Acute Care Neurosurgery by Case Management

Pearls and Pitfalls

P. B. Raksin
Editor

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ISBN 978-3-030-99511-9 ISBN 978-3-030-99512-6 (eBook)
https://doi.org/10.1007/978-3-030-99512-6

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

How many neurosurgeons take emergency call?

The answer: most of them—at least 80% of practicing neurosurgeons, according to some estimates. This is a huge percentage when one considers that most of these neurosurgeons have busy elective practices. Adding the burden of call onto the work of maintaining a practice can be stressful at least, to a neurosurgeon. At the very least, it makes long workdays. The reasons why we take call vary widely: hospital medical staff requirements, group practice contracts with hospitals, call stipends, or—for a larger number of neurosurgeons than many might expect—a sense of duty to the community.

Long gone are the days when a single individual could be expected to be knowledgeable in all areas of neurosurgery. Ever-increasing sophistication within its various branches has raised the level of care provided by neurosurgical subspecialists, with the result that they may sometimes take call only for their own area of specialization. Cerebrovascular neurosurgery and pediatric neurosurgery are perhaps the best examples. Less time-sensitive but still urgent problems in spine surgery, neuro-oncology, or other areas may eventually receive definitive treatment by the appropriate subspecialist. But the person who is on call for general neurosurgery is the initial point of contact with the emergency department or for outside facilities. He or she has the responsibility of triage and stabilization before deciding whether to contact a colleague with subspecialty expertise.

Recognition of this gradual evolution in contemporary neurosurgical practice was part of the motivation for the American Board of Neurological Surgery to change the format of its oral examination for certification. In the current structure, one of the three oral exam sessions is based on a candidate's own submitted case log, and the second session consists of standardized questions in the candidate's subspecialty area (candidates with a practice in general neurosurgery can elect to be examined on additional general neurosurgery cases). But for the third session, every candidate is examined on the same standardized questions in general neurosurgery, with an emphasis on urgent or emergency problems. The candidate may not be expected to know the technical nuances of coiling an aneurysm or inserting a deep brain stimulator. But he or she needs to know enough about assessment and management to provide initial treatment and be conversant in more sophisticated

interventions. Traumatic brain injury, spinal cord injury, spontaneous intracerebral hemorrhage, acute nontraumatic spine conditions, shunt failure, central nervous system infections, and other common emergency conditions are assumed to be within any neurosurgeon's capabilities.

It is against this backdrop that Dr. Raksin has produced this remarkable book. Just as a sailor cannot write about sailing unless he or she spends hours on the sea, a physician cannot write authoritatively on neurotrauma without living it. Dr. Raksin has devoted her career to neurotrauma and neurocritical care, including clinical practice, education, research, and volunteer representation of neurosurgery during interactions with other medical organizations. As a busy practitioner, she has hands-on experience with the challenges, frustrations, and rewards of this branch of medicine. Her experiences as a leader in the field afford her a broader perspective on the evolution of neurotrauma care and the gradual shifts in practice over the past few decades. She walks the walk as well as talks the talk.

The title of this book is taken from the specialty of acute care surgery, which was created several years ago in response to an existential threat to the field of trauma surgery. Back then, there was concern that the field of trauma surgery was unable to attract young surgeons to the field. One reason was that the number of surgical cases performed by trauma surgeons was dropping as the efficacy of nonoperative management became established for many conditions that had been previously treated in the operating room. Some trauma surgeons feared that they were becoming a largely nonoperative specialty that cared for many patients whose primary problems were orthopedic or neurosurgical. Frequent nights on call and long hours at work were another disincentive to choose a career in this field, especially among younger surgeons for whom work/life balance was a higher priority than it had been for their predecessors.

In response, trauma surgeons expanded their scope of practice to include nontraumatic emergencies. This broadening of scope increased their operative case volumes. The critical care portion of their practice was also strengthened, which allowed these specialists the opportunity to generate more nonoperative revenue. Work schedules were changed to a model of defined shifts so that these physicians could leave work at a scheduled time, knowing that they would not receive constant calls and pages while they were out of the hospital. The specialty was rebranded as acute care surgery to emphasize its broader scope, with nontraumatic surgical emergencies and surgical critical care now added to the traditional base of trauma care. By all accounts, this strategic repositioning of the role of acute care surgeons has been highly successful.

