: due to inadequate hemostasis, and the fact that the patient may have received heparin intraoperatively, in addition to preoperative dual antiplatelet therapy.
- An angiographic "slow-flow phenomenon," appearing as reduced or absent anterograde flow in the internal carotid artery proximal to filter-type embolic protection devices (EPD), may be caused by occlusion of the filter membrane pores by microemboli and debris. In a single-center case series of 453 carotid artery interventions using filter-type EPDs, slow flow occurred in 42 procedures (9%) [18]. E.mbolic protection devices are typically deployed following placement of the guidewire and sheath and are removed once the carotid artery stent has been deployed and expanded in the appropriate position.
- Dislodgement of atherosclerotic emboli from aortic wall during catheterization.

Question 10:
Surgery is now completed. However, the patient is not waking up. What is your differential diagnosis?

Answer:
Multiple causative factors are considered in delayed emergence from anesthesia. In this particular situation, some of the causes may include

- Residual anesthetic: residual inhalational agents/intravenous agents, excessive narcotics.
- Electrolyte imbalances.
- Hypoglycemia.
- Stroke.
- Intracranial hemorrhage.
- Subclinical seizures.
- Increased intracranial pressure.

Immediate recognition and treatment are important. Arterial blood gas analysis will aid in diagnosing electrolyte imbalances, glucose levels, and acid-base status. If stroke/intracranial hemorrhage is suspected, an immediate computed tomography (CT) scan of the brain is important in diagnosis. The patient may require postoperative intubation and mechanical ventilation until the clinical scenario improves.

Question 11:
You treat appropriately, and the patient is now waking up. What are your strategies for minimizing hemodynamic changes during emergence?

Answer:
It is important to minimize the sympathetic responses during emergence and extubation. Commonly seen are tachycardia and hypertension, both of which are not desirable in this patient due to her underlying coronary artery disease, as well as her recent carotid surgery. In addition, coughing or bucking on the endotracheal tube may disrupt the suture lines and hemostasis at the femoral vascular access site and increase the chances of hematoma. Various strategies can be employed to minimize this scenario. A bolus of Inj. lidocaine 1-–1.5 mg/kg or a bolus of any short-acting narcotic e.g., remifentanil can be used to facilitate a smooth wake up. Beta blockers e.g., esmolol can be used to treat the heart rate and blood pressure during emergence. Deep extubation may be considered; however, it is not desirable as it impedes immediate postoperative neurological examination.

Question 12:
What is cerebral hyperperfusion syndrome and how do you treat it?

Answer:
Cerebral hyperperfusion syndrome occurs as a result of hypertensive encephalopathy and is characterized by severe headache and various neurological deficits, the etiology of which is typically ischemia-reperfusion injury in the setting of impaired autoregulation.

Postoperative reperfusion injury: Cerebral hyperperfusion syndrome (CHS) is an extreme form of cardiovascular instability which occurs in 1% of patients undergoing CEA, typically 2–7 days after surgery. Patients usually present with a hypertensive encephalopathy, that is,

severe headache, variable neurological deficits, blurry vision, seizures, and marked hypertension. The etiology is probably an ischemia–reperfusion injury with impaired cerebral autoregulation in areas of the brain which were previously under-perfused. CHS can lead to cerebral edema and cerebral hemorrhage [19]. Treatment of CHS include strict blood pressure control and treatment of associated signs of increased intracranial pressure, if present.

Question 13:
What are the other postoperative complications you may encounter in this patient?

Answer:
Some of the other postoperative complications which may occur include wound hematoma, wound infection (appropriate timing of perioperative antibiotics is essential), re-exploration of the surgical site, contrast-related renal impairment, etc. Myocardial ischemia can occur in the postoperative period as well. Inadequate BP control due to disrupted baroreceptor function may pose a challenge in the postoperative period.

Carotid stent thrombosis and restenosis: Acute and subacute in-stent thrombosis has been reported in up to 5% of patients following carotid artery stenting, some of these may be related to discontinued or inadequate dual antiplatelet therapy [18]. Beyond 30 days, early restenosis after carotid revascularization is mainly due to neointimal hyperplasia, which is related to vascular injury due to stent overdilation or imperfect positioning of the carotid stent, seen more often in women and in patients with poorly controlled diabetes or hyperlipidemia or with history of prior radiation [8].

Question 14:
How would you manage postoperative pain in this patient?

Answer:
Control of postoperative pain is important in this patient given her cardiac risk factors, it is important to avoid tachycardia and hypertension. Local anesthesia can be used initially at the site of femoral access. In addition, carefully titrated narcotics such as Inj. fentanyl 25–50 μg or Inj. hydromorphone 0.2–0.4 mg titrated to effect can be used. Nonopioid analgesics are beneficial in reducing narcotic requirement, e.g., Inj. acetaminophen 1000 mg. NSAIDs are typically avoided due to bleeding risk in the immediate postoperative period. Adequate transition to oral pain medications when patient is able will be useful for long-term control.

Question 15:
Does this patient require postoperative ICU? Why?

Answer:
With the complex nature of this type of surgery, as well as preexisting risk factors, it is advisable for this patient to be monitored in the intensive care unit (ICU). ICU admission also facilitates frequent neurological exams, as well as strict control of BP and other parameters.

Following the CAS procedure, we recommend continuation of dual antiplatelet therapy with aspirin 325 mg daily and clopidogrel 75 mg once daily for at least 6 weeks (grade 1B). For patients with a history of neck irradiation, we suggest continuing these agents indefinitely (grade 2C). For all other patients, after CAS, we recommend continuing aspirin 325 mg daily indefinitely (grade 1B) [20].

Multiple Choice Questions

1. What is the efferent limb of carotid sinus baroreceptor reflex?
   (a) Trigeminal nerve.
   (b) Vagus nerve.
   (c) Facial nerve.
   (d) Optic nerve.
   Answer: b

   Vagus nerve. The carotid sinus baroreceptor reflex starts with specialized neurons called baroreceptors. These are stretch receptors located in the wall of the aortic arch and carotid sinus. Any manipulation or dilation of these receptors cause the reflex to be activated, sending signals to medullary nuclei, with the vagus nerve as one of the efferent limbs, causing bradycardia and hypotension.

2. Some of the potential intraoperative complications during carotid artery stenting include.
   (a) Carotid artery dissection.
   (b) Severe bradycardia.
   (c) Hematoma at femoral access site.
   (d) All of the above.
   Answer: d

   All of the above. Any of the above complications may be seen during carotid artery stenting. Constant vigilance and monitoring is essential for early diagnosis and treatment.
3. Causes of delayed wake up after carotid surgery include.
   (a) Residual anesthetic.
   (b) Cerebral hemorrhage.
   (c) Hypoglycemia.
   (d) All of the above.
   Answer: d

   All of the above. All of the above are potential causes of delayed emergence after carotid artery surgery.
4. Two days after successful carotid artery stenting, the patient complaints of headache and blurry vision. Heart rate is 90 b/m and BP is 190/100 mmHg. What is the initial treatment of choice?
   (a) Labetalol.
   (b) Nitroglycerin.
   (c) Aspirin.
   (d) Morphine.
   Answer: a

   Labetalol. This patient is most likely experiencing symptoms of cerebral hyperperfusion syndrome. Immediate recognition and timely treatment are important. Blood pressure control is the appropriate initial treatment. In this patient, titrated doses of Inj. labetalol are appropriate given the heart rate and blood pressure. Although morphine will help treat the pain, if any, the symptoms are due to cerebral hyperperfusion syndrome which needs to be addressed first.

References

1. Fleisher LA, et al. 2014 ACC/AHA Perioperative Guideline: Executive Summary.
2. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A, Goldman L. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100(10):1043–9.
3. Devereaux PJ, Goldman L, Cook DJ, Gilbert K, Leslie K, Guyatt GH. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. CMAJ. 2005;173(6):627–34.
4. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011;58:e44–122.
5. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg. 2011;54(3):e1–31.
6. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 1991;325(7):445–53.
7. Kernan WN, Ovbiagele B, Black HR, American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 45(7):2160–236.
8. Bonati LH, Gregson J, Dobson J, et al. Restenosis and risk of stroke after stenting or endarterectomy for symptomatic carotid stenosis in the international carotid stenting study (ICSS): secondary analysis of a randomised trial. Lancet Neurol. 2018;17:587.
9. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. Circulation. 2007;116:e418–500.

10. Leichtle SW, Mouawad NJ, Welch K, et al. Outcomes of carotid endarterectomy under general and regional anesthesia from the American College of Surgeons' National Surgical Quality Improvement Program. J Vasc Surg. 2012;56:81.
11. Gough MJ, Bonham A, Horrocks M, Colam B, Lewis SC, Rothwell PM, et al. GALA: an international multicentre randomised trial comparing general anesthesia versus local anesthesia for carotid surgery. Trials. 2008;9:28.
12. Kirchheim HR. Systemic arterial baroreceptor reflexes. Physiol Rev. 1976;56:100–77.
13. Ladak N, Thompson J. General or local anaesthesia for carotid endarterectomy? Contin Educ Anaesth Crit Care Pain. 2012;12(2):92–6.
14. Wu TY, Anderson NE, Barber PA. Neurological complications of carotid revascularisation. J Neurol Neurosurg Psychiatry. 2012;83:543.
15. Hill MD, Brooks W, Mackey A, et al. Stroke after carotid stenting and endarterectomy in the carotid revascularization Endarterectomy versus stenting trial (CREST). Circulation. 2012;126:3054.
16. Boulanger M, Camelière L, Felgueiras R, et al. Periprocedural myocardial infarction after carotid Endarterectomy and stenting: systematic review and meta-analysis. Stroke. 2015;46:2843.
17. Brott TG, Hobson RW 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med. 2010;363:11.
18. Casserly IP, Abou-Chebl A, Fathi RB, et al. Slow-flow phenomenon during carotid artery intervention with embolic protection devices: predictors and clinical outcome. J Am Coll Cardiol. 2005;46:1466.
19. Stoneham MD, Thompson JP. Arterial pressure management and carotid endarterectomy. Br J Anaesth. 2009;102:442–52.
20. https://www.uptodate.com/contents/carotid-artery-stenting-and-its-complications?sectionName=Bleeding%2Fhematoma%2Fpseudoaneurysm&topicRef=90608&anchor=H22&source=see_link#H101619074.

Management of Patient with Vein of Galen Malformation

29

Kiran Jangra, Sanket Agrawal, and Shiv Lal Soni

Stem Case Terminology

A 5-month-old female child brought to the emergency room with the history of failure to thrive, excessive sweating, and unable to take the breastfeed in single sitting. The patient is a preterm neonate delivered by cesarean section for fetal distress, with a birth weight of 1.5 kg.

Examination: The patient was lethargic with slowing of all movements. Heart rate—150/min, blood pressure—60/30 mmHg. On systemic examination, the child had a hyperdynamic precordium with a pansystolic murmur in the mitral area and hepatomegaly. Enlarged head size with bruit when auscultated through fontanel. Neurological examination revealed global delay in milestones.

Investigation: The blood investigations revealed a deranged coagulation profile with a raised activated partial thromboplastin time of 57 seconds. Serum electrolytes were Na—143 mEq/L, K—4.0 mEq/L, and the arterial blood gas showed pH —7.1, $PaCO_2$—39 mmHg, PO_2—69 mmHg, H_2CO_3—26.1 mEq/L. Two-dimensional transthoracic echocardiography demonstrated a severe pulmonary arterial hypertension with an atrial septal defect with the right to left shunt, biventricular hypokinesia with ejection fraction of 30%.

Imaging: Computed tomography scan showed ventriculomegaly. Magnetic resonance angiogram confirmed a large vein of Galen malformation (VOGM).

Key Questions

1. What is VOGM?
2. What is the embryology of VOGM?
3. What is the physiopathology of VOGM?

Case continued: The patient was intubated and shifted in the pediatric intensive care unit. Prognosis was explained and parents were counseled. The plan was made to stabilize the medical condition of the child first followed by emergency embolization. Certain investigations were done prior to the definitive intervention.

4. How will you classify?
5. What are the various clinical presentations of VOGMs?
6. What are the diagnostic modalities?
7. How will you plan the treatment?

Case continued: The child was posted for transarterial embolization. Partial occlusion was done and symptoms of heart failure started improving and all the vasopressors were weaned off. Child was followed up by serial ultrasonography of

K. Jangra (✉) · S. Agrawal · S. L. Soni
Department of Anaesthesia and Intensive Care, Postgraduate Institute of Medical Education and Research, Chandigarh, India

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_29

head and was called again at 8 months of age for redo embolization to achieve complete occlusion of the VOGM. The child came back again at 7 months with features of congestive heart failure. Prognosis was explained to the parents.

8. What are the anesthetic concerns for a patient with VOGM?
9. What special preparation will be required for the intraoperative care of this patient?
10. What monitors would you apply intraoperatively for the procedure?
11. What other intraoperative difficulties do you anticipate, and how will you manage them?
12. What is the prognosis of the diseases?

29.1 Discussion

29.1.1 Vein of Galen Malformation (VOGM)

The **vein of Galen** (VOG) is also known as the **great cerebral vein** or **great vein of Galen.** It is a short trunk that is formed by the union of both the internal cerebral veins and basal vein of Rosenthal (Fig. 29.1). It lies in the quadrigeminal cistern then it curves backward and upward around the splenium of the corpus callosum and finally drains into the confluence of inferior sagittal and straight sinuses. In utero, it arises from the median prosencephalic vein of Markowski as a normal structure. Vein of Galen malformations (VOGMs) are the rare congenital abnormalities that are believed to comprise <1 of all intracranial and up to 30% of all pediatric vascular malformations [1, 2]. VOGM is a misnomer, as it has been demonstrated that it represents the embryonic median prosencephalic vein rather than the vein of Galen. There is an aneurysmal dilatation of vein which may be fed by various abnormal arteriovenous connections. In 1895, Steinheil referred these as Galenic malformation for the first time and denoted as a "varix aneurysm." [3] Subsequently, these lesions are also known as the aneurysms or arteriovenous aneurysms of the vein of Galen, vein of Galen malformations/aneurysmal malformations, and median prosencephalic arteriovenous fistulas.

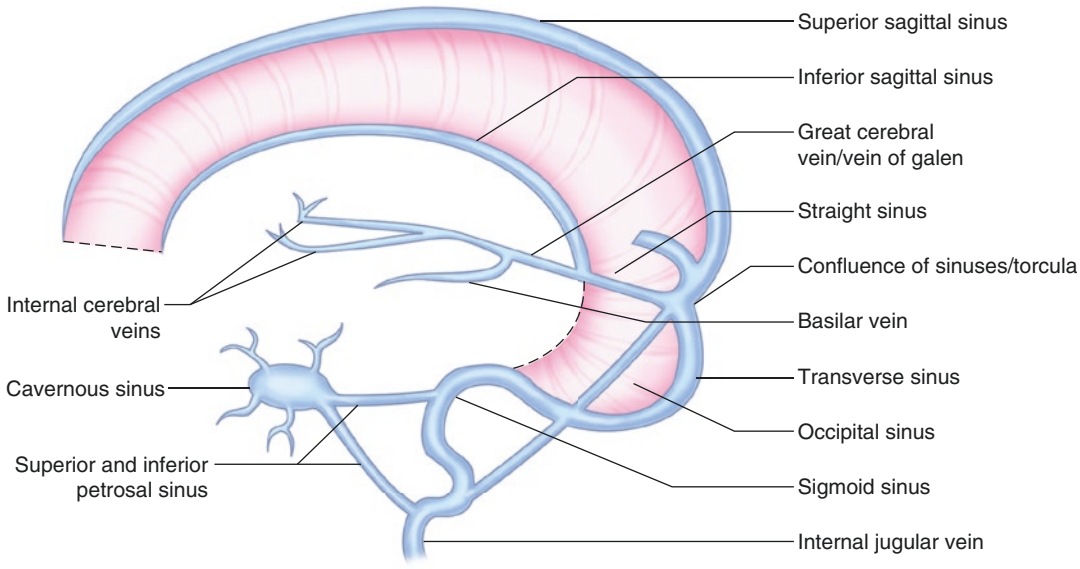


Fig. 29.1 Schematic illustration of cerebral venous drainage. Vein of Galen is the part of deep cerebral venous system which is formed by internal cerebral veins and basilar vein and finally drains into the confluence of inferior sagittal and straight sinuses

29.1.2 Embryology

The VOGMs are believed to represent the persistence of embryonic vascular arrangements particular to a developmental period. Hence, it becomes necessary to have sound knowledge embryology of the cerebral vasculature to understand the pathophysiological features and unique architecture of vessels in VOGMs. Cerebral vasculature develops in three stages including extraembryonal supply (open neural tube, nurtured by the amniotic fluid), extrinsic vascularization (highly vascularized neural crest surrounding the neural tube form the network of arteries and veins), and intrinsic vascularization (development of blood vessels within the cerebral parenchyma) [4, 5]. The normal vein of Galen originates from differentiation of arteriovenous tangles of prosencephalic vessel group, the median prosencephalic vein, which makes the arteriovenous fistulous connections during embryonic life. The fistulous connections normally involute between the fifth and seventh weeks of development, and later at around 3 months of developmental age, it forms the vein of Galen [4]. In true vein of Galen malformation, these primitive arteriovenous connections persist where the median prosencephalic vein receives feeders from prosencephalic (anterior and middle cerebral, anterior and posterolateral choroidal arteries) and median prosencephalic (posteromedial choroidal, posterior thalamoperforating, quadrigeminal, and superior cerebellar) arteries [2, 5]. These high-flow connection drain into the falcine sinus that connects to superior sagittal sinus, only during embryonic life (Fig. 29.2). Persistence of these fetal patterns interferes with the development of other sinuses such as the straight sinus and explains various vascular anomalies that are associated with VOGMs.

29.1.3 Angioarchitecture of VOGMs [6–8]

Vein of Galen malformations are the midline structures, extending from the interventricular foramen to the choroidal fissure, and laterally to the atria. The following vessels contribute to the formation of VOGMs.

Arterial Feeders: Feeders are usually bilateral and symmetrical. Following arteries supply the VOGMs:

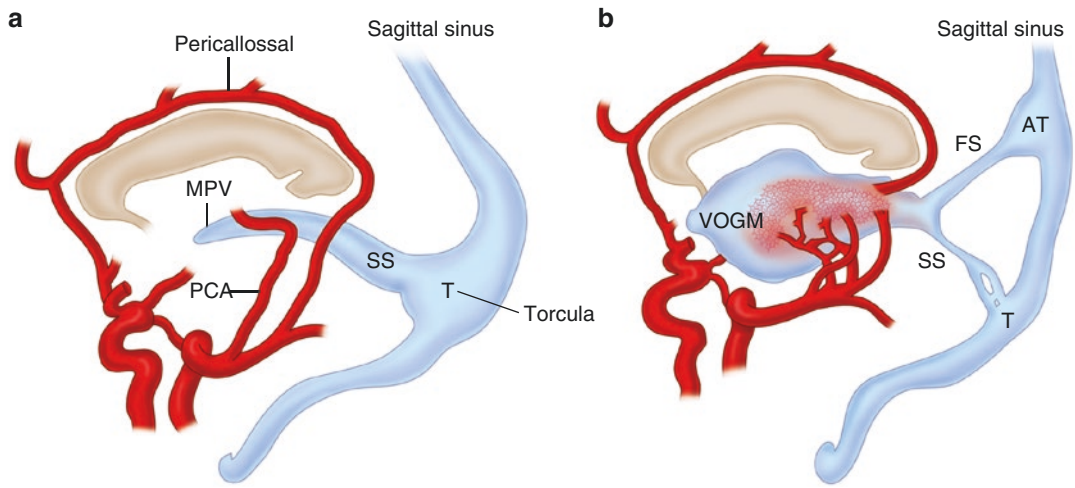


Fig. 29.2 Schematic illustration of the development of a vein of Galen malformation (VOGM). (**a**) Showing normal anastomosis between the posterior branches of the pericallosal arteries and distal branches of the posterior cerebral arteries (PCA) during fetal life. (**b**) Showing VOGMs where anastomoses degenerate and end up in the enlarged and malformed median prosencephalic vein of Markowski (MPV). Associated venous malformations are stenosis, fenestration, duplication, or absence of straight sinus (SS), decrease or absence of torcula (T), and sometimes an aberrant presence of falcine sinus (FS) and an accessory torcula (AT)

(a) Choroidal arteries: In most of the cases, all of the choroidal arteries feed the VOGMs.
(b) Subependymal arterial network: It arises from the posterior portion of circle of Willis.
(c) Thalamoperforators: These are the rare feeder.

Venous drainage: The embryonic venous drainage is persistent where the median vein of the prosencephalon (dilated vein is called as VOGM) drains through falcine sinus into the superior sagittal sinus or the posterior venous sinuses. These malformations interfere with the development of normal venous architecture and are associated with other venous abnormalities including:

(a) The straight sinus is hypoplastic or absent in most of the patients.
(b) Venous outlet obstruction may be present.
(c) There is preferential drainage away from the deep cerebral venous system.

Because of these malformations, the deep brain structures drain into alternate venous pathways that typically include thalamic and subtemporal or lateral mesencephalic veins, which have an epsilon shape on lateral view angiogram.

29.2 Classification

Various classifications are described in the literature for VOGMs, including Litvak categories, Mortazavi, Lasjaunias, and Yaşargil types. These classifications and their clinical importance are tabulated in Table 29.1.