Direct application of this model to neurosurgery is not possible. Unlike most acute care surgeons, and as mentioned earlier, most neurosurgeons who deliver emergency care spend the bulk of their time in elective practice. The growing demand for neurosurgical services by our expanding and aging population means that most elective neurosurgical practices are busy. Expecting most of the neurosurgeons who participate in the emergency care system to focus solely on neurosurgical emergencies would see many residents of their communities deprived of essential elective neurosurgical care. This is less of an issue for general surgeons because

they are much more numerous than neurosurgeons. In very broad terms, there are roughly six to seven times as many general surgeons with active board certification as there are neurosurgeons.

The upshot is that the vast majority of neurosurgeons do not devote themselves exclusively to emergency care, and yet these are the same neurosurgeons who provide the bulk of emergency neurosurgical care in this country. This book is perfect for them. A physician must first have a broad foundation in the care of all types of neurosurgical disease before he or she can become proficient in the management of neurosurgical emergencies. At the same time, neurotrauma is like every other field of medicine in that it is difficult for physicians to remain up to date in areas that are outside their primary focus. This book is a refresher course for experienced neurosurgeons, an introduction for those still in training, and a reference for acute care surgeons, emergency medicine physicians, intensivists, advanced practice professionals, nurses, prehospital providers, and the many other professionals who make up the emergency care team.

Most important, of course, is the group that will benefit the most from this book: our patients. Dr. Raksin and her contributors have provided a great service to the emergency care community. This volume will occupy a prominent place on my bookshelf.

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Preface

I was planning to use this space to tell the story of this book's birth, but it would be disingenuous to ignore the 10-ton public health emergency in the room. In fact, it is difficult not to think of this text as my personal pandemic project. In March 2020, as I was preparing to submit my proposal to Springer, life abruptly and fundamentally changed. Chicago's "stay at home" order went into effect on March 21. At work, I watched as successive ICUs—including my own—were swallowed up for the COVID cause. Elective surgeries were halted. The clinics were closed. A perfect time for academic diversion, you might say?

Well, not exactly. What happened over the next few months both underscored the importance of this endeavor and posed challenges to reaching the finish line.

While the ICUs were full and hospital services stretched to capacity, people quickly became tired of "stay at home" and found trouble—of the traumatic kind. Much has been said anecdotally about people driving faster in the absence of traffic, forgetting the rules of the road, growing frustrated with their quarantine roommates, or taking uncustomary risks during this period. Neurotrauma colleagues across the country reported an uptick in both blunt and penetrating injuries. At the same time, we noticed that the patients who dared venture into an emergency room for something other than symptoms of COVID were showing up in dramatic fashion—with atypical presentations, advanced stage disease, and uncontrolled medical comorbidities. In a word: *perfect* candidates for operative intervention.

Of course, we all had to adapt to an onerous "new normal" mode of practice—one imbued with CO_2 intoxication after hours of double-masking, the drone of HEPA filters to drown out the music, and rooms stripped bare of anything one might actually need when operating on a known positive or "person under investigation" (basically, any acute trauma patient).

Because I work at an institution where neurosurgical productivity was driven by urgencies and emergencies in the pre-COVID era, our surgical volume did not suffer much for the loss of elective O.R. time. In fact, while more elective-sensitive subspecialties saw cases slow to a trickle, we even managed to record a slight net positive at one point! The *acuity* of what we are called upon to do—daily, and independent of the public health crisis—was laid bare for administrators.

The American Association for the Surgery of Trauma (AAST) defines "acute care surgery" as incorporating elements of three disciplines: trauma, critical care, and emergency surgery (https://www.aast.org/AcuteCareSurgery.aspx). Acute care surgery adapts core principles of trauma care—systems-driven, evidence-based approaches—to the management of patients with other not necessarily traumatic, yet time-sensitive surgical conditions. While general surgeons have embraced the practice of acute care surgery, it remains a designation largely foreign to neurosurgeons.

It is interesting to note that the recent reconfiguration of the American Board of Neurological Surgery (ABNS) oral board exam has placed renewed emphasis on the initial evaluation and management of a range of potentially time-sensitive neurosurgical problems. The cases presented during the mandatory general session run the gamut of "things that go bump in the night," requiring rapid processing of data and application of clinical judgment to triage acuity and determine the need for urgent or emergent intervention—precisely those skills necessary to be successful in the exam, but also skills transferable to any clinician functioning as the first responder for patients presenting with a potential neurosurgical issue.

This text—for the first time—puts a recognizable face on a concept that is a natural outgrowth of the acute care surgery movement but has not been defined previously as such within organized neurosurgery. The acute care neurosurgeon should demonstrate mastery of both the emergent operative and critical care management of patients with surgical neurologic illness.

This volume reviews common clinical scenarios that might trigger emergent neurosurgical consultation, with attention to key components of the clinical interview and exam, optimal diagnostic evaluation, indications for and the goals of operative intervention, perioperative considerations, and strategies for complication mitigation. This is not intended to be a surgical atlas, but rather, a road map for the journey to the operating room door. The emphasis is on establishing a systematic, evidence-based action plan for the patient presenting in neurologic crisis.

The book is divided into three broad care settings—*In the Trauma Bay*, *In the Emergency Department*, and *In the ICU*. The chapters within each section highlight the breadth of the acute care neurosurgical field, encompassing not only cranial and spinal trauma, but also entities such as shunt failure, stroke, aneurysmal subarachnoid hemorrhage, pituitary apoplexy, cauda equina syndrome, and central nervous system infection that might require time-sensitive intervention. Additional chapters address issues requiring emergent neurosurgical response in the ICU setting, including sudden neurologic worsening, status epilepticus, delirium, and abnormal clotting/coagulopathy.

Each chapter opens with a relevant case vignette and then unfolds through uniform sections to tell the story of how one might approach the disease entity in question, from initial request for consultation to definitive management, emphasizing steps of the decision-making process:

- What are the highest yield questions to ask during a focused interview?
- What are the most pertinent objective exam findings?

- What is the proper differential diagnosis?
- What is the most appropriate and efficient plan for diagnostic evaluation—with respect to laboratories and imaging?
- Does this patient have an indication for emergent or urgent neurosurgical intervention?
- If so, what is the goal of that intervention?
- What are the most common potential complications of the proposed procedure, and what steps might be taken to mitigate those risks?

Each chapter is punctuated by 3–5 teaching pearls, summarizing these key elements. The overall goal is to establish a framework for assessment that might be applied in the emergency department, the trauma bay, or the ICU when a neurologic crisis arises.

The text should not only serve as a blueprint for the spectrum of acute care neurosurgery, but should also provide a valuable resource for those preparing to take the oral board exam, a targeted refresher for clinicians taking general neurosurgical call in the community, and an educational reference for mid-level practitioners and those in training who are serving as first responders on behalf of a neurosurgical service.

Chicago, IL, USA P. B. Raksin
2022

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Part I
In the Trauma Bay

Chapter 1
Acute Extra-Axial Hematoma

Shelly D. Timmons

Clinical Scenario

A 23-year-old male patient is brought into the trauma bay by ground ambulance from the scene of a motor vehicle crash. He was an unbelted driver who was ejected from the vehicle that had struck a guard rail at approximately 65 miles/h and flipped multiple times. The paramedics report that at the scene, he was not opening his eyes, exhibited extensor posturing, and was making guttural sounds. His GCS prior to resuscitation was therefore E1/V2/M2 = 5. He was unable to protect his airway, so he was intubated in the field without any drugs being required. This was approximately 30 min prior to arrival.

On examination, a large frontal scalp laceration with active venous bleeding is noted, as well as multiple ecchymoses and abrasions scattered over the face, head, neck, upper extremities, torso, and lower extremities. He has bilateral hemotympanum and blood per nares. There are bilateral breath sounds but rhonchi are noted. The abdomen is soft and non-distended. There is a right mid-thigh deformity and massive swelling. On neurological examination, the patient does not open his eyes. He is intubated. He exhibits decerebrate posturing on the right side, and he localizes to pain on the left. His GCS is therefore E1/V1T/M5 = 7T. His left pupil is 5 mm and sluggishly reactive, while the right pupil is 3 mm and briskly reactive. He has bilateral corneal reflexes, and gag reflex is intact.