Litvak et al., in the 1960s, proposed the classification system for VOGMs for the first time [9]. They classified VOGMs in three categories based on the review of the literature, personal experiences, clinicopathological considerations, and amenability to surgery. Category A was termed as "Aneurysms of the great vein of Galen," which included a singular dilation of VOG. It was continued with a dilated straight sinus and torcula, and various anomalous branches of the anterior and posterior circulation were the major feeders. Category B was termed as "Racemose Conglomerations of blood vessels" deep in the cerebral structures with dilated deep venous structures and included a vermiform tangle of arteries and veins in the midline. The deep cerebral structures drain centripetally into dilated deep veins and sinuses. Category C was termed as "transitional types of midline arteriovenous shunts" and included singular dilations of vessels other than the VOG. This classification had lost its popularity after the newer classifications which are currently more commonly used [6, 10].

Another classification, by Mortazavi et al., was based on arterial feeders, clinical features, and age [10]. A score of 0 includes any feeder other than P1–2 (posterior cerebral artery), thalamoperforators, choroidal and direct feeders from the basilar artery; absence of heart failure; and age $\geq$ 5 months. In the presence of feeders described above, the presence of heart failure, and age < 5 months, a score of 1 was given. The authors proposed that this classification will help in making an appropriate decision for the treatment.

Lasjaumas classified VOGMs as type 1 (choroidal) and type 2 (mural) [5, 8]. This classification is based on the concept that there are normally multiple capillary shunts in the early stages of development, and they disappear with development. If these shunts persist, then it results in vascular malformations. Type 1 is the most common and more complex form, where multiple feeding arteries enter the median prosencephalic vein from the anterior surface. These feeding arteries are arteries of anterior circulation including bilateral anterior and posterior choroidal, anterior cerebral, thalamoperforating, and collicular or quadrigeminal arteries [4, 11]. Clinically, this type of VOGMs is the most severe form and frequently present as a high-output car-

Table 29.1 Classifications of vein of Galen malformations

Classification	Basis	Categories	Clinical Importance
Litvak	• Review of literature • Personal experiences • Clinicopathological considerations • Amenability to surgery	**Category A:** A singular dilation of VOG (aneurysms of the great vein of Galen)	• In comparison with category A, category B tends to become symptomatic at an older age and manifests with hemorrhage rather than hydrocephalus and cardiac failure • Category B is probably true arteriovenous malformations (AVMs) • A or C is probably dural AVFs
		Category B: A vermiform tangle of arteries and veins in midline (racemose conglomerations of blood vessels)	
		Category C: Singular dilations of vessels other than the VOG (transitional types of midline arteriovenous shunts)	
Mortazavi	• Arterial feeders • Clinical features • Age	**Score 0:** • Any feeder other than – P1–2 (posterior cerebral artery) – Thalamoperforators, choroidal – Direct feeders from basilar artery • Absence of heart failure • Age of ≥5 months	• **Score 0–1**: Consider endovascular therapy • **Score 2:** Consider endovascular but urgent treat in multiple stages • **Score of 3:** Consider endovascular or palliative treatment and treated in multiple stages
		Score 1: • Presence of feeders from – P1–2 (posterior cerebral artery) – Thalamoperforators, choroidal – Direct feeders from basilar artery • Presence of heart failure • Age < 5 months	
Lasjaumas	Persistence of embryonic vasculature	**Type 1 (choroidal, most common):** Multiple feeding arteries enter the median prosencephalic vein from anterior surface	• Most severe form of the disease • Causes high-output cardiac failure in the newborn • Multiple high-flow fistulas • Little outlet restriction
		Type 2 (mural): Either single or multiple fistulas enter through the inferolateral wall of the median prosencephalic vein	• Smaller number of fistulas • More outflow obstruction • Associated with – More severe dilation of the median prosencephalic vein – Manifest later in infancy as macrocephaly, hydrocephalus – Failure to thrive • Cardiac failure, if present, is mild • Cardiomegaly may be asymptomatic

(continued)

Table 29.1 (continued)

Classification	Basis	Categories	Clinical Importance
Yasargil	Angioarchitecture	**Type I:** Relatively few fistulous connection and feeders arise principally from the pericallosal (both anterior and posterior) or posterior cerebral arteries	• Yaşargil's types I–III are comparable to Litvak's type A • Yaşargil's types IVA–B to Litvak's type B • Yaşargil's type IVC falls into Litvak's category C • Litvak and Yaşargil are important for considering open surgery • Lasjaunias's classification is important for endovascular management • the internal cerebral veins remain invisible on angiograms in types I–III • In type IV the internal cerebral and mesencephalic veins are dilated and synchronically filling with the dilated vein of Galen, the straight sinus, or the fetal parietooccipital vein on angiography
		Type II: Multiple fistulous connections and feeders mainly arise from the thalamoperforators	
		Type III (true or choroidal type): Most common type. High-flow feeders that are combination of both type I and type II	
		Type IV (secondary type): Dilatation of the vein of Galen resulting from shunting from adjacent parenchymal AVM or dural AV fistula, or outlet obstruction It has three subtypes **Type IVA**: Aneurysmal dilation of the vein of Galen resulting from shunting from an adjacent thalamic AVM **Type IVB:** Similar to type IVA but with the AVM being mesencephalic instead of thalamic **Type IVC:** Thalamomesencephalic or mesodiencephalic plexiform malformation along with an adjacent and separate cisternal AVF to the vein of Galen	

diac failure in the newborn due to the presence of several high-flow fistulas. In type 2, either single or multiple fistulas enter through the inferolateral wall of the median prosencephalic vein and may be unilateral or bilateral. The feeding arteries arise mainly from the collicular or quadrigeminal and/or the posterior choroidal arteries. There are a lesser number of fistulas, but an obstruction in the outflow results in more severe enlargement of the median prosencephalic vein. Patients with these lesions commonly manifest during infancy as head enlargement, obstructive hydrocephalus, and failure to thrive. Due to the small number of fistulas, cardiac failure is rarely seen, and if present, it is of mild severity and usually asymptomatic [8].

Yasargil classified VOGMs into four categories based on the angiographic findings (Table 29.1) [12]. Type 1, 2, and 3 lesions involve direct fistulous communication with the vein of Galen and with no other proximal nidus. Type 4 lesions represent parenchymal arteriovenous malformations (AVMs), which drain into the vein of Galen.

29.3 Pathophysiology

The presence of VOGMs not only affects a cerebral system but also has systemic effects. The most commonly affected system is the cardiac system due to increased shunting of blood in the fistulae. The cerebral system is usually affected by local mass effect and change in cerebrospinal fluid or blood flow dynamics. Figure 29.3 depicts the pathophysiology of VOGM.

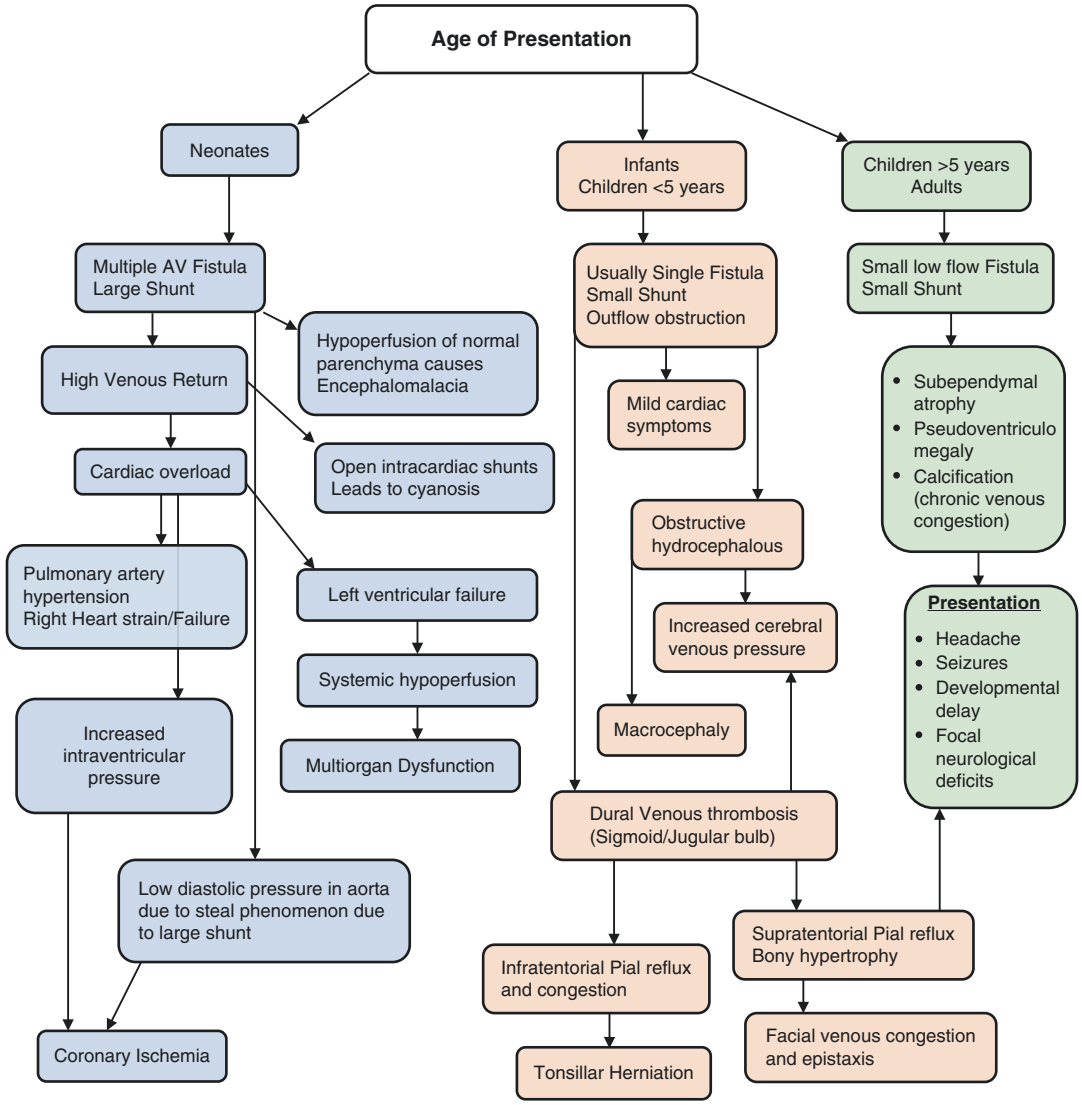


Fig. 29.3 Pathophysiology of vein of Galen malformations. Larger shunt due to high-flow fistulas generally present at early age while low-flow fistulas may go undetected to late childhood or adulthood

29.3.1 Cardiac Manifestations

During intrauterine life, the heart is usually protected from the high venous return of VOGMs due to the presence of low-resistance placental circulation. Here, the left ventricle predominantly supplies the brain (fistula) while the right ventricle works in parallel to the left ventricle and supplies the placenta and the rest of the body [13]. Hence the workload is shared by two low-resistance systems, the cerebral and placental, and overall workload on the heart is not affected (Fig. 29.4a). After birth, the intracardiac shunts (foramen ovale and ductus arteriosus) are closed, and both the ventricles work in series. The high output from fistula is received by right ventricle that supplies the high-resistant circuit (pulmonary vasculature), and this results in the increased

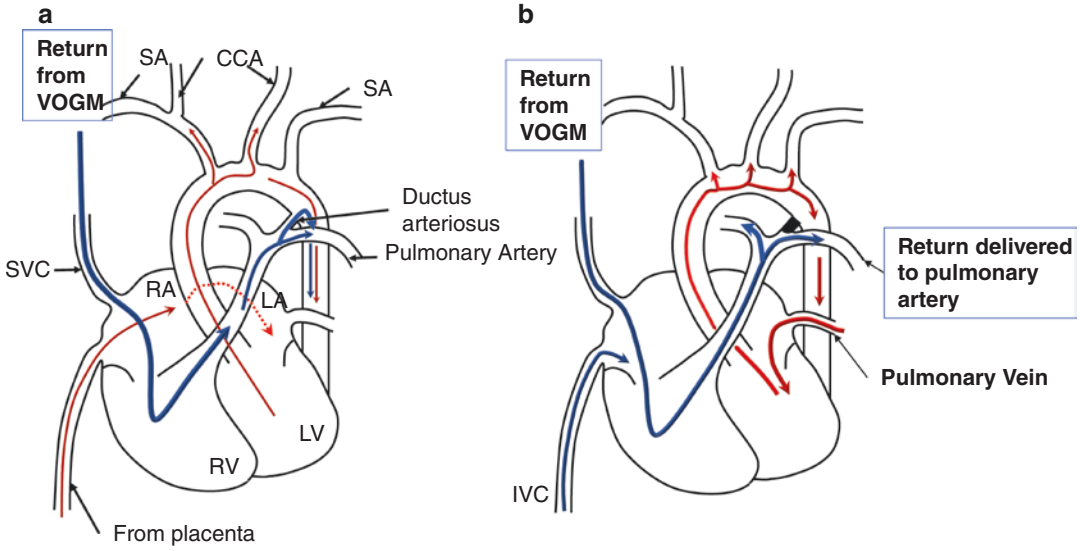


Fig. 29.4 Cardiac physiology in patients with vein of Galen malformations. (**a**) Fetal circulation: Low resistance of the placental circulation prevents high flow though the intracranial shunt. Both sides of heart work parallel to each other. (**b**) Early postnatal circulation: Cessation of placental flow suddenly increases the forward flow within the intracranial shunt and across the pulmonary vasculature and may result in congestive cardiac failure. Both sides of the heart work in series. Size of the arrowhead indicates volume of flow. Large arrowhead represents high flow and Small arrowhead represents low flow. Color of arrowheads indicates oxygen saturation. Red arrowhead represents high oxygen saturation and blue arrowhead represents low oxygen

venous return to the left ventricle. Thus, the work of both the ventricles is increased leading to cardiomegaly and finally cardiac failure (Fig. 29.4b). There is a drastic increase in fistula blood flow after exclusion of the low-resistance placental circulation. Being a low-resistance circuit in the brain (large arteriovenous fistula), most of the left ventricular output is diverted to the brain (~80%), and it compromises the systemic circulation. To compensate for this physiological change, the cardiac output and blood volume are increased to maintain the systemic perfusion. The volume overload in right atrium causes opening of foramen ovale and ductus arteriosus. These shunts lead to the flowing of blood from right to left circulation and result in the cyanosis. The increased blood flow in the pulmonary circulation results in pulmonary artery hypertension. Large shunts reduce the diastolic pressure of aorta that reduces coronary artery flow. Also, the ventricular intracavitary pressure is raised due to increased cardiac output. Both of these factors may contribute to the reduction in subendocardial blood flow and compromise the myocardial perfusion [13–15]. Thus, various factors are responsible for the cardiac failure in neonates/infants, and this failure is usually resistant to usual medical treatment.

29.3.2 Neurological Manifestations

Most of the neurological manifestations of VOGMs occur due to local mass effect and cerebral venous hypertension. As described in previous section, these malformations are associated with various other venous anomalies such as dysgenesis, stenosis, and occlusion of normal venous architecture. Venous occlusion distal to high-flow arterial feeders results in raised cerebral venous pressure. The arachnoid granulations are also not fully developed in infants, and most of the ventricular CSF is absorbed directly into the brain parenchyma across the ventricular ependyma which is subsequently drained through the medullary veins. The high venous

pressure, as found in VOGMs, is transmitted to the medullary veins that hamper the resorption of CSF, and this results in hydrocephalus and cerebral edema [16]. The hydrocephalus may also develop due to the aqueductal compression, but this is not very commonly seen [17, 18]. Chronic venous hypertension causes cerebral tissue hypoxia and progressive cerebral parenchymal damage that results in cognitive impairment, delayed milestones, and mental retardation [19]. In longstanding cases, pseudoventriculomegaly occurs secondary to parenchymal atrophy that mimics the hydrocephalous. Other consequences of cerebral venous hypertension include intracerebral hemorrhage and seizures from cortical venous (pial) reflux. The venous outflow obstruction may divert the blood flow into the cavernous sinus, and that has communications with the extracranial venous system such as facial veins, basilar, and pterygoid plexus. This obstruction results in prominent facial venous channels and epistaxis [20].

There may be occlusion of various venous channels that are typically observed in transverse sinus, sigmoid sinus, and the jugular bulb. In such a situation, blood from posterior fossa is drained mainly by superior and inferior petrosal sinuses. If cavernous sinus is also underdeveloped, then there may occur severe venous congestion in posterior fossa that leads to tonsillar herniation.

29.4 Clinical Presentation

The clinical classification system given by Gold et al. in 1964 categorizes the clinical presentation and pathophysiology in three age groups of patients including neonates, infants and children, and older children and adults [21].

29.4.1 Neonates

The patients with multiple fistulas and a more severe form of VOGMs usually present immediately after birth and develop high-output congestive cardiac failure. The clinical features depend upon the severity of disease and characteristics of the lesion such as the size of the shunt, venous drainage, arterial feeders, and the patient's response. The cardiac symptoms may vary from mild asymptomatic cardiomegaly to severe cardiac failure. Due to the higher venous return in the right atrium, its pressure rises above the left atrium pressure, resulting in the opening of the foramen of ovale or ductus arteriosus and right to left shunt. These shunts lead to the cyanosis that may be mistaken as congenital cyanotic heart disease [22].

The myocardial workload is raised in an attempt to increase cardiac output to maintain systemic flow as most of the cardiac out passes through low-resistance fistulas. These fistulas decrease the diastolic aortic flow that compromises the coronary blood supply. Also, there is increased ventricular chamber pressure due to higher blood volume returning to the heart. These factors lead to subendocardial ischemia that can be detected on electrocardiography [23, 24]. These patients may develop multiorgan failure including renal and hepatic failure due to low systemic perfusion pressure. Such failure is usually refractory to the medical management and responds only to the prompt reduction in shunt size.

29.5 Infants and Children

Infants and children may have a single fistula, and so cardiac manifestations are usually very mild or may be absent due to the smaller shunt. These patients commonly develop hydrocephalus and macrocephaly because of obstructed venous drainage leading to cerebral venous hypertension. As fontanelles are open in this age group, any lesion that increases intracranial pressure will lead to enlargement of the head size. Longstanding cerebral venous hypertension may lead to a delay in developmental milestones. Systemic and cerebral venous congestion lead to cardiac decompensation and hypothalamic and hypophyseal dysfunction that may cause failure to thrive [25].

29.6 Older Children and Adults

Low-flow fistulae may remain asymptomatic until late children and even adulthood. As cranium is closed, these patients may present with features of raised intracranial pressure including headache and seizures (secondary to parenchymal calcifications). These patients may also develop delay in the development, focal neurological deficits, proptosis, and epistaxis. Rerouting of blood into the pial veins leads to subarachnoid or intracerebral hemorrhage in this age group of patients [12].

29.7 Imaging

Imaging is needed to understand the anatomical and dynamic characteristics of VOGMs. The commonly used imaging techniques are transcranial Doppler ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI).

VOGMs can be detected by prenatal ultrasound during the third trimester of pregnancy [26–29]. Prenatal ultrasonography can also assess the fetal cardiovascular system [30]. Once discovered in antenatal period, these patients should be referred to higher centers for the delivery as early intervention of VOGMs can optimize the myocardial functioning and have a better neurological outcome. For the definitive management of VOGMs, an accurate and complete imaging of angioarchitecture is required to locate the fistula. Various imaging techniques include contrast-enhanced CT and MRI, magnetic resonance angiography (MRA), and digital subtraction cerebral angiography (DSA, gold standard modality). The role of imaging modalities is to noninvasively identify the number and sites of arteriovenous fistulae, the presence of thrombosis, other sinus abnormalities, and venous drainage of fistula. The use of DSA helps in the reduction of total contrast load during angiography and intervention can be planned in the same sitting to avoid multiple anesthesia exposures in neonates with cardiac failure [31, 32]. The multiplanar MRI is more sensitive over other noninvasive modalities such as CT angiography and MRA in demarcating even small feeders, the dynamic aspects of the venous drainage, and hemodynamic relationships of the arteriovenous shunt venous outflow and to plan for endovascular treatment [31]. Transcranial Doppler and CT or MRI are routinely used in older children and adults for follow-up of VOGMs.

29.7.1 Plain Radiograph

Pain X-ray is not being used commonly for the management. It may show calcified aneurysmal sac wall in nearly half of the thrombosed and 14% of the non-thrombosed aneurysm. Chest X-ray shows cardiomegaly and signs of congestive heart failure.

29.7.2 Ultrasound

This modality is useful during both the antenatal and postnatal periods. The VOGMs can be diagnosed during the antenatal period by the use of abdominal ultrasound in the third trimester. In addition to arteriovenous abnormalities, other complications such as hydrocephalus and cardiac dysfunction can also be detected on antenatal ultrasonography [26–30]. During the postnatal period, ultrasonography through open fontanel can help in confirming the diagnosis, and the use of Doppler ultrasonography helps in identifying the hemodynamic changes associated with the malformation (Fig. 29.5a,b) [33]. It is a useful and noninvasive modality for follow-up of patients with open fontanelles.