Laboratory values include hematocrit 32.2%, hemoglobin 10.9 g/dL, pO2 175 mmHg, pCO2 35 mmHg, lactate 2.8 mmol/L, base deficit −5.6, glucose 190 mg/dL, serum Na 142 mEq/L, PT 14.0 s, INR 1.6, PTT 75 s.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_1

1.1 History and Physical Examination

Any patient presenting with polytrauma must undergo a rapid primary trauma survey, including the "ABCs" of airway, breathing, and circulation first and foremost. Avoidance of hypoxia and hypotension in severe traumatic brain injury patients is paramount, as any single incidence of each negatively impacts outcome, and the presence of both portends an even worse prognosis [1]. Active bleeding should be staved with compression or rapid closure.

Modern concepts of the primary trauma survey also include additional elements, called "ABCDE," with "D" standing for disability or neurological status. The letter "E" stands for exposure and environmental control. Clothing is cut away and removed to allow for a thorough external examination for injuries. Attention then is turned toward keeping the patient from becoming hypothermic by controlling the environment (ambient temperature, warming blankets, etc.).

Key to the assessment of any neurologically injured patient is the rapid evaluation of consciousness and neurological status. The post-resuscitation Glasgow Coma Scale score [2] shown in Table 1.1 is a predictor of prognosis in patients with acute traumatic brain injury (TBI) and should be obtained on all patients presenting with evidence of TBI. The best response in each category is scored. This scale is commonly used to assess progress over time and can change rapidly, especially in the face of expanding extra-axial lesions, so obtaining an accurate post-resuscitation score is a critical element of the exam in the trauma bay.

Speech and orientation are not testable in comatose patients or even sometimes in responsive, but intubated patients. However, basic levels of responsiveness should be noted, such as looking toward an examiner's voice, nodding yes or no, following commands that are either simple (one step) or complex (multi-step or requiring awareness of numbers or lateralizing right-left). Occasionally, only subtle changes in these findings will signal precipitous decline due to herniation from mass lesions like extra-axial hematomas.

Table 1.1 The Glasgow Outcome Score is calculated based upon the patient's best response in each category. 1-I is the author's own modification to differentiate an intubated patient from a patient who has already had a tracheostomy; historically 1-T has been used for any type of artificial airway or "tube"

Eye opening		Motor		Verbal response	
None	1	None	1	None	1
To pain/pressure	2	Decerebrate posturing	2	Incomprehensible sounds	2
To speech/sound	3	Decorticate posturing	3	Inappropriate words	3
Spontaneous	4	Withdraws from pain	4	Regular speech but confused	4
Not testable	NT	Localizes pain	5	Regular speech and oriented × 3	5
		Follows commands	6	Not testable	NT
		Not testable	NT	Intubated	1-I
				Tracheostomized	1-T

Asymmetry of motor and pupillary responses must be noted as potential lateralizing signs. Unilateral weakness or posturing most commonly signals the contralateral location of an extra-axial hematoma such as an epidural hematoma (EDH) or subdural hematoma (SDH). The presence of an ipsilateral pupil dilation or decrease in reactivity can further help localize a compressive lesion. A less common finding is weakness ipsilateral to a compressive extra-axial hematoma, known as the Kernohan's notch phenomenon. This is a false localizing sign with ipsilateral motor weakness caused by compression of the contralateral cerebral peduncle against the tentorium cerebelli.