29.7.3 Computed Tomography (CT)

VOGMs appear as intensely enhancing lesion located in the midline in the cisterns on contrast-enhanced CT scan of the brain (Fig. 29.6a). Contrast CT delineates the angioarchitecture and parenchymal collateral veins. With CT scan, we can also detect hydrocephalous (Fig. 29.6b), periventricular white matter hypodensities, diffuse cerebral atrophy, diffuse chronic ischemic changes, parenchymal calcifications, focal parenchymal infarcts, and the brain stem compression

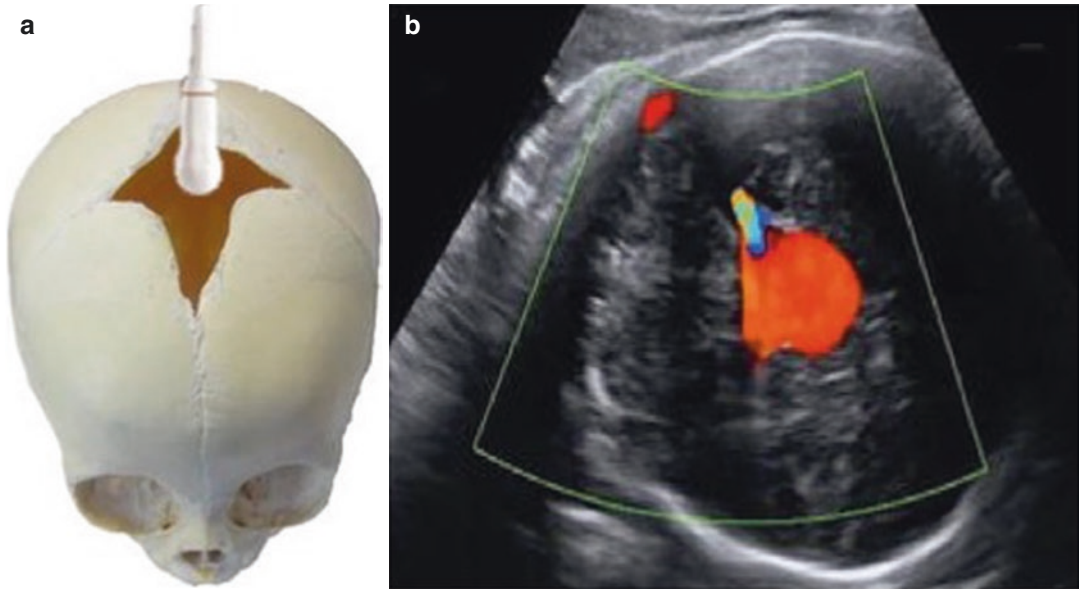


Fig. 29.5 (**a**) Schematic illustration of ultrasound (USG) through open fotanelle. (**b**) Scalp USG Doppler showing pulsatile blood flow in the vein of Galen malformation

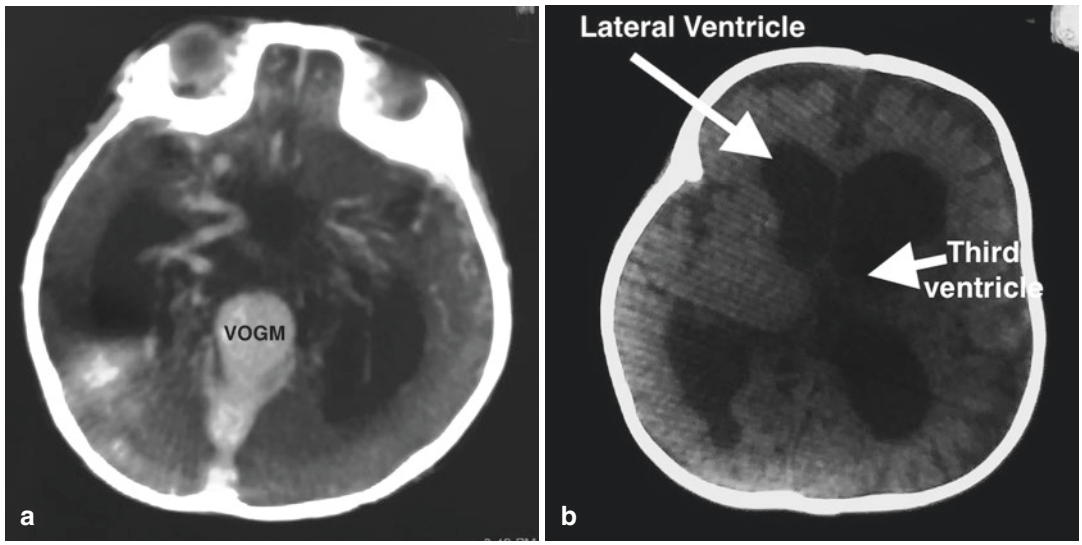


Fig. 29.6 Computed tomography (CT) head axial section. (**a**) Contrast CT showing midline hyperdense space occupying lesion. (**b**) Plain CT head showing ventriculomegaly

[5, 19]. The thrombosis within the aneurysmal sac appears as mixed hypodense, isodense, and hyperdense areas due to variable maturation stage of the clot. Central thrombus with peripheral circulating blood makes the "Target Sign" on contrast CT scan [32]. There may be peripheral calcification seen as a crescentic rim of hyperdensities which is a poor prognostic sign.

29.7.4 Magnetic Resonance Imaging (MRI)

MRI (Fig. 29.7a) and MR angiography (Fig. 29.7b–d) are gaining popularity for identifying the location of fistula, the presence of nidus, complete angioarchitecture (arterial feeders, venous sac, and venous drainage), and associated

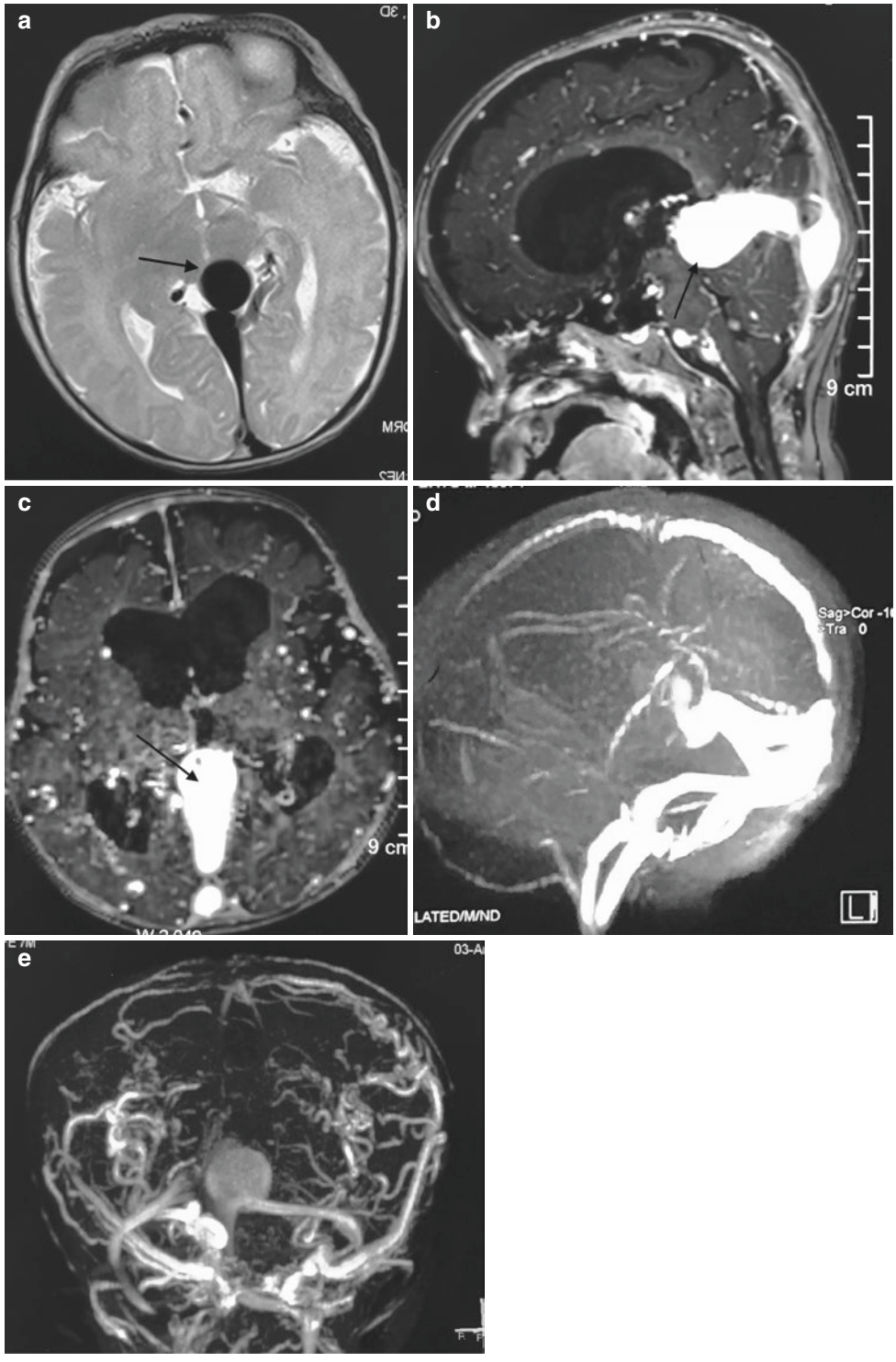


Fig. 29.7 Magnetic resonance imaging of brain. (**a**) T2-weighted image axial section showing hypointense lesion (VOGM, as shown by arrow). (**b**) MR angiography sagittal view. (**c**) MR angiography axial view. (**d**) Venous drainage of VOGM. (**e**) Three-dimensional reconstruction of MRA showing complete angioarchitecture of VOGM

venous abnormalities. The cerebral parenchymal changes are better appreciated on MRI.

29.7.5 Digital Subtraction Angiography

Angiography is the gold standard modality for the evaluation of VOGMs. It is considered to be superior to the other noninvasive modalities such as CT and MR angiography in recognizing small feeders, the dynamic aspects of the venous drainage, and hemodynamics of venous drainage VOGMs (Fig. 29.8).

29.8 Treatment Options

If untreated, VOGMs with large shunts have a very grave prognosis [34, 35]. The mortality is very high due to congestive cardiac failure in the patients who present during the neonatal period. So, it is essential that cardiac failure should be managed rapidly and aggressively. Any intervention should be delayed until the child is optimized. In a few cases, where shunt size is huge and heart failure is refractory to the medical management, an emergency embolization of the malformation may be attempted to reduce the shunt size [35]. Even after good emergency embolization, the neurological outcome may be disastrous in patients with encephalomalacia, severe brain damage, or severe parenchymal loss.

Various options are available for the management of VOGMs including surgery, embolization (transarterial, transvenous, and transtorcular) and gamma knife therapy.

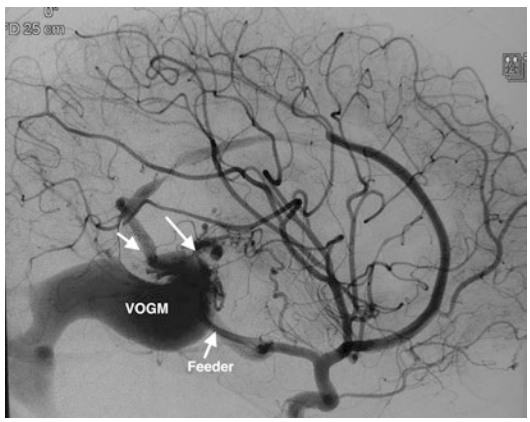


Fig. 29.8 Digital subtraction angiography showing complete angioarchitecture of VOGM

29.8.1 Surgery

Before the advent of embolization, microsurgical ligation of feeder and draining veins played some role in the management of VOGMs. Microsurgery provides an immediate cure, but it is technically difficult to perform and is less effective for treating complex VOGMs. Nowadays surgery is just an adjuvant to the embolization to treat the residual lesion. Surgery is poorly tolerated and is associated with very high mortality in neonates and patients with multiorgan dysfunction [17–19]. Even with advancement in technology, the complete elimination of the lesion by microsurgery is rarely achieved and is associated with severe complications including mortality [35–37].

29.8.2 Endovascular Embolization

Currently, endovascular treatment is considered as the treatment of choice for VOGM. The goal of treatment varies as per the age and clinical symptoms of the patients. In small neonates with congestive heart failure refractory to the treatment, the goal is to arrest or improve the heart failure by decreasing the shunt size and volume load to the heart. In this group of patients, even partial occlusion by emergency embolization is acceptable [38]. In neonates with compensated cardiac failure, the decision of treatment should be balanced between safe embolization (after the age of 5 months) and the risk of cerebral parenchymal damage. In stable children without features of cardiac failure, the goal of endovascular therapy is to prevent complications secondary to chronic cerebral venous hypertension and to stimulate the normal cerebral development [39]. In large lesion, the procedure should be performed in a staged manner to minimize complications.

Table 29.2 Bicêtre neonatal evaluation score[a]

Points	Cardiac function	Cerebral function	Respiratory function	Hepatic function	Renal function
5	Normal	Normal	Normal	–	–
4	• Overload • No medical treatment	• Subclinical • Isolated EEG abnormalities	• Tachypnea • Finishes bottle	–	–
3	• Failure • Stable with medical treatment	• Nonconvulsive intermittent neurologic signs	• Tachypnea • Does not finish bottle	• No hepatomegaly • Normal hepatic function	Normal
2	• Failure • Not stable with medical treatment	• Isolated convulsion	• Assisted ventilation • Normal saturation FIO_2 25%	• Hepatomegaly • Normal hepatic function	Transient anuria
1	Ventilation necessary	Seizures	• Assisted ventilation • Normal saturation FIO_2 25%	Moderate or transient hepatic insufficiency	Unstable diuresis with treatment
0	Resistant to medical therapy	Permanent neurological signs	• Assisted ventilation • Desaturation	• Abnormal coagulation • Elevated enzymes	Anuria

Maximal score = 5 (cardiac), 5 (cerebral), 5 (respiratory), 3 (hepatic), 3 (renal) = 21
Reprinted after permission from Lasjaunias P et al. The Management of Vein of Galen Aneurysmal Malformations. Neurosurgery 2006;59:(S3)184–194
[a]EEG electroencephalogram; FIO_2 fractional inspired oxygen

Lasjaunias et al. introduced a 21-point "**Bicêtre neonatal evaluation score**" to guide the treatment options that were based on the functioning of various major organ systems including cardiac, cerebral, hepatic, respiratory, and renal (Table 29.2) [8]. The neonates with a score of <8 usually carry a poor prognosis, and further treatment is not indicated. Whereas a score of 8–12 warrants an emergency endovascular management. Neonates having a score of >12 are well-preserved, and the medical management should be continued till the age of 5 months before an endovascular procedure.

There are three major routes of embolization including transarterial, transvenous, and transtorcular, and the choice of technique depends upon angioarchitecture of VOGMs [40].

The transarterial technique is employed where angiogram shows that feeding arteries are accessible and having sufficient caliber to negotiate the microcatheters. In this technique, the arterial feeders are approached through the umbilical artery or femoral artery to occlude of the fistula. Super-selective microcatheters are placed beyond the origin of any normal vessel. Currently, two embolization materials are being used including N-butyl-cyanoacrylate (NBCA) and Onyx liquid (ethylene vinyl alcohol in dimethyl sulfoxide solvent and tantalum powder). Postprocedural angiography is done to see the extent of shunt reduction [41]. Patients can also be later followed up by transcranial Doppler USG if fontanels are open.

The transvenous route is particularly useful where the caliber of feeding arteries is not sufficient to negotiate the microcatheter or if the shunt is having extremely high flow (to avoid migration of the embolic material). Occasionally it may be required to use both techniques (transarterial and transvenous) as occlusion of feeding arteries decreases the pressure gradient and flow through the fistula. The fistula veins are approached through the internal jugular vein, femoral vein, or direct torcula puncture. The sac is approached through the various structures including sigmoid sinus, transverse sinus, torcula, and straight sinus. If sigmoid sinuses are thrombosed, then it may be

approached through a persistent suboccipital and straight sinus. The sac is filled with pushable micro coils or Guglielmi detachable coils (GDC) initially followed by a mixture of NBCA and lipidol. The scaffold of coils is placed to prevent migration of embolic materials. After achieving the substantial reduction of flow, an arterial route is used for staged embolization. The normal cerebral veins should not be connected directly to the sac, as in such scenario, transvenous route may lead to cerebral venous hypertension that results in immediate or delayed hemorrhagic complications [42–44].

In transtorcular route, varix is approached through the occipital bone over the torcula where occipital bone is penetrated with a large bore needle to reach the varix. This approach is used for embolization of high-flow choroidal malformations which are not accessible through the femoral route [38].

29.8.2.1 Complications of Embolization [8, 45, 46]

After the complete or near-complete occlusion of large arteriovenous fistulas, normal perfusion pressure breakthrough, a potentially lethal complication, occurs where cerebral edema and hemorrhages develop even when the perfusion pressure was kept within normal limits [45]. The hypothesis behind this complication is that as arteriovenous fistula is a low-resistance circuit, hence the majority of cerebral blood flow is delivered to the fistula while rest of the brain develops a state of chronic low perfusion. To compensate for reduced blood supply, blood vessels in rest of the brain are chronically vasodilated. When the large fistula is closed completely in one stage and blood flow restored, the dilated blood vessels of the normal brain cannot constrict at the same time and breakthrough occurs. Another potentially fatal complication is intracerebral hemorrhage secondary to venous hypertension [45]. These complications are largely avoidable by doing embolization in stages.

Other complications inherent to the endovascular procedures include wire perforation of the venous sac during coil embolization, pulmonary embolization, and ischemic neurological deficits due to the migration of embolization material. Various complications and their management are described in Table 29.3.

Table 29.3 Complications of neurointerventions for Vein of Galen malformations

1.	**Local site:** Femoral hematoma or bleeding; ensure immobility till complete hemostasis is achieved
2.	**Vascular complication:** *Thrombotic:* Thrombosis of normal vessels leads to cerebral venous hypertension, venous infarcts, hemorrhage, herniation; increase perfusion by increasing systemic blood pressure *Hemorrhagic:* Wire perforation of vessels leads to massive intracranial hemorrhage; reverse heparin, manage hemodynamics (decrease blood pressure), and decrease ICP (maintain cerebral perfusion pressure/head up/hyperventilation/mannitol/burr hole evacuation in radiology suite)
3.	**Contrast-related complications:** *Contrast reaction:* Mild hypotension to anaphylaxis; managed as anaphylaxis guidelines (100% oxygen, remove the offender/rush fluids/antihistaminics/steroids/adrenaline) *Contrast overload:* Diuresis leading to dehydration, osmotic nephrosis; closely monitor the hydration

29.8.3 Gamma Knife Treatment

Gamma knife surgery is done by using gamma radiation that hit a particular target area in the brain from different directions. It acts by depolarizing the cell that leads to cell death. This is a slow process, so no immediate reduction is achieved in arteriovenous shunting, and hence, it is not an option for patients who need emergency surgery [47]. This technique is relatively safe, and the results in the form of cure of the lesion are comparable to microsurgery in simple malformations. The major disadvantage is the absence of instant benefit from the treatment. The slow occlusion of the malformation has an advantage that it provides time for normalization of the cerebral hemodynamics before the complete obliteration of VOGM, and hence, the complications, such as normal perfusion pressure breakthrough, are not observed [47]. The literature on

the use of Gamma knife treatment for VGAM is sparse. Most of the case reports and case series have shown it to be complimentary to the complex lesion and may be used as a sole modality for very small fistulas [48, 49]. Gamma knife surgery should be kept an option for treating VOGMs in medically stable patients. This therapy is used for partially treated malformations by other modalities to achieve complete obliteration without any increased incidence of mortality or morbidity [10, 50].

A multimodal approach is needed to manage the unusual vascular malformation. The management for symptomatic newborn and infants includes the combinations of medical and endovascular therapy. For the relatively stable patients, microsurgery may be considered where the lesion could not be treated completely using the endovascular technique. Endovascular therapy is the most widely accepted treatment of choice to reduce the shunt as much as possible before surgery or completely occlude the lesion. In medically and neurologically stable patients, gamma surgery offers more appropriate therapy for the cure with a lesser risk of complications.

29.9 Preoperative Optimization and Anesthetic Challenges for a Patient with VOGM

The major anesthetic challenges include the pediatric patient, having poor reserves and disease pathophysiology (associated multiorgan failure, hydrocephalus). In addition, the endovascular treatment has its inherent problems including remote location (non-operating room anesthesia), radiation hazard, contrast reaction, hemodynamic manipulations, and identifying and managing the complications. A detailed preoperative assessment and optimization are required before definitive intervention.

Electrocardiography, echocardiography, and lab tests are essential to manage the patients with VOGMs. Echocardiography may demonstrate biventricular failure and patent foramen ovale or other intracardiac shunts. Flow reversal may occur in the aorta during diastole, indicating "steal phenomenon" due to diversion of cardiac output to the low-resistance intracranial shunt. Electrocardiography may show the signs of ischemia due to low coronary perfusion and elevated intraventricular pressure. Lab test must include evaluation of kidney (serum electrolytes/urea/creatinine) and liver functions (hepatic enzymes/bilirubin/coagulations studies) [48]. Neuroimaging studies should be performed to assess the parenchymal damage [51].

The immediate goal of the management is to optimize/support cardiac function and maintain cerebral perfusion. In patients with high pulmonary artery pressure, inhaled nitric oxide may be helpful in reducing RV workload [52]. In patients having LV dysfunction, vasoactive medications such as dopamine, dobutamine, or milrinone are required to maintain the systemic perfusion. The patients should be optimized as much as possible prior to the embolization, but if emergency embolization is planned in patients with refractory congestive cardiac failure, medical management should be continued during the endovascular therapy [53, 54]. Inhaled NO and vasopressor should be continued perioperatively.

During endovascular treatment, general anesthesia with muscle relaxation and endotracheal intubation is required to prevent catheter-related complications. Due to poor cardiac reserve, these patients poorly tolerate the inhalational anesthetic agents. Hence, the dose of anesthetic agents should be closely titrated. In addition to routine intraoperative monitoring, arterial line should be secured for beat-to-beat monitoring of blood pressure. A separate arterial line should be secured for the monitoring as the caliber of arterial access inserted for the procedure is very small and may not be useful for monitoring. With the hands of experienced neuroradiologist, the blood loss is minimal. The major concern here is a large amount of heparinized fluid used for flushing the microcatheters [55]. Excessive fluid administration tends to aggravate cardiac failure, while fluid restriction may cause sudden cardiovascular collapse. Another important factor is the volume of contrast injected in the neonate which can invariably produce osmotic diuresis and cause an imbalance in the hydration [56].

In older children, the anesthetic plan is more straightforward as they may be more stable. Most of the children are usually extubated postprocedure, but patients should remain calm to achieve femoral artery hemostasis. Postanesthetic apnea is commonly seen in premature neonates till 48–60 postgestational weeks, and there are various potential risk factors for postoperative apnea in these patients including anemia, infection, central nervous system pathology, and other comorbidities [57]. Patients may require anticoagulation to prevent thrombotic complications.

29.10 Prognosis

The outcome of patients with untreated VOGMs is grave with approximately 45–100% mortality based on the age of presentation and severity of symptoms. The neurological outcome may also be poor in patients with large fistula even after satisfactory treatment due to the parenchymal damage [51]. Historically, surgical isolation of fistula was carrying a very high mortality. Endovascular embolization has revolutionized the treatment of VOGMs. Both cognitive and functional outcomes are quite good after timely endovascular therapies. The most important parameter governing the outcome is the selection of appropriate patients and preoperative optimization. The neonates who present at birth with congestive cardiac failure and mutiorgan dysfunction are at high risk for mortality and develop neurological deficits if they survive. The patients without associated systemic problems tend to have a good neurological outcome in approximately 75% of cases [58, 59].

Multiple Choice Questions

1. A newborn presents with congestive heart failure, on examination has bulging anterior fontanellae with a bruit on auscultation. Transfontanellar USG shows a hypoechoic midline mass with dilated ventricles. Most likely diagnosis is
   (a) Encephalocele
   (b) Arachnoid Cyst
   (c) Vein of Galen Malformation
   (d) Aneurysm

   Answer: c

   Vein of Galen malformation is characterised by high flow arterio-venous connections that contribute to higher venous return to the right heart resulting in congestive cardiac failure. Bruit occurs due to high flow through the fistula. It is associated to obstruction to venous drainage and/or compression of cerebral aqueduct that causes dilated ventricles. Encephalocele is a type of neural tube defect that presents as sac-like protrusions of the brain and the meninges through the openings in the skull. Arachnoid cyst and aneurysm do not present with failure.
2. Which of the following statement is true regarding vein of Galen malformation?
   (a) The vein of Galen is also known as the great cerebral vein
   (b) Vein of Galen malformations are formed by abnormal dilation of normal arterial system
   (c) In most of the cases there are acquired malformations
   (d) Most of cases presenting in neonatal period are having good prognosis

   Answer: a

   The vein of Galen is also known as the great cerebral vein or great vein of Galen. Vein of Galen malformations are the rare congenital abnormalities. These malformations represent the persistent embryonic median prosencephalic vein rather than the vein of Galen. There is an aneurysmal dilatation of vein which may be fed by various abnormal arteriovenous connections. Most severe types present at birth and are associated with the worst prognosis.
3. The following cardiovascular changes are seen in VOGMs, **except**
   (a) Congestive heart failure
   (b) Systemic Hypertension
   (c) Myocardial Ischemia
   (d) Opening of foramen Ovale

   Answer: b

   VOGMs with large fistulous connections forms a low resistant circuit that receives majority of cardiac output. This high flow when returns back to heart, it increases right atrial

pressure more than left atrium and results in opening of foramen ovale and heart failure. The myocardial workload increases and systemic flow decreases due to diversion of flow to the VOGM that results in myocardial ischemia.

4. Which of the following statement is **not** true regarding treatment of VOGMs?
   (a) The patients with larges fistulous VOGMs if not treated patient may die mostly due to congestive heart failure
   (b) Microsurgical ligation of feeder and draining veins plays an important role in the management of VOGMs
   (c) Endovascular embolization is treatment of choice now-a-days
   (d) Normal perfusion pressure break-through is usually not observed after Gamma-Knife surgery

   Answer: b

   VOGMs with large shunts leads to cardiac failure to due high output that is leading cause of mortality, if untreated. Microsurgical ligation of feeder and draining veins played some role in the management of VOGMs before the advent of embolization. Surgery was associated with high intraoperative mortality due to excessive bleeding. Currently, endovascular treatment is considered as the treatment of choice for VOGM. Gamma knife surgery causes slow occlusion of the malformation and provides time for normalization of the cerebral hemodynamics before the complete obliteration of VOGM, and hence, normal perfusion pressure breakthrough is usually not observed.

References

1. Drake CG. Cerebral arteriovenous malformations: considerations for and experience with surgical treatment in 166 cases. Clin Neurosurg. 1979;26:145–208.
2. Casasco A, Lylyk P, Hodes JE, Kohan G, Aymard A, Merland JJ. Percutaneous transvenous catheterization and embolization of vein of Galen aneurysms. Neurosurgery. 1991;28:260–6.
3. Ciricillo SF, Edwards MS, Schmidt KG, Hieshima GB, Silverman NH, Higashida RT, et al. Interventional neuroradiological management of vein of Galen malformations in the neonate. Neurosurgery. 1990;27:22–8.
4. Raybaud CA, Strother CM, Hald JK. Aneurysms of the vein of Galen: embryonic considerations and anatomical features relating to the pathogenesis of the malformation. Neuroradiology. 1989;31:109–28.
5. Berenstein A, Lasjaunias P. Arteriovenous fistulas of the brain. In: Surgical Neuroangiography 4. Endovascular treatment of cerebral lesions. Berlin: Springer; 1992. p. 267–317.
6. Lasjaunias P, Terbrugge K, Piske R, Lopez Ibor L, Manelfe C. Dilatation of the vein of Galen. Anatomoclinical forms and endovascular treatment apropos of 14 cases explored and/or treated between 1983 and 1986. Neurochirurgie. 1987;33:315–33.
7. Alvarez H, Garcia Monaco R, Rodesch G, Sachet M, Krings T, Lasjaunias P. Vein of galen aneurysmal malformations. Neuroimaging Clin N Am. 2007;17:189–206.
8. Lasjaunias PL, Chng SM, Sachet M, Alvarez H, Rodesch G, Garcia-Monaco R. The management of vein of Galen aneurysmal malformations. Neurosurgery. 2006;59:S184–94.
9. Litvak J, Yahr MD, Ransohoff J. Aneurysms of the great vein of Galen and midline cerebral arteriovenous anomalies. J Neurosurg. 1960;17:945–54.
10. Mortazavi MM, Griessenauer CJ, Foreman P, Bavarsad Shahripour R, Shoja MM, Rozzelle CJ, Tubbs RS, Fisher WS 3rd, Fukushima T. Vein of Galen aneurysmal malformations: critical analysis of the literature with proposal of a new classification system. J Neurosurg Pediatr. 2013;12(3):293–306.
11. Lasjaunias P, Ter Brugge K, Berenstein A. Vein of Galen aneurysmal malformation, in: surgical Neuroangiography 3. Clinical and interventional aspects in children, ed 2. Berlin: Springer, 2006, Vol 3, pp 105–226.
12. Yasargil MG. Microneurosurgery IIIB. New York: Thieme Medical Publishers; 1988. p. 323–57.
13. Hoffman HJ. Malformations of the vein of Galen. In: Edwards MSB, Hoffmann HJ, editors. Current neurosurgical practice: cerebral vascular disease in children and adolescents. Baltimore: Lippincott, Williams and Wilkins; 1989. p. 239–46.
14. Crawford JM, Rossitch E Jr, Oakes WJ, Alexander E 3rd. Arteriovenous malformation of the great vein of Galen associated with patent ductus arteriosus. Childs Nerv Syst 1990;6:18–22.
15. Pellegrino PA, Milanesi O, Saia OS, Carollo C. Congestive heart failure secondary to cerebral arterio-venous fistula. Childs Nerv Syst. 1987;3:141–4.
16. Bhattacharya JJ, Thammaroj J. Vein of Galen malformations. J Neurol Neurosurg Psychiatry. 2003;74:142–4.
17. Zerah M, Garcia-Monaco RG, Terbrugge K, Tardieu M, de Victor D, et al. Hydrodynamics in vein of Galen malformations. Childs Nerv Syst. 1992;8:111–7.
18. Sainte-Rose C, La Combe J, Pierre-Kahn A, Renier D, Hirsch JF. Intracranial venous sinus hypertension: cause or consequence of hydrocephalus in infants? J Neurosurg. 1984;60:727–36.

19. Lasjaunias P, Garcia-Monaco R, Rodesch G, Ter Brugge K, Zerah M, Tardieu M, et al. Vein of Galen malformation: endovascular management of 43 cases. Childs Nerv Syst. 1991;7:360–7.
20. Gulati S, Kalra V. An uncommon variety of vein of Galen malformation. Indian Pediatr. 2002;39:307–8.
21. Gold AP, Ransohoff JR, Carter S. Vein of Galen malformation. Acta Neurol Scand. 1964;40:5–7.
22. Kothari SS, Naik N, Juneja R, Saxena A. Aneurysm of vein of Galen in the neonates: report of four cases. Indian Heart J. 2001;53:499–502.
23. Cumming GR. Circulation in neonates with intracranial arteriovenous fistula and cardiac failure. Am J Cardiol. 1980;45:1019–24.
24. Garcia-Monaco R, de Victor D, Mann C, Hannedouche A, Terbrugge K, Lasjaunias P. Congestive cardiac manifestations from cerebrocranial arteriov- enous shunts: endovascular management in 30 children. Childs Nerv Syst. 1991;7:48–52.
25. Lasjaunias P, Terbrugge K, Lopez Ibor L, Chiu M, Flodmark O, Chuang S, et al. The role of dural venous anomalies in vein of Galen aneurysms: report of six cases and review of the literature. AJNR Am J Neuroradiol. 1987;8:185–92.
26. Vintzileos AM, Eisenfeld LI, Campbell WA, Herson VC, DiLeo PE, Chameides L. Prenatal ultrasonic diagnosis of arteriovenous malformation of the vein of Galen. Am J Perinatol. 1986;3:209–11.
27. Mendelson DB, Hertzanu Y, Butterworth A. In utero diagnosis of a vein of Galen aneurysm by ultrasound. Neuroradiology. 1984;26:417–8.
28. Reiter AA, Huhta JC, Carpenter RJ Jr, Segall GK, Hawkins EP. Prenatal diagnosis of arteriovenous malformation of the vein of Galen. JCU. 1986;14:623–8.
29. Hirsch JH, Cyr D, Eberhardt H, Zunk el D. Ultrasonographic diagnosis of an aneurysm of the vein of Galen in utero by duplex scanning. J Ultrasound Med. 1983;2:231–3.
30. Jeanty P, Kepple D, Roussis P, Shah D. In utero detection of cardiac failure from an aneurysm of the vein of Galen. Am J Obstet Gynecol. 1990;163:50–1.
31. Seidenwurm D, Berenstein A, Hyman A. Vein of Galen malformation: correlation of clinical presentation, arteriography and MR imaging. AJNR Am J Neuroradiol. 1991;12:347–54.
32. Nikas DC, Proctor MR, Scott RM. Spontaneous thrombosis of vein of Galen aneurysmal malformation. Paediatr Neurosur g. 1999;31:33–9.
33. Surana UM, Patel BN, Patel SB, Dhebar M. Images: vein of Galen malformation. Ind J R adiol Imag. 1999;9:21–2.
34. Johnston IH, Whittle IR, Besser M, Morgan MK. Vein of Galen malformation: diagnosis and management. Neurosurgery. 1987;20:747–58.
35. Hoffmann HJ, Chuang S, Hendrick EB, Humphreys RP. Aneurysms of the vein of Galen: Experience at the Hospital for Sick Children, Toronto. J Neurosurg. 1982;57:316–22.
36. Diebler C, Dulac O, Renier D, Ernest C, Lalande G. Aneurysms of the vein of Galen in infants aged 2 to 15 months. Diagnosis and natural evolution. Neuroradiology. 1981;21:185–97.
37. Amachar AL, Shillito J Jr. The syndromes and surgical treatment of aneurysms of the great vein of Galen. J Neurosurg. 1973;39:89–98.
38. Rao V, Mathuriya SN. Pediatric aneurysms and vein of Galen malformations. J Pediatr Neurosci. 2011;6:S109–17.
39. ter Brugge KG. Vein of Galen management in neonatal period. Am J Neuroradiol. 2001;22:1403–9.
40. Khullar D, Andeejani AM, Bulsara KR. Evolution of treatment options for vein of Galen malformations. A review. J Neurosurg Pediatr. 2010;6:444–51.
41. Lasjaunias P, Rodesch G, Terbrugge K, Pruvost P, Devictor D, Comoy J, et al. Vein of Galen aneurysmal malformations. Report of 36 cases managed between 1982 and 1988. Acta Neurochir (Wein). 1989;99:26–37.
42. Gailloud P, O'Riordan DP, Burger I, Lehmann CU. Confirmation of communication between deep venous drainage and the vein of galen after treatment of a vein of Galen aneurysmal malformation in an infant presenting with severe pulmonary hypertension. AJNR Am J Neuroradiol. 2006;27:317–20.
43. Lasjaunias P, Garcia-Monaco R, Rodesch G, Terbrugge K. Deep venous drainage in great cerebral vein (vein of Galen) absence and malformations. Neuroradiology. 1991;33:234–8.
44. Levrier O, Gailloud PH, Souei M, Manera L, Brunel H, Raybaud C. Normal galenic drainage of the deep cerebral venous system in two cases of vein of Galen aneurysmal malformation. Childs Nerv Syst. 2004;20:91–9.
45. Spezler RF, Wilson CB, Weinstein P. Normal perfusion pressure breakthrough theory. Clin Neurosurg. 1978;25:651–72.
46. Young WL, Dowd CF. Interventional Neuroradiology: Anesthetic management. In: Cottrell JE, Young WL, editors. Cottrell and Young's Neuroanesthesia. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010. p. p247–63.
47. Payne BR, Prasad D, Steiner M, Bunge H, Steiner L. Gamma surgery for vein of Galen malformations. J Neurosurg. 2000 Aug;93(2):229.
48. Hansen D, Kan PT, Reddy GD, Mohan AC, Jea A, Lam S. Pediatric knowledge update: approach to the management of vein of Galen aneurysmal malformations in neonates. Surg Neurol Int. 2016;7:S317–21.
49. Triffo WJ, Bourland JD, Couture DE, McMullen KP, Tatter SB, Morris PP. Definitive treatment of vein of Galen aneurysmal malformation with stereotactic radiosurgery. J Neurosurg. 2014 Jan;120(1):120–5.
50. Shin M, Kurita H, Tago M, Kirino T. Stereotactic radiosurgery for tentorial dural arteriovenous fistulae draining into the vein of Galen: report of two cases. Neurosurgery. 2000;46(3):730–3.
51. Gailloud P, O'Riordan DP, Burger I, Levrier O, Jallo G, Tamargo RJ, Murphy KJ, Lehmann CU. Diagnosis and management of vein of Galen aneurysmal malformations. J Perinatol. 2005;25(8):542–51.

52. Frawley GP, Dargaville PA, Mitchell PJ, Tress BM, Loughnan P. Clinical course and medical management of neonates with severe cardiac failure related to vein of Galen malformation. Ch Dis Child Fetal Neonatal Ed. 2002;87(2):F144–9.
53. Thiex R, Williams A, Smith E, Scott RM, Orbach DB. The use of Onyx for embolization of central nervous system arteriovenous lesions in pediatric patients. Am J Neuroradiol. 2010;31(1):112–20.
54. Ashida Y, Miyahara H, Sawada H, Mitani Y, Maruyama K. Anesthetic management of a neonate with vein of Galen aneurysmal malformations and severe pulmonary hypertension. Paediatr Anaesth. 2005;15(6):525–8.
55. Landringan-Ossar M, McClain CD. Anesthesia for intervention radiology. Pediatr Anaesth. 2014; 24(7):698–702.
56. McClain CD, Landrigan-Ossar M. Challenges in pediatric neuroanaesthesia: Awake craniotomy, intraoperative magnetic resonance imaging, and interventional neuroradiology. Anesthesiol Clin. 2014; 32(1):83–100.
57. Davidson AJ, Morton NS, Arnup SJ, de Graaff JC, Disma N, Withington DE, Frawley G, Hunt RW, Hardy P, Khotcholava M, von Ungern Sternberg BS, Wilton N, Tuo P, Salvo I, Ormond G, Stargatt R, Locatelli BG, ME MC. Postoperative apnea after awake regional and general anaesthesia in infants: the general anaesthesia compared to spinal anaesthesia study-comparing apnea and neurodevelopmental outcomes, a randomized controlled trial. Anesthesiology. 2015;123(1):38–54.
58. Ellis JA, Orr L, Ii PC, Anderson RC, Feldstein NA, Meyers PM. Cognitive and functional status after vein of Galen aneurysmal malformation endovascular occlusion. World J Radiol. 2012;4(3):83–9.
59. Deloison B, Chalouhi GE, Sonigo P, Zerah M, Millischer AE, Dumez Y, Brunelle F, Ville Y, Salomon LJ. Hidden mortality of prenatally diagnosed veon of Galen aneurysmal malformation: retrospective study and review of literature. Ultrasound Obstet Gynecol. 2012;40(6):652–8.

Part IV

Special Circumstances

Management of Patient with Pregnancy and Brain Tumor

30

Sonal Patel and Sabri Barsoum

Stem Case Terminology

A 29-year-old primipara woman (162 cm, 78 kg) at 36-week gestation was admitted from the ER with the complaint of severe headache localized to the left frontal area for 3 months, accompanied by nausea/vomiting of 1 week duration.

Her past medical history was unremarkable.

Physical examination revealed mild apathy and bilateral grade 1 papilledema.

Laboratory examination results were within normal range.

Cranial MRI revealed a large intracranial mass (6 × 7 cm in diameter) with peripheral edema in frontoparietal location, causing left-to-right midline shift.

Question 1:
What is the differential diagnosis of headache in pregnancy?

Answer:
Headache is a common symptom in pregnancy, reported in up to 35% of women during their antenatal period. The International Headache Society (IHD) classifies headaches as primary, like tension-type headache and migraine, and secondary headaches, like hypertension, preeclampsia, idiopathic intracranial hypertension, subarachnoid hemorrhage, cerebral venous thrombosis, and reversible cerebral vasoconstriction syndrome. Headaches may be an initial symptom of a life-threatening condition, such as central venous thrombosis (CVT).

Question 2:
What would be the ideal approach to manage this patient?

Answer:
All neurosurgical procedures during pregnancy must be considered major interventions. Hence, a multidisciplinary and well-planned strategy and team approach are advisable. If an emergency situation arises, initial stabilization of the mother should take priority, although subsequent treatment has to consider both the mother and child.

Provision of anesthesia for a pregnant neurosurgical patient who needs surgical treatment is a major challenge. A balance between competing and even contradictory clinical goals may need to be achieved, like application of some neuroanesthesia techniques or protective interventions may benefit the mother but carry the risks of harming the fetus. Throughout the continuum of care, maintenance of uteroplacental perfusion and fetal oxygenation by avoidance of maternal hypoxia, hypotension, hypocarbia, and acidosis are of

S. Patel · S. Barsoum (✉)
Cleveland Clinic, Cleveland, OH, USA
e-mail: BARSOUs@ccf.org

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_30

utmost importance for fetal survival in a pregnant neurosurgical patient.

Decision to proceed for neurosurgery depends on the site, size, and type of the tumor, neurological signs as well as the patient's wishes and considerations.

In this case, due to the size of the intracranial mass causing midline shift in the dominant hemisphere, there was an increased risk of cerebral herniation. Hence, an emergent craniotomy had to be performed.

Question 3:
What are the physiological changes of pregnancy that impacts the anesthetic management?

Answer:
There are anatomical and physiological changes in pregnancy to meet the metabolic demands of the mother and fetus.

(a) **Respiratory Changes**.

Anatomically, there is capillary engorgement resulting in swelling and friability of the nasopharyngeal and oropharyngeal tissues. Hence, the airway can become compromised and tracheal intubation more difficult. This in conjunction with enlarged breasts, tongue, and increased obesity can make laryngoscopy more difficult. The nasopharyngeal approach should be avoided because of the increased risk of epistaxis.

Physiologically, there is 60% increase in oxygen demand and CO_2 production. There is an early increase in the tidal volume which increases the minute ventilation. The driving force for this is progesterone which lowers the carbon dioxide response threshold of the respiratory center.

As the uterus expands, the diaphragm gets pushed in a cephalic direction decreasing the functional residual capacity. Hence, the parturients become hypoxic very quickly. So adequate preoxygenation for 3–5 min or longer helps before intubation. Increased minute ventilation and a reduced FRC facilitate gas exchange at the alveolar level resulting in increased rate of uptake of inhalation agents and more rapid changes in depth of anesthesia. While ventilating a parturient, there is equivalent gradients between end-tidal CO2 and $PaCO_2$ due to the decrease in alveolar dead space as there is increased blood perfusion due to increased maternal CO. Hence, excessive hyperventilation can cause severe alkalosis, shifting the O_2 dissociation curve to left and hence resulting in decreased oxygen transfer to the fetus.

The chest wall compliance reduces due to the upward push by the gravid uterus, requiring higher airway pressure to maintain adequate ventilation.

(b) **Cardiovascular Changes**.

There is hyperdynamic circulation in pregnancy. The early hormonal effects lead to peripheral vasodilatation which causes a decrease in the systemic vascular resistance (SVR).

Initially, there is increase in store volume (SV), but as pregnancy progresses, there is an increase in the heart rate.

There is an overall increase of up to 2000 mL in blood volume compared with the nonpregnant individual. As a result of this, the pregnant patient compensates well for blood loss, and the classical symptoms and signs of hypovolemia such as tachycardia, hypotension, and oliguria are evident after more than 1500 mL in blood volume may have already been lost.

Despite an increased CO, there is an early transient decrease in arterial pressure, resulting in a widened pulse pressure and a reduced mean arterial pressure. This activates the renin–angiotensin system leading to retention of water and sodium and ultimately an increase in plasma volume. While the increase in plasma volume is in the region of 40–50%, the increase in red blood cell mass is only 20% resulting in the dilutional physiological anemia of pregnancy.

By the time enlarging uterus approaches the level of the umbilicus, the mechanical effects of the enlarging uterus cause compression of both the inferior vena cava and the descending aorta in the supine position.

This leads to a reduced venous return and decreased cardiac output. As the uteroplacental circulation has no autoregulation properties, this causes a decreased uterine blood flow and reduced placental perfusion and therefore leads to maternal hypotension and a subsequent fetal acidemia.

Peripheral vasodilatation facilitates venipuncture and I.V. cannulation. Epidural veins become dilated with increased risk of intravascular injection—"bloody tap" during epidural anesthesia. This is exacerbated during uterine contractions. IV and inhalation anesthetic agents cause a reduction in SV and CO, and neuraxial block causes sympathetic block and hence both increases the risk of supine hypotension. Hence pregnant patients are positioned with left lateral tilt.

Labor and delivery further increase the cardiac workload by pain and auto-transfusion. Those parturients with decreased cardiac reserve are at particular risk of ventricular failure and pulmonaryedema in the second stage of labor and early postpartum period.

Pregnancy is a hyper-coagulable state. All clotting factors are increased except factor XI and XIII, and there is a decrease in natural anticoagulants and a reduction in fibrinolytic activity, and hence, there is a high risk for postpartum thromboembolic disease. All pregnant women should routinely undergo a thromboembolic risk assessment in the antenatal period and appropriate thromboprophylaxis prescribed. As low molecular weight heparins (LMWHs) are being used increasingly in the antenatal period, the anesthetist has to be aware of the last dose administered before providing regional block.

(c) **Gastrointestinal Changes**.

The upward displacement of the stomach by the gravid uterus leads to increased intragastric pressure, and this with decreased esophageal sphincter tone leads to the symptoms of heartburn in pregnancy.

Gastric emptying is delayed in labor due to pain, anxiety, and administration of opiates by any route, including the epidural or subarachnoid route. This increases the risk of aspiration.

The safest and most effective way of aspiration prophylaxis is the effective use of regional anesthesia. Also antacid premedication, H2-receptor antagonists used in combination with sodium citrate, increases the mean pH and decreases the percentage of patients with a gastric pH <2.5 required to cause a chemical pneumonitis.

If general anesthesia is necessary, after pre-oxygenation, a rapid sequence induction technique with cricoid pressure should be used and the airway secured with a cuffed tracheal tube. Due to engorged, edematous airways, friable oropharyngeal mucosa, and large tongue, a smaller size tube is always recommended.

Question 4:
What factors determine the drug transfer across the placenta?

Answer:

(a) **Lipid solubility**.

Lipophilic molecules diffuse readily across placenta and reach the fetal circulation. All induction agents, inhalational agents, and opioids are highly lipid soluble.

(b) **Molecular weight**.

It influences the rate and amount of drug transferred across the placenta. Drugs with molecular weight less than 500 Da readily diffuse through the placenta. All muscle relaxants depolarizing and non-depolarizing have a high molecular weight and do not cross the placenta.

(c) **Protein binding**.

Drugs that are protein bound do not cross the placenta, only the free unbound portion of the drug is free to cross the placental cell membrane. Any disease process associated with hypoalbuminemia will result in a higher portion of unbound drug and therefore promote drug transfer across the placenta.

(d) **Degree of ionization**.

Only the non-ionized fraction of the partially ionized drug crosses the placenta. The degree to which a drug is ionized depends on its PKa and the Ph of the maternal blood. Most drugs used in anesthesia are poorly ionized; therefore, they diffuse readily through the placenta. The exception is the neuromuscular blocking agents which are highly ionized; therefore, their transfer is negligible.

Question 5:
What preparations are required before proceeding with craniotomy and cesarean delivery at the same session?

Answer:
Fetal monitoring with ultrasound and Doppler for fetal heart rate to ensure that the fetus is well should be done. A close communication with the neonatologist and NICU should be done to establish fetal compatibility with life after cesarean delivery.

All gravid patients, presenting with intracranial mass and increased intracranial pressure who are at high risk of developing seizure disorder should be treated with prophylactic anticonvulsant therapy. It is crucial to avoid seizures as hypoxia and acidosis resulting from seizure disorder may have more impact on fetus compared with anticonvulsant therapy. Also the side effects from anticonvulsant therapy after organogenesis are infrequent.

Anesthetic management is quite often challenging due to the effect of the physiological changes of pregnancy on the cerebral circulation and tumor.

It is vital to maintain the hemodynamic stability all the time, while avoiding aortocaval compression, hypoxemia, and hypercarbia for the fetal and maternal well-being.

Aspiration prophylaxis in the form of nonparticulate antacids, H2-receptor antagonists used in combination with sodium citrate and pro motility medication should be given while on the way to the operating room.

Question 6:
What technique of anesthesia should be employed?

Answer:
The patient was placed in supine with left lateral tilt in order to maintain venous return and decrease pressure on the inferior vena cava by avoiding the aortocaval compression by the gravid uterus. Also, a 15 degree reverse Trendelenburg was maintained to decrease intracranial pressure.

Preoxygenation for 3–5 min is ideal in obstetric patients. Also continuous oxygen can be delivered through the high-flow nasal cannula during the process of intubation too.

Once the surgeons had prepared and draped the patient and were ready for incision, a rapid sequence induction was done with propofol 2 mg/kg, remifentanil 1 mcg/kg, lidocaine 1.5 mg/kg, and rocuronium 1 mg/kg while maintaining the cricoid pressure. After intubation and confirmation of bilateral breath sounds was done by auscultation, an extra-large bore peripheral IV was started. Right radial arterial line provided beat-to-beat control of the blood pressure, and body core temperature was monitored throughout.

Anesthesia was maintained with 50% oxygen, 50% air, and 0.5 Mac of sevoflurane. A continuous infusion of remifentanil 0.25 μg/minute was started to maintain hemodynamic stability.

Controlled ventilation was maintained providing 8 mL/kg tidal volume and respiratory rate sufficient to maintain end tidal CO_2 at 30–32.

Succinylcholine was avoided for the concern of increasing intracranial pressure.

Nitrous oxide should not be administered in pregnant neurosurgical patients for a variety of reasons. In the mother, it may increase the ICP and cerebral oxygen metabolic rate, expanding the size of an occult pneumothorax and contributing to postoperative nausea and vomiting. In the fetus, nitrous oxide may have adverse effects on development because of its propensity to oxidize cobalamin and inhibit methionine synthase activity, affecting, for example, DNA production and myelin deposition.

Question 7:
Can opioids be given before the delivery of the baby?

Answer:
Normally, opioids should be withheld until after the baby is born because of the risk of neonatal depression. However, in this case, due to the maternal increased stress response and intracranial pressure, a short-acting opioid remifentanil was administered.

Remifentanil has a unique metabolism by plasma and tissue esterases and a context-sensitive half-life of 3–4 min independent of the duration of infusion. Despite crossing the placenta, remifentanil can be metabolized and redistributed to both mother and fetus rapidly.

In this case, APGAR scores of the baby was 7 and 10 at 1 and 5 min following delivery. Remifentanil allows both control of the intraoperative stress response and a more rapid recovery than the commonly used opioids. Because of its fast metabolism and short duration of action, remifentanil can be considered safe and effective for general anesthesia for emergency cesarean sections in patients with neurological risk factors.

Remifentanil infusion is an excellent anesthetic adjunct when hemodynamic stable anesthetic is the main goal as in this case.

Question 8:
How does the maintenance of anesthesia change after the delivery of the baby?

Answer:
In this case, a healthy neonate was delivered within 4 min of induction. The obstetrician started bimanual uterine massage and compression to help uterine contraction and tone to minimize bleeding that can lead to hemodynamic instability. Oxytocin infusion of 20 U in 500 mL of saline was started immediately after delivery of placenta. Oxytocin is the uterotonic agent of choice in patients with intracranial tumors. Methergin has been associated with hypertensive response which can further increase intracranial pressure.

Neuroanesthetic techniques should be designed to avoid fetal hypoxia, hypercarbia, hypotension, and teratogenicity and acknowledge pregnancy-related changes in maternal physiology. Neuroprotective measures such as hyperventilation or induced hyper-osmolarity should only be used with caution and to a limited extent, because hypocarbia, reduced uterine perfusion, and fetal hyper-osmolarity or dehydration pose serious threats to the fetus. Neuroanesthesia must therefore strive to offer optimal care for the mother and minimize or eliminate risks to the fetus, while also ensuring the shortest possible exposure to anesthesia drugs. The following medications were started.

Dexamethasone 0.1 mg/kg, mannitol infusion of 0.5 mg/kg, and furosemide 0.1 mg/kg were administered to decrease brain edema and ICP. Dexamethasone is used to decrease cerebral edema and is safe for premature fetus if given 24–48 h prior to delivery, to facilitate fetal lung maturity.

Osmotic diuresis with mannitol is routinely used for decreasing brain bulk and intracranial pressure, it has been shown to cause fetal hypovolemia and electrolyte imbalance in both animal and human studies. However, there is no evidence that mannitol at 0.5–1 g/kg has any significant effect on fetal fluid balance.

30.1 Intraoperative

Anesthesia was maintained with oxygen/air/sevoflurane and remifentanil infusion. Vital signs remained stable during operation. A 1000 gm of IV phenytoin was given as an anti-convulsant agent. Sevoflurane and remifentanil were stopped during stapling.

Muscle relaxation was reversed with neostigmine 1.5 mg and atropine 0.5 mg IV. The trachea was extubated after 5 min from the end of anesthesia, when the patient responded to verbal stimulation.

Frozen section of the tumor confirmed the diagnosis of anaplastic oligodendroglioma grade III.

30.2 Postoperative Course

The patient was transferred to ICU from the OR; vaginal bleeding was at normal range. Control CT revealed persistent brain edema. After resumption of intestinal peristalsis, the patient was started on oral intake at postoperative day 1.

Postoperative Day 2
The patient had generalized convulsions in spite of being on the treatment of dexamethasone 4 mg q 6 h and phenytoin 300 mg q 8. Convulsions were controlled with diazepam. Dexamethasone dose was increased, and 50 mL of 20% mannitol infusion six times a day was started.

Postoperative Day 3
Generalized convulsions were noted again. Carbamazepine 200 mg q 8 h was started, and phenytoin and mannitol were decreased gradually and stopped.

Lactation was stopped with bromocriptine, and commercial formula was used for infant feeding to prevent the side effects of the drugs to the baby via breast-feeding.

After 5 days in the ICU, the patient was discharged on postoperative day 10 to follow up in the medical oncology as an outpatient.

Multiple Choice Questions

1. Which of the following neurosurgical pathologies are more common in pregnancy?
   (a) Gliomas.
   (b) Bleeding from arteriovenous malformations.
   (c) Pituitary tumors.
   (d) Bleeding from intracerebral aneurysms.
   (e) Meningiomas.
   Answer: d
   Although intracranial aneurysms are uncommon during pregnancy, normal hemodynamic changes in pregnant women may increase vascular stress and the risk of aneurysm formation, progression, and rupture. Ruptured aneurysms in pregnancy deserve prompt surgical treatment.
2. Pregnancy is normally associated with:
   (a) An increase in intracranial pressure.
   (b) A normal $PaCO_2$ of 30–32 mmHg.
   (c) A reduction in factors II, V, and X.
   (d) Decreased renal excretion of bicarbonate.
   (e) Reduced platelet count.
   Answer: b
   During the first trimester of pregnancy, the arterial oxygenation increases from nonpregnant levels to 107 mmHg due to greater alveolar ventilation, the decline in $PaCO_2$, and a lower AV oxygen difference (reducing the reduction in PaO_2 due to venous admixture). Throughout pregnancy, oxygen consumption increases and cardiac output increases to a lesser extent, lowering mixed venous oxygen content.
   Oxygenation further decreases in the supine position at midgestation because the FRC becomes less than the closing capacity leading to atelectasis. Minute ventilation rises during pregnancy due to progesterone acting as a respiratory stimulant and as a result of increased carbon dioxide production (increased by 30%). pCO_2 declines to approximately 30 mmHg by 12 weeks and stays constant through the remainder of pregnancy. This results in a respiratory alkalosis. Metabolic compensation for this reduces serum bicarbonate to approximately 20 mEq/L with a base excess of 2–3 mEq/L. Arterial PaO_2 is increased about 10 torr during pregnancy (increased minute ventilation). $PaCO_2$ is decreased about 10 torr during pregnancy.
   $PaCO_2$ is about 32 mmHg but pH is normalized secondary to a compensatory metabolic acidosis, with HCO_3 decreasing from 25 meq/L to 21 meq/L.
   All factors are increased in pregnancy excluding XI and XIII. There is increased renal excretion of bicarbonate to compensate for the respiratory alkalosis. In pregnancy, platelet production and consumption both increase with resultant normal.
3. Which of the following is recommended during craniotomy in a pregnant patient with raised intracranial pressure?

(a) Moderate hypothermia should be implemented for neuroprotection.
(b) Simultaneous cesarean section should be considered if pregnancy is 28 weeks.
(c) Slow neuro induction with propofol, fentanyl, and rocuronium is advisable.
(d) Modest hyperventilation to decrease ICP.

Answer: d

Modest hyperventilation ($PaCO_2$ 25–30 mmHg) should be instituted within physiological parameters appropriate for gestational age. Maternal hyperventilation can facilitate surgical exposure by deceasing cerebral blood volume. However, severe hypocarbia may impair fetal oxygen delivery and also decrease maternal cardiac output by raising intrathoracic pressure.

4. Regarding pharmacology in pregnancy:
(a) MAC values are 10% greater.
(b) Gastrointestinal absorption of drugs is increased.
(c) Larger doses of induction agents are required due to bigger volumes of distribution.
(d) Pseudocholinesterase levels are reduced.

Answer: d

Serum pseudocholinesterase falls progressively during pregnancy, falls further in the first few days of the puerperium, and then returns to normal by about the sixth week. The cause of this fall is uncertain; hemodilution, a general effect on hepatic function and a specific effect of estrogen have all been suggested.

5. All of the following pertain to the anesthetic management of pregnant women undergoing neurosurgery except.
(a) The MAC value decreases by 30% leading to greater risk of cardiovascular depression.
(b) FRC decreases by around 20%, and closing capacity remains unchanged.
(c) Placental transfer of highly ionized drugs is rapid.
(d) Placental transfer of propofol, etomidate, and thiopental are high.

Answer: c

This statement is false and is the correct answer for this question. Highly ionized agents like depolarizing and non-depolarizing muscle relaxants are minimal. The muscle relaxant reversal drugs like neostigmine and edrophonium are also highly ionized and demonstrate minimal placental transfer.

6. Regarding the conduct of anesthesia:
(a) 15 degrees left lateral tilt should be applied from 24 weeks gestation to prevent aortocaval compression.
(b) Ephedrine is the vasopressor of choice.
(c) Fetal heart rate monitoring is a useful predictor of fetal well-being from 20 weeks gestation.
(d) Hyperventilation to manipulate $PaCO_2$ and cerebral vascular tone should be within the limits of 25–30 mmHg.
(e) Esmolol is an effective way to reduce pressor responses to laryngoscopy with no impact on fetal well-being.

Answer: d

7. A 32-year-old female who is at 30 weeks gestation comes to the hospital with C/O headache and numbness over the face. Imaging was done, and she was found to have an intracranial AV malformation. When is a pregnant woman with intracranial AVM at greatest risk of rupture?
(a) second Trimester
(b) third Trimester
(c) During labor.
(d) Immediate postpartum.

Answer: b

The risk of rupture for both AVMs and aneurysms is highest in the third trimester. Incidence of hemorrhage increases with advanced gestation, possibly due to increases in cardiac output or, possibly, from hormonal influences on vascular integrity.

8. Which of the following is an absolute indication for surgery during pregnancy?
(a) Disc herniation causing symptomatic nerve root compression.
(b) ER/PR-positive meningioma causing headaches in pregnancy.
(c) Macroprolactinoma in pregnancy.

(d) Ruptured berry aneurysm presenting with headache.

Answer: d

SAH is an indication for immediate neurosurgical intervention. The involvement of an experienced neurosurgeon and a neuroradiologist play a central role in the management of SAH in pregnant women. Endovascular coiling is one of the treatment modalities for cerebral aneurysms which is a minimally invasive technique to reduce the risk of rebleeding.

9. Which of the following parturients are not candidates for neuraxial block during cesarean section?
   (a) Patients with pseudotumor cerebra.
   (b) Parturients with intracranial aneurysm.
   (c) Parturients with tethered cord.
   (d) None of the above parturients qualify.

   Answer: c

   Spinal anesthesia for adult TCS (tethered cord syndrome) should be avoided because it can cause complex neurological complications. When a patient has mild symptoms such as back pain, neurogenicbladder, motor, or sensory change, it is extremely important for the anesthesiologist to be aware of the possibility of TCS. When acute onset of paresthesia or weakness in the lower extremities occurs after surgery, MRI should be promptly performed to make the diagnosis.

10. Intravenous magnesium therapy during pregnancy is NOT indicated in which of the following situation?
    (a) Treatment of primary seizure in preeclampsia.
    (b) Prolonged management of preterm labor.
    (c) Treatments of recurrent seizures in eclampsia.
    (d) Prophylaxis against cerebral palsy in preterm deliveries.

    Answer: b

    Intravenous magnesium sulfate is commonly encountered during the practice of obstetric anesthesia, because it is frequently used by obstetricians for various reasons. The most likely use of magnesium in pregnancy is for seizure prophylaxis in preeclampsia and treatment of eclampsia. The current medical literature demonstrates that magnesium is not an effective therapy for preterm labor beyond 48 h.

    Fetal neuroprotection is the most recent addition to the clinical uses of magnesium in obstetrics, with maternal administration of magnesium used to minimize the risk of subsequent cerebral palsy in preterm infants.

    Magnesium levels in the serum are controlled by the kidneys. Renal insufficiency, either chronic or acute, may be associated with toxic serum levels of magnesium without careful observation of the patient and appropriate dose adjustments. Therapeutic serum levels of magnesium for seizure prophylaxis are 5–9 mg/dL. A common clinical assessment for magnesium toxicity is to check patellar tendon reflexes, which are absent at serum magnesium levels above 12 mg/dL. Further increases in magnesium levels can lead to respiratory arrest and asystole.

    The most likely practical interaction between magnesium therapy in pregnancy and anesthetic management is the potentiation of skeletal muscle relaxants by therapeutic magnesium levels during general anesthesia. Magnesium can prolong the effects of either depolarizing or nondepolarizing muscle relaxants. However, the usual clinical impact on an intubating dose of succinylcholine is minimal. In contrast, therapeutic magnesium levels can markedly prolong the clinical effects of nondepolarizing muscle relaxants, resulting in otherwise unnecessary postoperative ventilatory support. In the presence of therapeutic magnesium levels, it is prudent to avoid nondepolarizing muscle relaxants during general anesthesia or at least use a very small dose (e.g., 10% of a usual dose). Sugammadex has been used to reverse the profound neuromuscular blockade from rocuronium in patients receiving magnesium.

Bibliography

1. Centre for Maternal and Child Enquiries (CMACE). Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer: 2006–08.
2. The Eighth Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG 2011; 118 (Suppl. 1): 1–203.
3. Dias MS, Sekhar LN. Intracranial hemorrhage from aneurysms and arteriovenous malformations during pregnancy and the puerperium. Neurosurgery. 1990;27:855–65.
4. Hunt HB, Schifrin BS, Suzuki K. Ruptured berry aneurysms and pregnancy. Obstet Gynecol. 1974;43:827–37.
5. Shah AJ, Kilcline BA. Trauma in pregnancy. Emerg Med Clin N Am. 2003;21:615–29.
6. Weinberg L, Steele RG, Pugh R, Higgins S, Herbert M, Story D. The pregnant trauma patient. Anaesth Intensive Care. 2005;33:167–80.
7. Fast A, Shapiro D, Ducommun EJ, Friedmann LW, Bouklas T, Floman Y. Low back pain in pregnancy. Spine. 1987;12:368–71.
8. Ng J, Kitchen N. Neurosurgery and pregnancy. J NeurolNeurosurg Psychiatry. 2008;79:745–52.
9. Cook T, Woodall N, Frerk C. 4th National Audit of the Royal College of Anaesthetists and the difficult airway society: major complications of airway management in the United Kingdom 2011. http://www.rcoa.ac.uk/index.asp?PageID=1089. Accessed 23 Mar 2012.
10. NganKee WD, Lee A, Khaw KS, Ng FF, Karmakar MK, Gin T. A randomized double-blinded comparison of phenylephrine and ephedrine combinations given by infusion to maintain blood pressure during spinal anesthesia for cesarean delivery: effects on fetal acid-base status and hemodynamic control. Anesth Analg. 2008;107:1295–302.
11. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MS. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for caesarean delivery. Anesthesiology. 2002;97:1582–90.
12. Brown MD, Levi ADO. Surgery for lumbar disc herniation during pregnancy. Spine. 2001;26:440–3.
13. http://www.fass.se/LIF/miljo_splash/index_en.jsp. Accessed 23 Mar 2012.
14. Cottrell and Young's Neuroanesthesia. 5th Edition. Chapter 23. Pg: 419.
15. Guida M, et al. Aneurysmal subarachnoid Haemorrhage in pregnancy: a case series. Transl Med UniSa. 2012 Jan-Apr;2:59–63.
16. Jing-Jie Liu MD, Zheng Guan MD, et al. Complications after spinal anesthesia in adult tethered cord syndrome. Medicine (Baltimore). 2016;95(29)
17. Dean C, Douglas J. Magnesium and the obstetric anaesthetist. Int J Obstet Anesth. 2013;22:52–63. https://doi.org/10.1016/j.ijoa.2012.10.003.
18. Oddie S, Tuffnell DJ, McGuire W. Antenatal magnesium sulfate: neuro-protection for preterm infants. Arch Dis Child Fetal Neonatal Ed. 2015;100:F553–7. https://doi.org/10.1136/archdischild-2014-307655.
19. Shnider SM. Serum cholinesterase activity during pregnancy, labour and the puerperium. Anesthesiology. 1965;26:335.
20. Robertson GS. Serum cholinesterase deficiency 11: pregnancy. Br J Anaesth. 1966;38:361.
21. MacDonald AG, Graham IH. Suxamethonium apnoea in a pregnant patient. Br J Anaesth. 1968;40:711.
22. Evans DB, Lehmann H. Pseudocholinesterase activity in liver transplantation. Lancet. 1971;1:1040.
23. Wang LP, Peach MJ. Neuroanesthesia for the pregnant woman. Neurosurgical Anesthesiology. 2008;107(1):193–200.

31 Management of Immunosuppressed Patient with HIV and Hepatitis B and Brain Tumor

Rakhi Pal and Anand Rajan

31.1 Introduction

Important insights have been gained into the pathogenesis of human immunodeficiency virus (HIV) infections and hepatitis B infections, but managing these patients still remains challenging. Anesthesiologists should be aware of the implications of dealing with increasing numbers of both diagnosed and undiagnosed, symptomatic and asymptomatic HIV-infected patients in the operating room.

Stem Case Terminology

A 57-year-old male is admitted with H/O seizures and weakness of his right side. He also complains of headaches. He has been diagnosed with HIV (human immunodeficiency virus) infection last year and is on antiretroviral medication. A recent CT scan after the second episode of seizures shows an enhancing brain tumor on the left partial region along with some edema surrounding it. The neurosurgeon wants to operate on him to resect this tumor. He is on levetiracetam and dexamethasone.

R. Pal (✉)
University Hospitals, Cleveland, OH, USA

A. Rajan
Ohio State University, Columbus, OH, USA

31.2 Preoperative

Question 1:
What are the preoperative concerns in a patient with HIV infection coming for a brain tumor resection?

Answer:
There are a number of concerns to think about during the preoperative evaluation.

1. Respiratory impairment due to concurrent infections and pneumonia should be considered.
2. Impairment of neuronal functions (related to viral factors, host response, and environmental factors such as alcohol, drug addiction, and HCV co-infection) inducing a cognitive dysfunction or a peripheral neuropathy. Autonomic neuropathy can be a serious problem under anesthesia [1].
3. Lipodystrophy, dyslipidemia, and insulin resistance are the main metabolic combined antiretroviral therapy (ART)-related side effects, responsible for atherosclerosis and coronaropathy.
4. Nutritional impairment. Anesthesia for HIV patients is almost the same than usual, without HIV-related contraindication to regional anesthesia.
5. Anesthetic drugs can have drug interaction with antiretroviral therapy. The main restriction belongs to the protease inhibitors, which could

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_31

affect the metabolic pathways of opioids, NSAIDs, and benzodiazepines (overdose risks).

Question 2:
What is the current treatment of HIV?

Answer:
After the introduction of antiretroviral combination (ARV) therapies, mortality has been reduced by half. The goal with ARV is to sustain plasma viral load levels to <50 copies/mL on ultrasensitive viral load assays. Increase in CD4 count and decrease in viral load are indicators of effective treatment [2]. The treatment plan must therefore include ARV drugs with different resistance profiles to minimize the chances of a viral strain that will be resistant to all the prescribed drugs.

Antiretroviral drug (ARV) class classification [3].

Five broad classes of ARVs are being used, often in combination.

1. Protease inhibitors (PIs).
2. Nucleoside reverse transcriptase inhibitors (NRTIs).
3. Non-nucleoside reverse transcriptase inhibitors (NNRTIs).
4. Cell membrane fusion inhibitors.
5. Integrase inhibitor-based HAART is HIV treatment.

Question 3:
What are the side effects to keep in mind while considering HIV patients for brain tumor surgery?

Answer:
Ideally all patients on HAART should continue with their treatment protocol.

Below is the list of antiretroviral drugs and their side effects [4].

Protease inhibitors (PIs)—GI disturbances, hyperbilirubinemia, hyperlipidemia, lipodystrophy.

Nucleoside analog reverse transcriptase inhibitors (NRTIs)—peripheral neuropathy, pancreatitis.

Renal toxicity, increased LFTs, GI.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)—GI, increased LFTs, rash, p450 induction.

Pentamidine—arrhythmias, bronchospasm (aerosolized), electrolyte abnormalities.

Question 4:
What is the preoperative management of associated infections of different organ systems in HIV patients?

Answer:
Since HIV can affect almost every organ system, preoperative assessment should involve evaluation of every organ system.

Respiratory system
1. Look for association of opportunistic infections in HIV/AIDS due to *Pneumocystis carinii* pneumonia (PCP), aspergillosis, herpetic infections, oral and pharyngeal candidiasis, and cytomegalovirus (CMV) pneumonia.
2. Evaluation of pulmonary function, which may include arterial blood gas analysis and spirometry.
3. The need for postoperative ventilatory support.

Cardiovascular system
1. Any brain tumor pathology affecting brainstem function may provoke arrhythmias.
2. Echocardiography to rule out any vegetation especially in IVDUs, myocarditis, or dilated cardiomyopathy.
3. Rule out any opportunistic bacterial infections causing endocarditis and/or congestive cardiac failure.

Gastrointestinal system
1. Fluid and electrolyte imbalance is common, and preoperative correction is important.
2. Kaposi's sarcoma in the mouth and upper airway may pose a hazard to endotracheal intubation.

Nervous system
- Evaluation of HIV patients for the following neurological complications.
- Encephalitis, meningitis, neoplasia (primary cerebral lymphoma), polyneuropathy, and HIV-related dementia.

Hematological complications

- Anemia, thrombocytopenia, and leucopenia are common.
- Chemotherapeutic agents and radiotherapy may aggravate these abnormalities necessitating blood and blood product transfusions. CMV adrenalitis and/or exogenous corticosteroid administration in the treatment of peripheral neuropathy may cause adrenal suppression requiring perioperative steroid supplementation.
- Other problems include anesthesia in the IVDU group (multisystem disease, poor venous access) and problems related to drug interactions (e.g., PIs may decrease metabolism of benzodiazepines and opioids).

Question 5:
What preoperative investigations are required?

Answer:
CBC—complete blood count.

Electrolytes, renal function, LFTs, and coagulation profile.

CD4 count and viral load <3 months.

ECG looks for prolonged QT time, conduction defects, ischemic changes, pericarditis, and pericardial effusion.

CXR should be routinely performed, as well as a chest CT if CD4 count <200; also look for cardiac shadow abnormalities as above, infection, *Pneumocystis carinii*, Kaposi sarcoma of airway of mediastinum, mediastinal lymph nodes or compression, and tuberculosis.

MRI of brain or spine if demyelinating neuropathy suspected.

Liver function especially if on nevirapine (raised liver enzymes are common on ARV, albumin levels are often low).

Question 6:
What are the special considerations for HIV patients for anesthesia?

Answer:
Consider delaying an elective case if CD4 < 200 due to an increased risk in postoperative infectious complications. If CD4 < 50, there is increased 6-month mortality following surgery. HIV medications should not be stopped; ID specialist should be consulted if the patient is unable to take PO postoperatively. The perioperative care should take into account the underlying conditions.

31.3 Intraoperative

Question 7:
What are the common pharmacological interactions between antiretroviral drugs and anesthetic drugs?

Answer:
Benzodiazepines: PIs with midazolam and diazepam can cause major respiratory depression and dangerous sedation [5].

Opiates: PIs and NNRTIS can cause acute withdrawal of methadone [6]. Methadone is a drug of choice for opiate dependence in HIV patients as almost 30% of HIV patients are IVDU.

Etomidate, atracurium, remifentanil, and desflurane are not dependent on cyt p450 metabolism, so they are preferred agents to minimize drug interaction [7].

ARV can cause impairment of fentanyl and alfentanil metabolism, resulting in higher serum levels and hence major respiratory depression [7].

Question 8:
What is cross infection and how does cross infection occur in operating room environment?

Answer:
Cross infection occurs in patients who have not been cured with antiretro viral medications and due to urgency of brain tumor surgery from patient to patient or from anesthetist to patient. HIV can be transmitted to the anesthetist through a sharps injury or from splashing of a mucosal surface or broken skin by body fluid. In operating rooms, most injuries occur during unsafe disposal of sharps or when re-sheathing needles. Until today, risks of HIV transmission following needle stick injury and mucocutaneous transmission are 0.3% and 0.03%, respectively.

Question 9:
What are the factors for determining cross infection and how do we prevent this?

Answer:
1. Volume of blood inoculated during needle stick injury.
2. Depth of puncture by infected needle.
3. Contamination of anesthetic equipment like laryngoscope and circuits with HME devices.

We anesthesiologists carry a cumulative risk over our anesthetic career may be as high as 4.5%.

The universal precautions remain the most important in the prevention of cross infection of HIV in operative room environment.

Wearing gloves associated with a 10–100 fold reduction in the inoculum from a needle stick injury.

Use of disposable equipment should be recommended where available.

Question 10:
Should succinylcholine be used for endotracheal intubation?

Answer:
While succinylcholine has been found to increase intracranial pressure, as long as the brain is well anesthetized and $PaCO_2$ controlled, the effects should be negligible, while utilizing succinylcholine with regard to hyperkalemia, it has not been found to significantly raise potassium in either early or delayed surgery.

Question 11:
What are the anesthetic consideration in patients with HIV and a brain tumor?

Answer:
HIV patients with significant cardiac disease is identical to management of all other patients with coronary artery disease. Maximizing myocardial oxygen supply and reducing oxygen demand are priority. Supply may be increased with increasing FiO_2, transfusions as necessary, and reduction of heart to maximize diastolic perfusion. Demand can be reduced by augmenting heart rate, contractility, and afterload.

Under general anesthetic, attention should be paid to altered gas exchange from pneumonia, presence of secretions that can cause alteration in pulmonary mechanics and pressures, and the need for intraoperative pulmonary toilet (bronchodilators, recruitment, and bronchoscopy).

The clinician should be aware that aerosolized pentamidine can cause significant perioperative bronchospasm.

An arterial line may be useful to evaluate gas exchange as well as to monitor mean arterial pressure (MAP) and hence ICP. Immediate treatment of cardiovascular abnormalities in patients with significant degrees of autonomic dysfunction is possible.

While no special equipment is required, at the conclusion of the procedure, all equipment should be cleaned with appropriate anti-infective solutions.

Maintenance of renal perfusion pressure, with avoidance of excessive and prolonged hypotension or alternatively, high vasopressor use.

Patients with HIV and AIDS encephalopathy or AIDS-related dementia complex tend to be more sensitive to opioids and benzodiazepines, reflecting the extent.

Antiseizure medications for the treatment of neurological disorders (especially seizure medications, treatments for spasticity) can cause significant neurological involvement. Significant interaction with multiple anesthetic drugs, particularly at the level of liver metabolism (i.e., muscle relaxants), often decreasing the duration of action. Frequent twitch monitoring is indicated if muscle relaxation is required.

Biochemical or clinical adrenal insufficiency should be ruled out. Primary or secondary adrenal insufficiency is the most serious complication of HIV/AIDS. Secondary causes include infection (CMV, Neisseria meningitis) or drugs (ketoconazole, rifampin, etomidate).

For patients who are on insulin preoperatively, their regimen should be adjusted according to their fasting status as hyperglycemia can cause worsening of cerebral ischemia.

Hyponatremia in neurosurgery patients presents a unique challenge in the perioperative period. It should be corrected accordingly.

Intraoperative monitoring is based on patient's underlying concomitant system involvement. No additional monitoring is required other than routine craniotomy for brain tumor surgery. If significant cardiovascular disease is present, central venous catheter, transesophageal echocardiographic [TEE], may be warranted.

31.4 Postoperative

Question 12:
How would you control postoperative pain in these patients?

Answer:
The treatment of pain in HIV infection is similar to cancer pain management and should be via multidisciplinary approach through history and physical examination, including medication history, history of substance use or misuse, and neurological and psychological assessment.

1. Possible etiologies, infections and malignancies, should be ruled out.
2. The psychological and emotional contribution to pain should be explored.
3. A specialist in pain management should be consulted, when necessary. Painful peripheral neuropathy is the most common neurological disorder associated with HIV [8].

After brain tumor surgery, neurological assessment should be considered before administering long-acting narcotics. Current pain management modalities include non-narcotic and narcotic analgesics, tricyclic antidepressants, anticonvulsants, physical therapy, and psychological techniques.

Question 13:
What are the postoperative considerations in HIV-positive patients?

Answer:
Postoperatively, continued pulmonary toilet, incentive spirometry, and nebulizer treatments may be required. Antibiotics should be continued. Patients with severe preoperative respiratory failure but required a surgical intervention consider the need for possible postoperative continued intubation and/or mechanical ventilation. Another contributing factor of post op ventilatory support is that significant musculoskeletal disease exists.

Establishment of full muscle strength should precede extubation, otherwise patients may require postoperative mechanical ventilation.

In postoperative period, the follow-up should include the thromboembolism prevention (increased risk compared to main people), the cardiovascular side effects, the nutritional status, and the continuation of the treatment. Moreover, the related psychological status and a close collaboration with the corresponding physician is critical.

Multiple Choice Questions

1. While providing safe anesthetic for managing HIV patents under anesthesia, which of the following is not necessary?
   (a) Evaluation for various organ involvement.
   (b) Pharmacology and adverse reactions of antiretroviral agents.
   (c) Understanding basic knowledge of HIV infection.
   (d) Worldwide incidence and prevalence of HIV.
   Answer: d
2. Neurologic involvement associated with HIV infections are except.
   (a) Lymphoma.
   (b) Autonomic neuropathy.
   (c) Cerebral aneurysm.
   (d) Polyneuropathy.
   Answer: c
3. Which of the following is not true regarding pharmacokinetics of antiretroviral medication?

(a) NNRTIs have inhibitory effect on CYP and reduce fentanyl clearance.
(b) ARV (PIs and NNRTIs) can inhibit midazolam metabolism and prolong midazolam effect.
(c) Activation of CYP 450 3A4 enzyme can enhance hypotensive effect of calcium channel blockers or increase level of lidocaine.
(d) PIs and NNRTIS can cause acute withdrawal of methadone.

Answer: c

4. Which endocrine abnormality is not associated with HIV?
   (a) Insulin resistance.
   (b) Hypercortisolism.
   (c) Lipodystrophy and hyperlipidemia.
   (d) Hypoglycemia.

   Answer: d
5. While considering cross contamination, which of the following is not true?
   (a) A single significant needlestick injury with HIV-infected blood may be associated with a 0.31% risk of HIV transmission.
   (b) Constant vigilance and the use of universal precautions when caring for all patients are required by the anesthetist in the operating theater in order to avoid contracting infection from patients.
   (c) Contamination of laryngoscope blades and handles with visible and occult blood occurs frequently cause transmission of disease.
   (d) Post exposure prophylaxis should be administered 2 weeks after the injury.

   Answer: d
6. Which of the following statement is not true?
   (a) Increased risk in postoperative infectious complications if CD4 count less than 200.
   (b) CD4 < 50, increased 6-month mortality following surgery.
   (c) HIV medications should be stopped 1 week before surgery.
   (d) Check CD4 count and viral load <3 months as part of pre op test.

   Answer: c
7. In regard to preoperative investigation, which statement is not true?
   (a) Echocardiography to rule out any opportunistic bacterial infections causing endocarditis and/or congestive cardiac failure.
   (b) CXR to rule out infection i.e., *Pneumocystis carinii*, TB, Kaposi sarcoma of airway of mediastinum, mediastinal lymph nodes, or compression.
   (c) All patient with HIV should get evaluation of pulmonary function, which may include arterial blood gas analysis and spirometry.
   (d) CBC, electrolyte blood glucose.

   Answer: c
8. Regarding cross infection, which one is not a contributory factor?
   (a) Volume of blood inoculated during needle stick injury.
   (b) Depth of puncture by infected needle.
   (c) Contamination of anesthetic equipment like laryngoscope and circuits with HME devices.
   (d) Use of nondisposable equipment.

   Answer: d
9. During the intraoperative period, under a general anesthetic, which of the following is true?
   (a) Attention should be paid to altered gas exchange from pneumonia, presence of secretions that can cause alteration in pulmonary mechanics and pressures, and the need for intraoperative pulmonary toilet.
   (b) There is no change in pharmacokinetics of fentanyl and alfentanil.
   (c) There is no risk of cross contamination.

   Answer: a
10. Which statement regarding HIV is false?
    (a) Hyponatremia is common.
    (b) Adrenal insufficiency is a common occurrence.
    (c) Protease inhibitors could interact with the metabolic pathways of opioids, NSAIDs, and benzodiazepines.
    (d) Use of atracurium is not favorable in HIV-infected patients under anesthesia.

    Answer: d.

References

1. Boise L, Gill MJ, Power C. HIV infection of the central nervous system: clinical features and neuropathogenesis. Neurol Clin. 2008;26:799–819.
2. Weller I. Williams I. ABC of AIDS. BMJ. 2001;June 9;322
3. Wynn G, Zapor M, Smith B, et al. Antiretrovirals part 1: overview, history and focus on protease inhibitors. Psychosomatics. 2004;45:262–70.
4. Avidan MS, Jones N, Pozniak AL. Anaesthesia. 2000;55:344–54.
5. Dasgupta A, Okhuysen P. Pharmacokinetic and other drug interactions in patients with AIDS. Ther Drug Monit. 2001;23:591–605.
6. Foisy M, Tseng A. Interactions between sedatives/hypnotics and protease inhibitors/NNRTIs. www.tth-hivclinic.com 2002; September 20: 1–7.
7. Rainey P. HIV drug interactions: the good, the bad and the other. Ther Drug Monit. 2002;24(1):26–31.
8. Penfold J, Clark AJ. Pain syndromes in HIV infection. Can J Anaesth. 1992;39:724–30.

Management of Patients with Intracerebral Hemorrhages

32

Alexis Steinberg, Kate Petty, and Brian T. Gierl

Stem Case Terminology

A 68-year-old man of Asian ethnicity presents after being found down in his bedroom. His wife states that he had a cardiac stent placed 1 year ago and had been taking clopidogrel and aspirin since that time, but recently stopped taking the clopidogrel due to the cost of the drug and instead increased his aspirin dose to 325 mg daily.

Question 1:
What is the epidemiology of ICH?

Answer:
ICH accounts for roughly 10% of strokes and ~40% of ICH victims will die within 30 days. Deaths from ICH total ~20,000 annually in the US alone. Asians, African-Americans, Mexicans, and Native Americans all have higher rates of ICH than Caucasians and the reason for that discrepancy is unproven. Increasing age portends the highest relative risk for ICH; one study found that approximately one-third of all ICH occurs to patients over the age of 80. Hypertension, smoke exposure, alcohol, and cocaine abuse are the main modifiable risk factors.

Question 2:
What is the etiology of ICH? How does location predict etiology?

Answer:
The etiology of ICH is divided into primary ICH due to chronic disease by hypertension or cerebral amyloid angiopathy (CAA). These two etiologies account for ~80% of all ICH. In both HTN and CAA, the diminutive walls of small vessels are easily damaged. Eventually they rupture and bleed.

ICH due to hypertension most commonly occurs in "perforators" which are small vessels that branch directly off of much larger vessels at abrupt angles to perfuse white matter in the basal ganglia, thalamus, pons, and cerebellum. The proximal segments of these vessels are subjected

A. Steinberg
Department of Neurology, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Department of Critical Care Medicine, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA, USA
e-mail: steinberga2@upmc.edu

K. Petty
Department of Anesthesiology and Perioperative Care, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA, USA
e-mail: pettykl@upmc.edu

B. T. Gierl (✉)
Division of Neuroanesthesiology, Department of Anesthesiology and Perioperative Care, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA, USA
e-mail: gierlbt2@upmc.edu

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_32

to shear forces due to the abrupt branching. Perforating vessels also lack the long arteriolar segments that protect vessels of that size so that a portion of the vessel with a diminutive muscularis is subjected to high forces. These forces cause the vessels to form atheromas, which further weaken the vessel walls.

Amyloid plaques tend to accumulate in cortical gray matter. Apolipoprotein E (ApoE) is the main lipoprotein of the brain. It is produced by astroglia and microglia and carries cholesterol and some proteins within the CNS and can also bind to neuronal receptors to act as a signaling molecule. The ApoE allele $\epsilon 2$ increases the risk for amyloid plaques and Alzheimer's disease.

Secondary causes are structural or due to acute hemodynamic changes and they account for ~20% of the incidences of ICH. They include trauma, arteriovenous malformation or aneurysm rupture, eclampsia, hemorrhagic conversion of ischemic stroke, tumors, and the abuse of stimulants. Both cocaine and methamphetamines can cause a vasculitis that can weaken vessel walls. Renal cell carcinoma and melanoma are the two cancer types that are the most likely to bleed.

Question 3:
What is the pathophysiology of ICH? What are the primary and secondary pathologies?

Answer:
Primary ICH begins as a disease of the blood vessel wall, as described above. Initially, vessel disruption ends blood flow to the capillary bed served by that vessel. The mass effect of the expanding hemorrhage also reduces the cerebral perfusion pressure in the adjacent tissue. High pressure blood can dissect adjacent tissue. As that hematoma expands, it may tear other diseased vessels nearby and they may bleed as well.

The outcome of the disease is largely influenced by the extent of the expansion of the hematoma in the first few hours after symptom onset, which is why it is crucial to identify ICH early and to begin treatment immediately.

Secondary damage occurs when an inflammatory cascade releases and activates matrix metalloproteinases, glutamate, and cytokines. These substances perpetuate a variety of insults to the brain, including an inflammatory milieu that produces free radicals that damage local structures. Metalloproteinases and other substances breakdown the blood-brain barrier, which allows macrophages and platelets to arrive and trigger cytotoxic and apoptotic cell death and edema that damages neurons that were still viable after the initial bleed.

A second wave of edema and further toxicity occurs from 48 h to 7 days after the event. This fact has complicated clinical trials, as it is believed that for a nonsurgical therapy to be effective, it would have to be applied continually over 7 days or more. Nonetheless, therapies to limit this edema and its toxic effects are ongoing. The breakdown of blood products in the hematoma is known to release heme and free iron, which are cytotoxic and inflammatory, making iron removal or neutralization a potential therapy. Several compounds that chelate iron have been tested, but so far each compound has failed—many chelators have had toxic side effects with escalating doses before reaching a therapeutic level.

The clinician should be aware that the surrounding brain is fragile and that the patient's physical examination may worsen without a treatable or identifiable etiology in this time period.

Question 4:
What is the timeframe for initial treatment per the available guidelines? Has treatment per those Guidelines been shown to reduce morbidity or mortality?

Answer:
Guidelines published by the AHA/ASA and the European Stroke Organization (ESO) have evaluated the current evidence for treatment of ICH and those guidelines as well as the relevant literature pertaining to the treatment of ICH will be discussed throughout this chapter. The Neurocritical Care Society (NCS) published guidelines for ICH treatment as part of its Emergency Neurologic Life Support (ENLS) series. The NCS' guideline refers to the first hour within presentation for medical care as the "Golden Hour." They recom-

mend that each of these issues be reviewed and addressed in that first hour.

1. Stabilization and reassessment of the patient's airway, breathing, and circulation (ABC's).
2. Rapidly determine an accurate diagnosis using neuroimaging (usually non-contrast CT Head).
3. Perform a concise clinical assessment regarding ICH characteristics and the patient's condition. This is important in determining whether the patient is clinically deteriorating without performing an exorbitant number of CT scans.
4. Targeted assessment for potential early interventions including:
   (a) Control of elevated blood pressure.
   (b) Correction of coagulopathy.
   (c) Need for early surgical intervention.
5. Anticipation of specific patient care needs such as:
   (a) Specific treatment aspects related to underlying ICH cause.
   (b) Risk for early clinical deterioration and hematoma expansion.
   (c) Need for intracranial pressure (ICP) or other neuromonitoring.

There is not a specific trial of the influence of these guidelines on patient outcome. Overall, some cohort and population studies have concluded that the morbidity and mortality of ICH has been declining in countries with modern medical care—specifically the control of HTN. However, some studies have not witnessed a change in the rate of ICH in those same countries. Sub-Saharan Africa has seen an increase in the diagnosis of ICH and has a fatality rate of ~40% as opposed to the fatality rate of ~25% in Great Britain's' modern health system.

Question 5:
What is the level of evidence behind the guidelines?

Answer:
Due to the relatively high frequency of this disease and the impact to society, many trials have been initiated in the past 5–6 years, so expert's knowledge of ICH is rapidly evolving.

The ESO's panel of experts published their most recent guidelines for ICH treatment in 2014 and only found four strong recommendations. However, the AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage updated their guidelines 1 year later in 2015 and included 14 Class I recommendations.

Question 6:
What is the appropriate neuroimaging and how is it interpreted? Is an MRI/MRA or CTA helpful?

Answer:
Classically, the patient presenting with headache and somnolence should receive a non-contrast CT of the head in order to identify a hemorrhage. ICH can often mimic the signs and symptoms of ischemic stroke. Both of these conditions warrant prompt, aggressive therapy but they are treated in an opposing manner in terms of blood pressure goals and anticoagulation, so it is necessary to differentiate between them promptly and correct coagulation deficits and reduce blood pressure in ICH patients.

A few trials have correlated various hematoma shapes or patterns within the ICH hematoma with a hemorrhage expansion >33%, which is considered to be indicative of a poor outcome. The signs on non-contrast CT include an irregularly shaped hematoma including the presence of lakes or island sign, intrahematoma hypodensities, black hole sign, swirl sign, blend sign, and heterogeneous hematoma density. A table that accompanies the suggested reading "Blood pressure reduction and noncontrast CT markers of ICH expansion" defines each of these signs. The presence of *any* of the "signs" predicts an increased risk of hematoma expansion, poor outcome, and 90-day mortality.

A combination of the presence or absence of multiple signs combined with hematoma volume may be more specific for certain good and bad outcomes. In this manner, these signs may be important for end of life decision-making in appropriate populations. They may also be a useful means to further risk-stratify patients being enrolled in clinical trials of ICH therapies.

At the time of this publication, no society has endorsed a CT Angiogram of the head (or MRA of the Brain) as a standard of care for ICH evaluation. However, the presence of a bright "spot" within the hemorrhage on CTA is known as "spot sign." It suggests continued extravasation and has been widely accepted as a marker for continued hematoma expansion and a poorer prognosis. The "spot sign" has demonstrated the highest odds ratio of poor outcome.

An MRI (with and without contrast) and MRA brain and neck can be helpful in diagnosing the etiology of the ICH. It can help identify markers of CAA and the presence of a tumor or vascular malformation. MRI can also be utilized to estimate the age of hemorrhage based on the appearance of blood degradation products on different sequences. A digital subtraction angiography (or conventional angiography) can be useful for evaluating the underlying cause of ICH. However, both MRI and digital subtraction angiography should be deferred until the patient is stable.

Question 7:
Is there a proven temperature target for patients with ICH?

Answer:
Deep hypothermia is neuroprotective for patients who require induced cardiac arrest for many procedures. This was transitioned to treating patients post cardiac arrest with mild hypothermia to reduce inflammatory responses and free radical formation, and possibly induce the production and release of neuroprotective compounds. Early studies of mild hypothermia demonstrated a profound benefit for a temperature of 33–35 °C after cardiac arrest. Large randomized controlled trials clearly demonstrated worse functional outcomes in patients who were hyperthermic in the early post-arrest period.

Simialry, patients recovering from traumatic brain injury (TBI) have worse outcomes when hyperthermic. The POLAR trial did not demonstrate a benefit of early hypothermia for TBI patients.

Several small studies have been performed to determine whether mild hypothermia will benefit patients after ICH, but none has conclusively answered that question. Most providers treat patients for hyperthermic, as in the same manner that was effective for post cardiac arrest and TBI patients. A large RCT—the Cooling in INtraCerebral Hemorrhage (CINCH) trial—is ongoing and its results may determine whether therapeutic temperature management is appropriate for ICH patients.

Question 8:
Is there a simple vehicle for predicting the outcome of patients with ICH? Is there a model to predict functional independence at 90 days?

Answer:
The original and most widely used outcome measure is the ICH Score. It was developed by a group led by Claude Hemphill and determined that low Glasgow Coma Score (GCS) on presentation, age 80 or above, hematoma volume greater than 30 cm^3, a location below the tentorium, and hemorrhage extension into the ventricles were all harbingers of poor outcome. See Table 32.1.

The FUNC Score similarly scores the likelihood of functional independence at 90 days post-bleed. It includes a slightly different scoring system for similar variables to the ICH Score, but also includes whether the patient had significant cognitive impairment prior to their hemorrhage. See Table 32.2. However, caution should be utilized when using these prognostic scores. Initially, aggressive medical treatment should be offered to patients even with high ICH scores, in order to prevent the self-fulfilling prophecy of using bad prognostic scores and seeing bad outcomes. The guidelines currently recommend against early withdrawal of intervention in the emergency department and recommend offering aggressive therapy with reevaluation and goals of care discussions at 24 h, based on the patients' preference and their clinical course.

Table 32.1 FUNC score likelihood of functional independence at 90 days

Feature	Points
GCS	
3–4	2
5–12	1
13–15	0
Age	
≥80	1
<80	0
Location	
Infratentorial	1
Supratentorial	0
ICH volume	
≥30 cm^3	1
<30 cm^3	0
Intraventricular blood	
Yes	1
No	0

ICH score	30 day mortality (%)
0	0
1	13
2	26
3	72
4	97
5	100
6	100

ICH Score = 0–6 points

Table 32.2 ICH score predicts 30 day mortality

Feature	Points
ICH volume (cm^3)	
<30	4
30–60	2
>60	0
Age (years)	
<70	2
70–79	1
≥80	0
ICH location	
Lobar	2
Deep	1
Infratentorial	0
GCS	
≥9	2
≤8	0
Pre-ICH cognitive impairment	
No	1
Yes	0

FUNC score	% Functionally independent at 90 days
0–4	0
5–7	13
8	42
9–10	66
11	82

Total FUNC Score = 0–11

32.1 Preoperative

Question 9:
How can you calculate the hemorrhage volume in your patient?

Answer:
The ABC/2 volume formula is a simple tool that was developed for use at the bedside to provide a rapid clinical assessment for estimation of the hemorrhage volume. First, identify the axial CT slice with the largest area of hemorrhage.

Formula

$$\text{Volume} = A \times B \times C / \text{shape}$$

A and *B* are the two largest diameters on this slice.

C is the section thickness multiplied by the number of sections the lesion was visible.

Shape = 2 in lesions that are round/ellipsoid and 3 for other shapes.

The initial studies found that the ABC/2 is a reliable test that is easily reproducible by multiple providers. The ABC/2 volume formula tends to overestimate the hemorrhage size in large, complex shaped lesions. Its accuracy is acceptable to prognosticate outcome for ellipsoid shaped lesions and was used to develop the ICH score. Software programs rapidly calculate hemorrhage volumes more accurately especially in complex lesions as well as other lesions such as arteriovenous malformations.

32.1.1 Blood Pressure and Coagulopathy Management

Question 10:
What is the target blood pressure goal?

Answer:
Many patients with ICH present with severe hypertension, which theoretically can exacerbate hemorrhage expansion and edema. Yet, aggressive blood pressure control must be balanced against the need for maintaining adequate cerebral perfusion pressure in those patients with large hemorrhages. Two randomized clinical trials, INTERACT2 and ATACH2, have provided information about blood pressure goals. Both trials randomized patients to either a systolic blood pressure of less than 140 or 180 mmHg. Neither trial demonstrated a benefit in primary outcome of death or major disability from aggressive blood pressure control, but there were some secondary outcomes suggesting possible benefit. Therefore, in patients where there is no concern for elevated ICP, a general approach is to rapidly correct blood pressure to <140 or < 160 mmHg for the first 24 h. Given the lack of clear evidence, practice is quite variable, and some centers still target an SBP <180 mmHg in the acute period. Aggressive hypertension control may cause relative or absolute hypotension, which can lead to end organ damage.

Question 11:
What antihypertensive should be used?

Answer:
Commonly used medications for blood pressure control initially after ICH include intermittent intravenous labetalol and continuous infusions of a calcium channel blocker. The two calcium channel blockers that are available for continuous infusion are nicardipine and clevidipine. Clevidipine has a shorter half-life than nicardipine, which allows the provider to more quickly titrate clevidipine so that the target blood pressure can be met quickly and robustly maintained. Hydralazine is an option but it is a long acting medication and its clinical effect is not as easy to predict. Although readily titratable, nitroglycerin and sodium nitroprusside are generally avoided because they cause global cerebral vasodilatation and can lead to rebound cerebral hyperemia after they are stopped.

Reversal of Coagulopathy Prior to going to the operating room for an ICH, it is vital for the anesthesiologist to determine if the patient was taking any antiplatelet agents or an anticoagulant.

Aspirin (acetylsalicylic acid)
- Patients commonly take aspirin on a daily basis for primary and secondary protection against myocardial infarction and ischemic strokes. Aspirin irreversibly binds with cyclooxygenase-1 enzyme leading to decreased thromboxane A2, which results in impaired platelet aggregation. The effect of aspirin lasts 7 days, which is the duration of the platelet lifespan.
- There is limited data in the literature regarding reversal of aspirin therapy after an acute intracranial hemorrhage. Unless a patient is diagnosed with vWD Ty 2B (rare), they can receive DDAVP (trade name desmopressin) 0.4 μg/kg with minimal risks. The NCS recommends that no reversal be undertaken in nonsurgical candidates.
- If the patient is planned for a surgical intervention, it is recommended to test the platelet function. If this testing is not readily available, empiric platelet transfusion may be a reasonable option. If there is documented platelet dysfunction then platelet transfusion is given to mitigate the salicylate effect. The suggested dose is a single donor apheresis unit or six pooled platelets for patients on aspirin alone. Then it is suggested to guide further transfusions by repeated platelet function tests or to dose based on clinical judgment in the case of ongoing bleeding.

Clopidogrel
- Clopidogrel is a P2Y12-ADP receptor inhibitor that is prescribed along with aspirin to limit platelet-induced thrombus formation in patients with coronary or intracranial stents, as well as some patients with vasculopathies. Clopidogrel has an active metabolite that persists after discontinuation of the medication. This metabolite can be persistent up to 4 days after the last dose of clopidogrel. Determine

the last dose taken and be aware of the possibility of a prolonged effect secondary to the active metabolite.
– Patients on clopidogrel have longer platelet inhibition that those on aspirin, though only one single donor apheresis unit or 6-pooled platelets is recomended for transfusion.

Vitamin K Antagonists
– Vitamin K antagonists (VKAs) inhibit the synthesis of vitamin K dependent coagulation factors in the liver including II, VII, IX, X resulting in a prolonged prothrombin time on laboratory testing. The most commonly used VKA is warfarin. Providers should promptly reverse VKAs in patients with intracranial hemorrhage.
– Evaluation of the INR will help to guide further management and dosing of reversal. All patients should receive 10 mg IV of vitamin K. The effect of vitamin K has a delayed onset, though it creates a sustained reversal of the VKA.
– Other methods to reverse VKAs include replacing the vitamin K dependent factors. It is recommended that reversal be carried about with prothrombin complex concentrates (PCC). PCCs contain factors II, VII, IX, X, protein C, and S. The amounts vary based on the method of manufacture. There are 3-factor PCCs and 4-factor PCCs, which differ in that the four factors contain appreciable amounts of factor VII, while 3-factor PCCs do not. The neurocritical care society strongly recommends using 3 or 4 factor PCC in patients with an INR greater than 1.4 for intracranial hemorrhage reversal in patients on warfarin. Use of PCCs results in better functional outcomes, less hematoma expansion, and more reliable and faster INR reversal versus those receiving fresh frozen plasma (FFP).
– If PCC is not possible at the institution, then FFP is a suitable alternative. FFP has advantages that include widespread availability and lower cost. Conversely, FFP is associated with a longer time and a large volume required to correct the INR.
– It is not recommended to use recombinant factor VIIa for reversal of VKAs due to the high thrombosis rate cited in clinical trials.

Direct Factor X Inhibitors
– FX is a factor common to both the extrinsic and intrinsic pathways. Activated factor X inhibitors (FXa) block factor X (FX) activity. The current FXa inhibitors used in clinical practice are rivaroxaban, apixaban, and edoxaban. Practitioners should determine the last dose of the FXa inhibitor for any patient who presents with ICH. If it is within 2 h of ingestion and the patient is not at risk for aspiration it is recommended to administer 50 g of charcoal orally, which can reduce the drug exposure by 50%.
– Andexanet alfa is a recombinant FXa analog that competes with the native Xa to bind the currently available FXa inhibitors. It was FDA approved in 2018. For those that have access to this it may provide more complete anticoagulation reversal and should be considered first line. A recent trial administered andexanet alfa to patients taking anti-FXa medications who developed life-threatening bleeding due to gastrointestinal or intracranial bleeds. Andexanet alfa was associated with reduced anti-FXa activity and was found to achieve hemostasis in 79% of the patients.
– As an alternative to andexanet alpha, a number of studies demonstrated that 4-factor PCCs or activated PCCs achieved at least partial reversal of FXa inhibitors.

Direct Thrombin Inhibitors
– Direct thrombin inhibitors (dabigatran, argatroban, bivalirudin) work via inhibition of factor IIa which includes thrombin-mediated platelet activation and aggregation. For reversal, determine the last dose and if more than 3–5 half lives have passed simple discontinuation may suffice in a patient with normal renal function.

– If a dose has been given within 2 h of presentation, administer oral activated charcoal. For dabigatran ingestion within 3–5 half lives or in patients with concurrent renal failure, we recommend to administer idarucizumab 5 g IV. If idarucizumab is not available or the direct thrombin inhibitor is not dabigatran give activated PCC or 4-factor PCC. Using a 3- or 4-factor PCC has only been validated in animal studies and healthy volunteers. If the hemorrhage is significant and there is renal failure consider hemodialysis since dabigatran has a low protein binding (35%) and high rates of renal excretion.

Unfractionated Heparin (UFH)

– UFH inhibits factor IIa and FXa via indirect mechanisms with antithrombin III. For those patients with intracranial hemorrhage, first stop the heparin infusion. To dose protamine determine heparin in the previous 3 h and give 1 mg of protamine per 100 units with a maximum dose of 50 mg. Subsequent dosing can be based on the follow-up PTT.

Low Molecular Weight Heparin (LMWH)

– LMWHs includes enoxaparin and dalteparin, which bind to both FXa and FIIa. There is no specific reversal agent although protamine is given. The reversibility varies significantly. There has been some efficacy using FVIIa for reversal of LMWH. It is not recommended to reverse patients receiving prophylactic dosing of LMWH.

Reversal of Anticoagulation

Classification	Agent	Laboratory test	Reversal	Comments
Antiplatelet	Aspirin	Aspirin response assay	(1) DDAVP 4mcg/kg (2) + surgical intervention, platelet transfusion, 1 apheresis unit	If no aspirin response, and surgical intervention is planned, empiric platelet transfusion is reasonable
	Clopidogrel	n/a	(1) DDAVP 4cmg/kg (2) Platelets, 1 apheresis unit	
Vitamin K antagonist	Warfarin	PT/INR If INR > 1.4 reversal warranted	(1) 10 mg IV vitamin K (2) 3- or 4-factor PCC (based on weight, PCC type, and INR)	If PCC not available FFP 10–15 mL/kg
FXa antagonist	Rivaroxaban Apixaban Edoxaban	FX activity	(1) Charcoal 50 g if last dose <2 h (2) Andexanet alpha low dose/high dose regimen	If andexanet alpha is not available, 4-factor PCC or activated PCC 50 IU/kg
Direct thrombin inhibitor (DTI)	Dabigatran (oral) Desirudin (subcutaneous) Bilirudin (IV) Argatroban (IV)	No recommendations levels correlate with thrombin time (though not available in a timely fashion)	(1) Charcoal 50 g if last dose <2 h (2) If dabigatran Idarucizumab 5 g IV (3) PCC or 4-factor PCCs (50 U/kg) if Idarucizumab is not available or it is a DTI other than dabigatran	Consider hemodialysis if renal insufficiency or dabigatran OD or if idarucizumab is unavailable
Heparin	Unfractionated heparin	PTT, FXa	(1) Protamine	Maximum dose of 50 mg for the first dose
Low molecular weight heparin (LMWH)	Enoxaparin Dalteparin	FXa	(1) Reversal when using full anticoagulation dosing (2) Protamine	If protamine is contraindicated, consider FVIIa (90mcg/kg IV)

32.2 Intraoperative

32.2.1 Surgical Intervention

Question 12:
Should clot evacuation with craniotomy be performed for a patient with supratentorial CINCH?

Answer:
For patients with supratentorial ICH, acute surgical intervention for clot evacuation and decompressive craniectomy is indicated only in those patients with clear mass effect leading to herniation. STITCH I and II trials randomized patients to early surgical evacuation or medical management and demonstrated that there is no role for early operative intervention of supratentorial bleeds in the absence of substantial mass effect causing decreased level of arousal. The STICH II analysis used lower age, smaller hematoma size, and higher initial Glascow Coma Scale and found that for patients with good prognostic scores, an initial conservative approach is warranted.

Question 13:
What are possible minimally invasive techniques for supratentorial ICHs?

Answer:
Advances in surgical technique and inferior results with craniotomy have led to an era of minimally invasive approaches of clot evacuation in supratentorial ICHs. MISTIE protocols allow for stereotactic catheter placement and aspiration of hematoma combined with fibrinolytic agents. MISTIE II and III trials randomized patients to standard medical management versus catheter placement with hematoma aspiration and fibrinolytic administration. The MISTIEII trial demonstrated safety and provided reproducible results. Patients who received the intervention demonstrated improved modified Rankin Scores (mRS) at 12 months that was greater for patients where a larger clot burden was removed. Although the intervention was associated with increased brain re-bleeding (9.7 versus 5.0%), mortality was equal between groups. However, MISTIE III showed no difference in mRS at 365 days between the intervention and control groups.

The ENRICH trial is also ongoing and aims to compare early hematoma evacuation using minimally invasive parafascicular surgery (MIPS) compared to medical management alone for moderate and large hematomas. MIPS is type of surgical system whereby surgical ports are placed in sulci and thus between lobes in order to minimize parenchymal trauma. Preliminary studies using this technique are promising and will be applied to a large cohort with full results expected in 2020.

Question 14:
When should the placement of an external ventricular drain (EVD) occur?

Answer:
Intraventricular hemorrhage (IVH) occurs in 40% of patients with ICH and is an independent factor associated with poor long-term outcomes. Development of hydrocephalus is a common complication of ICH, especially if there is IVH and occurs in up to 50% of cases. Hydrocephalus can lead to elevated ICP necessitating placement of an EVD to provide both ventricular drainage of CSF and allow for monitoring of ICP. Hydrocephalus is seen more frequently in younger patients, those with lower GCS and with deep hemorrhages. For patients with GCS < 8, evidence of herniation, extensive IVH, or hydrocephalus, the placement of an ICP monitor should be considered.

Question 15:
Are there other techniques to improve outcomes for ICH with IVE?

Answer:
Despite the use of EVDs to control hydrocephalus, patient outcomes for ICH with IVE remains poor. Intraventricular tPA via EVD has shown to accelerate clot removal without increasing bleeding or causing ventriculitis in some patients with extensive IVH. Given this, a randomized controlled trial, CLEAR III, was designed to assess whether intraventricular administration of fibrinolytics

through a ventricular drain improved outcomes. Patients within the treatment arm with small or moderate size ICH (< 30 mL) received alteplase via ventriculostomy catheters in effort to resolve intraventricular clot burden, whereas controls received saline injections via their EVDs. There were similar rates of good functional outcomes at 6 months between the two groups but mortality was lower in the alteplase group, although there was a concurrent increase in severe disability in those who survived. The failure to show benefit from the intervention may be related to poor goal achievement as the blood reduction goal was only achieved in 30% of alteplase recipients. Even though the results were neutral, CLEAR III did demonstrate safety and low rates of complications (infection, re-hemorrhage, and death), and provides a basis for further studies of more aggressive clearance.

Question 16:
When should neurosurgery be done for patients with infratentorial ICHs?

Answer:
Patients with cerebellar hemorrhages >3 cm in diameter or with symptomatic mass effect from a hemorrhage, should undergo decompression (suboccipital) as soon as possible. The infratentorial space is small and has poor elastance so any increase in infratentorial volume is transmitted onto the pons and medulla, making this condition life-threatening. The use of an EVD in this scenario is not sufficient and could lead to upward herniation, worsening outcomes.

32.2.2 Induction

Question 17:
How would you induce anesthesia in this patient? What are your hemodynamic goals during induction of anesthesia?

Answer:
During induction of anesthesia in a patient with an intracranial hemorrhage it is likely that these patients have elevated ICP and the anesthesiologist must maintain cerebral perfusion pressure (CPP). A smooth induction is imperative. The titration of anesthetic agents is used to avoid hypertension with laryngoscopy and tracheal intubation. Paralytic is used to avoid coughing upon tracheal intubation in to avoid further increases in ICP.

Question 18:
Would you premedicate this patient?

Answer:
Typically, in patients presenting with an intracranial hemorrhage, acutely there is an altered level of consciousness when they come to the operating room rendering no need for anxiolytic agents. These agents produce a decrease in consciousness, leading to a depressed respiratory drive resulting in elevated pCO_2 and cerebral vasodilation. Furthermore, these agents may delay a rapid emergence from anesthesia making a timely postoperative neurologic assessment difficult. Premedication is determined on an individual basis and some patients with a better clinical grade may benefit from premedication that is slowly titrated to reduce anxiety and any hypertension associated with it prior to induction.

Question 19:
Prior to induction how would you decrease ICP? Or avoid further increases?

Answer:
Prior to induction, it is critical to avoid further elevation in ICP due to the risk of possible herniation, while maintaining CPP. Start with the patient in a head up position to promote venous drainage and minimize positional changes in ICP. Before induction, during the pre-oxygenation phase, the anesthesiologist must avoid hypoventilation. This period of hypoventilation as well as long periods of apnea must be avoided, as it is associated with a predictable rise in pCO2 and cerebral vasodilation.

Question 20:
What induction agents would you use?

Answer:
The ideal agent to induce hypnosis is an agent that causes cerebral vasoconstriction, decreases cerebral blood flow, and reduces the cerebral metabolic rate leading to decreased intracranial pressure. One can use propofol, etomidate, or thiopental (not currently in the US) all of which achieve these goals. These agents can all be used safely in a patient with elevated ICP as long as they are dosed and titrated appropriately for the each patient and take into account their comorbidities. Other agents such as ketamine previously have been associated with elevations in intracranial pressure and cerebral blood flow, but literature suggests that this is not true. Some studies suggest there is a decrease in ICP with ketamine bolus dosing and using ketamine in a hemodynamically unstable trauma patient it is a reasonable option for induction.

Question 21:
How would you blunt the hemodynamic response to direct laryngoscopy and tracheal intubation?

Answer:
Practitioners can employ several different strategies to reduce the hemodynamic response to stimulation. Overall, the goal is to blunt the sympathetic response to avoid further elevation in ICP. Agents such as lidocaine 1.5–2.0 mg/kg, esmolol or short acting opioids are used to blunt the hypertensive response seen with intubation. Beware with these medications that some result in significant hypotension and should be titrated carefully. Many anesthesiologists strive to decrease blood pressure about 20% from baseline just prior to direct laryngoscopy in anticipation of the blood pressure and heart rate response during intubation.

Question 22:
What muscle relaxant would you use?

Answer:
Muscle relaxation is of great importance to avoid coughing and minimize the stimulation associated with direct laryngoscopy and tracheal intubation. The use of a depolarizing agent such as succinylcholine is used for its fast onset and quick metabolism. Many older studies suggest that it increases ICP, while a few newer studies suggest there is no elevation in ICP. Due to the lack of evidence, and few incidences of documented mortalities associated with succinylcholine in patients with elevated ICP, one can assume that it is probably safe to use in clinical situations. Other ways to decrease the possible elevation in ICP with succinylcholine is by using hyperventilation and using a de-fasciculation dose prior to administering succinylcholine. These strategies may offset the possible increase in ICP. Other caveats; determine if the patient is in the acute phase of an ICH in which succinylcholine is safe to use. While using succinylcholine in a patient in the subacute or chronic phase of an illness with associated motor deficits could be associated with a significant potassium rise resulting in cardiac arrhythmias or arrest.

Many providers prefer using a non-depolarizing agent such as rocuronium, which is not associated with an elevation in ICP. It has a similar onset time as succinylcholine when using a dose of 1.2 mg/kg and now can be reversed with sugammadex 16 mg/kg. Another consideration with the use of a non-depolarizing agent is to determine the neuromonitoring used, especially if MEPs are planned, as this is not compatible with neuromuscular blockade.

Once muscle relaxant is given, one must ensure that paralysis at the neuromuscular junctions is completed prior to tracheal intubation to avoid coughing. If the blood pressure continues to elevate on starting laryngoscopy cease the intubation and continue to titrate additional adjuncts to ensure no increase in ICP during tracheal intubation.

32.2.3 Maintenance of Anesthesia and Early Tracheostomy

Question 23:
What are your goals during maintenance of anesthesia?

Answer:
The four major goals during anesthesia for craniotomy for aneurysm clipping are to (1) maintain

CPP (2) brain relaxation, minimize surgical retraction (3) rapid titration of BP and rapid emergence from anesthesia.

Question 24:
How can you achieve brain relaxation? How long do these measures last?

Answer:
The first step in achieving surgical relaxation is placing the patient in a position that will promote venous drainage, even 10% reverse trendelenberg will suffice. The most rapid means of achieving surgical exposure is via hyperventilation. For each 1 mmHg of pCO_2 change there is a concurrent 2–3% change in cerebral blood flow. The typical goal is to achieve a pCO_2 between 30 and 35 mmHg. These changes are seen almost immediately, and the effects last around 8 h. The goal is to relax the brain via cerebral vasoconstriction while avoiding cerebral ischemia. Another method is via osmotic agent or hypertonic saline. A lumbar drain may be placed to allow further decrease of intracranial pressure and there should be extreme caution when placing, as drainage of too much CSF can result in herniation.

Question 25:
What are you goals for emergence? Which patients should you consider early tracheostomy?

Answer:
Recovery of patients after ICH is unpredictable. If there is uncertainty for neurological recovery postoperatively we would advise to leave the endotracheal tube in place and maintain controlled ventilation. During transportation, sedation is critical to avoid the patient awaking causing elevation of blood pressure and increases in ICP. If preoperatively, the patient did not have significant neurologic deficits and the patient remained hemodynamically stable consideration for extubation is reasonable. For the extubation it is similar to induction, the goal is to avoid coughing with further elevation of ICP and blood pressure.

In patients with significant ICH or ischemic strokes the TRACH score was developed in order to try and predict those patients who would require a tracheostomy. The study looked at 41 patients and determined the independent predictors for requiring a tracheostomy. They included the GCS, location of the hemorrhage, presence of hydrocephalus, and septum pellucidum shift. In order to calculate this, first the R-scale is determined;

$$\mathrm{R-Scale} = \mathrm{L} + \mathrm{H} + \mathrm{S}$$

L = Location, +2 thalamus.
H = Hydrocephalus, if present +1.5.
S = Septum pellucidum if present +3

$$\text{TRACH score} = 3 + \left(1 \times \mathrm{R-scale}\right) - \left(0.5 \times \mathrm{GCS}\right)$$

TRACH scores of zero, +1, and +2 predict a 50%, 80%, and 90% chance of the need for a tracheostomy, respectively.

The TRACH score was found to have a sensitivity of 94% with specificity of 83% in their population of patients. The Trach Score attempts to predict those patients who will require a tracheostomy, but it does not elicit if there is a benefit to early tracheostomy. The SET POINT trial looked to determine if early tracheostomy (defined as within 3 days of intubation) was associated with a shortened ICU admission compared to standard tracheostomy (defined as 7–14 days post intubation). It found no difference in length of ICU stay, but did have a decreased sedation requirement for patients who had early tracheostomy versus standard management. The study did find that there was a six-month mortality benefit in those who had early tracheostomy placement but due to the small sample size, a larger, multicenter trial called the SET POINT 2 trial is currently being conducted. The primary outcome measure is six-month mortality benefits in patients with early tracheostomy.

Determining if a patient with an ICH requires a tracheostomy may benefit from using the TRACH score and other clinical data points to help determine if early tracheostomy may be of value in patients. It may improve mortality in this subset of patients and provides expedited ventilator weaning trials as well.

32.3 Postoperative

32.3.1 Seizures

Question 26:
What is the incidence of seizures after ICH?

Answer:
Incidence of seizures varies significantly depending on the study and the more recent widespread use of continuous EEG. The incidence is anywhere from 1.7 to 31%. Seizures usually develop early after spontaneous ICH, with 90% of seizures occurring within the first 3 days but can occur 7–14 days from hemorrhage onset. There is also a risk of late seizure development, with unclear etiology and incidence. Seizures can either be convulsive or nonconvulsive in semiology. Proximity of ICH to the cortex is the most consistent risk factor associated with seizure development, but critically ill patients with either subcortical and infratentorial ICHs are also at high risk for seizures. The CAVE score is one prognostic tool to determine the risk of seizure development, however, its performance in validation has been low.

Question 27:
Should prophylactic antiepileptic drugs be initiated after ICH?

Answer:
Both the 2015 American Heart Association and 2014 ESO guidelines do not recommend the use of prophylactic antiepileptic drugs (AEDs), since no studies currently have shown neurologic functional or mortality benefit from prophylactic AED administration. As well, studies have not yet shown the use of prophylactic AEDs preventing the development of long-term epilepsy. However, data is limited given the lack of prospective randomized control trials available for prophylactic AED use after ICH.

Question 28:
When should a continuous EEG be used and for how long?

Answer:
Given that prophylactic AED use is not recommended after ICH, continuous EEG (cEEG) can be used to monitor for nonconvulsive seizures with the goal of preventing secondary brain injury by starting AEDs and stopping future seizures from occurring. There should be a low threshold for cEEG monitoring. Patients with depressed mental status or fluctuating level of consciousness, active or impending herniation, or cortical location (involving or within 1 mm of cortex) are considered high risk for developing seizures and so should be placed on continuous EEG to monitor for nonconvulsive seizures. Monitoring with continuous EEG for at least 24–48 h is advised. If the patient is comatose, then monitoring should occur for 48 h because there is high likelihood of detecting seizures after the initial 24 h. If continuous EEG is not available in patients with high risk features, then it is reasonable to administer AEDs for at least 7 days.

32.3.2 Temperature Management and Anticoagulation

Question 29:
Why should patients with ICH be monitored for fevers? When should patients be treated for fevers and how?

Answer:
Fevers are common after ICH and have been independently associated with worse outcomes. A temperature >38.5 °C should be treated however, consideration should be given for treating elevated temperatures below 38.5 °C. Sustained fevers can be addressed with acetaminophen, cooled saline infusion, or cooling blankets. If fevers are refractory, temperature targeted management can be initiated with endovascular cooling.

Question 30:
When should venous thrombemobolism (VTE) chemoprophylaxis therapy be initiated?

Answer:
Hematoma expansion occurs within the first few hours up to the first 24 h. Given concerns for re-bleeding, VTE in patients with ICH is a problematic complication to treat. Almost 15% of ICH patients will develop DVT within the first 30 days, and approximately 80% of these occur within the first 10 days (CLOTS I trial). A multicenter, large retrospective review of over 575,000 patients from 2004 to 2013 examined trends in medical complications including VTE after ICH and showed that the prevalence of deep venous thrombus was 2.7% and pulmonary embolism was 0.7%.

Overall, data on VTE prophylaxis efficacy is limited in patients with ICH. During the initial window for hematoma expansion, SCDs were found to reduce occurrence of proximal DVT when implemented on day of admission (CLOTS 3 trial). With regard to types of parenteral VTE prophylaxis, direct comparisons of efficacy of low dose unfractionated heparin (UFH) versus low molecular weight heparin (LMWH) are inconclusive, though both are thought to be likely safe. A meta-analysis of more than 1000 patients with ICH found initiation of LMWH or UFH started 1–6 days after ictus reduced rates of PE but not DVT, and were not associated with hematoma enlargement.

The 2015 guidelines from the American Heart Association/American Stroke Association based on available data provide a general approach to ICH patient care. The current recommendations are as follows: In the first 24 h of admission, SCDs use is recommended in all patients with ICH (Class 1, Level B). After 24–96 h (1–4 days) and documented cessation of bleeding, prophylactic low dose UFH or LMWH can be started, especially in those considered to be high risk (bed-bound, hemi-paretic) (Class 2b, Level B).

Multiple Choice Questions

1. Which one is not commonly associated with ICH?
   (a) Cerebral amyloid angiopathy.
   (b) Antithrombotic therapy.
   (c) Reversible cerebral vasoconstriction syndrome, PRES, eclampsia.
   (d) Vascular malformations.
   (e) All of the above are associated with ICH.

   Answer: Reversible cerebral vasoconstriction syndrome, PRES and preeclampsia are relatively rare etiologies of ICH. However, a personal history of Pregnancy Induced Hypertension or preeclampsia may increase the risk of ICH later in life.
2. A 59-year-old male on aspirin and hydrochlorothiazide is brought to the emergency department with altered mental status. A CT head was completed, showing a supratentorial intracranial hemorrhage and neurosurgery plans to take him to the operating room for emergent craniotomy. The patient's aspirin response assay was abnormal. What is the best course of action for reversal of this patient's aspirin therapy?
   (a) Nothing, it does not warrant reversal.
   (b) Give platelets and FFP.
   (c) DDAVP and one unit apheresis platelets.
   (d) DDAVP only.

   Answer: The NCS has published that due to the low risk of serious side effects and the relatively low cost, providers should consider administering a single dose of DDAVP (0.4 mcg/kg) in intracranial hemorrhage patients exposed to antiplatelet agents. Further, any ICH patients should receive DDAVP in addition to a platelet transfusion prior to any neurosurgical procedures.
3. A 72-year-old woman with a past medical history of hypertension, breast cancer, and dementia presented to an outlying hospital after being found down. A CT angiogram at the outside facility demonstrated a "bright spot" that was noted on your report. What is the significance of this radiographic finding?
   (a) The etiology is likely amyloid angiopathy.
   (b) The etiology is likely hypertension.
   (c) The etiology is likely a metastatic lesion.
   (d) It worsens the patient's prognosis.
   (e) It warrants transfusion of clotting factors and/or platelets.

   Answer: A "bright spot" on a CT angiogram of the head is also known as "spot sign." It is

significant in that it demonstrates active extravasation into the hematoma bed. It also portends a poor prognosis. Its presence is not specific for a particular etiology for the hemorrhage. "Spot sign" alone does not warrant transfusion.

4. Which of the following does NOT raise the ICH score?
   (a) Infratentorial location.
   (b) INR 2.2.
   (c) ICH volume 30 cm^3.
   (d) Patient age 80 years.
   (e) Aphasia.

   Answer: INR or any other marker of coagulopathy is not a part of the ICH score. An ICH Volume greater than or equal to 30 cm^3 increases the ICH score. Patient age greater than or equal to 80 years increases the ICH score. While not a specific part of the ICH score, aphasia reduces the GCS and a reduced GCS increases the ICH score and portends a poorer prognosis.

Suggested Reading

Babi MA, James ML. Spontaneous Intracerebral Hemorrhage: Should We Operate? Front Neurol. 2017 Dec 4;8:645.

Frontera JA, Lewin JJ III, Rabinstein AA, Aisiku IP, Alexandrov AW, et al. Guideline for reversal of antithrombotics in intracranial hemorrhage. Neurocrit Care. 2016;24:6): 6–46.

Hemphill CJ, Lam A. Emergency neurological life support: intracerebral hemorrhage. Neurocrit Care. 2017;27:89–101.

Hemphill CJ, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. Stroke. 2015;46:2032–60.

Morotti A, Boulouis G, Romero JM, Brouwers HB, Jessel MJ, Vashkevich A, Schwab K, Afzal MR, Cassarly C, Greenberg SM, Martin RH, Qureshi AI, Rosand J, Goldstein JN. Blood pressure reduction and noncontrast CT markers of intracerebral hemorrhage expansion. Neurology. 2017;89(6):548–54.

Correction to: Management of Patient with Brachial Plexus Injury

Hossam El Beheiry

Correction to: H. Prabhakar et al. (eds.), Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care, https://doi.org/10.1007/978-981-15-0458-7

In chapter 2, the abstract content was inadvertently duplicated as first paragraph of the chapter in the original version of this book. It has been corrected now and duplication of abstract content was removed and updated with correct stem cells content.

The updated online version of this chapter can be found at https://doi.org/10.1007/978-981-15-0458-7_2

© Springer Nature Singapore Pte Ltd. 2020

H. Prabhakar et al. (eds.), *Problem Based Learning Discussions in Neuroanesthesia and Neurocritical Care*, https://doi.org/10.1007/978-981-15-0458-7_33