Transtentorial or uncal herniation from a mass lesion is signaled initially by confusion progressing to unconsciousness, contralateral motor dysfunction, and an ipsilateral third nerve palsy. Contralateral motor dysfunction is caused by direct compression of the hemisphere by a mass lesion affecting the motor strip. Third nerve palsy is caused by compression of the third nerve against the ipsilateral tentorial incisura by the medially shifted temporal lobe uncus and is evidenced by a mydriatic, sluggishly reactive or non-reactive pupil, ptosis, and "down and out" position of the globe with the eye position pointed lateral and inferior when looking straight ahead with the unaffected eye. The pupillary abnormality occurs first due to the peripheral location of the autonomic nerve fibers within the nerve being compressed first. In the unconscious patient, the eye position and ptosis may be untestable. Altered consciousness is caused by progressive brainstem compression. As the situations progresses, the contralateral cerebral peduncle compression against the opposite tentorial incisura results in the ipsilateral motor dysfunction of the Kernohan's notch phenomenon.

An alert patient with a third nerve palsy and craniofacial trauma should raise the suspicion of a direct injury to cranial nerve (CN) III or a so-called traumatic third nerve palsy and should be distinguished from uncal compression of the third nerve.

Central or downward herniation is identified by rostral to caudal loss of neurological function progressing from headache, nausea, vomiting, and confusion to deep coma, respiratory arrest, and loss of brainstem reflexes. This progression can indicate a large extra-axial mass lesion with or without major cerebral edema, but typically is seen with significant primary brain injury and edema.

The Cushing reflex and resultant Cushing's triad are related to elevated intracranial pressure. The triad is comprised of bradycardia, hypertension, and irregular respirations (Cheyne–Stokes breathing). The pulse pressure (difference between systolic and diastolic blood pressure) is also widened. Since respiratory patterns are often masked by mechanical ventilation in intubated patients, this aspect of Cushing's triad is often obscured. This phenomenon is caused by the Cushing reflex, i.e., hypothalamic dysfunction affecting the autonomic nervous system due to poor perfusion caused by intracranial pressure elevation. Sympathetic tone is increased, resulting in increased peripheral vascular resistance and blood pressure, which then activates the parasympathetic response from carotid baroreceptors and vagal-nerve induced bradycardia.

If signs of transtentorial/uncal herniation, central/downward herniation, or Cushing's triad are present in a patient with head trauma, an extra-axial hematoma should be suspected.

Direct or vascular trauma to the limbs can affect motor responses, so any external traumatic findings should be noted. Blunt vascular injury (BVI) of the craniocerebral vasculature can also result in cerebral ischemia and unilateral motor findings, so signs of skull base fracture and neck trauma should be noted (e.g., seat belt marks, crepitus, hematoma/swelling, petechiae of the sclera, and soft tissues of the head and neck) [3, 4].

The patient should be checked for bleeding from the nares or into the oropharynx, hemotympanum, and for periorbital ecchymoses (racoon's eyes) or mastoid area ecchymoses (Battle's sign), which could signal the presence of facial fractures, injury to facial vessels, or skull base fractures. This degree of craniofacial trauma is more often associated with significant primary brain injury; therefore, SDH should be suspected if localizing signs are also present.

Limited brainstem reflex and cranial nerve examinations can be done quickly and should include testing the pupillary reactivity and size (CN III) and the corneal reflexes (CN V) at a minimum. Breathing patterns in non-intubated or spontaneously breathing patients should be noted. The gag reflex may be tested while making certain not to dislodge any endotracheal tube (ETT) or other airway. This can be done in an intubated patient with minimal manipulation of the ETT as long as the balloon is inflated and there is no tracheal injury. Alternatively, a catheter can be inserted into the mouth to carefully touch the posterior tongue or pharynx. Deep suctioning that induces coughing is not an indicator of an intact gag reflex but rather a cough reflex. Both gag and cough reflexes are subserved by CN X with additional contribution of CN IX to the gag reflex. Oculocephalic reflexes (CN III, IV, VI, VIII) are generally not tested in comatose patients in the trauma bay due to the common co-existence of cervical spinal injuries with traumatic brain injuries [5] and because the cervical spine has not yet been cleared. Oculovestibular reflexes can be checked in cases of suspected brain death through the so-called cold caloric test.

In more responsive patients, even if intubated, extraocular movements can be tested easily to assess CN III, IV, and VI by commands to look up, down, and to each side. Nystagmus should be noted if present. Gross vision (CN II) can be assessed in responsive patients by asking them to hold up the same number of fingers they see or to report verbally if non-intubated. Blinking to visual threat is a rapid and gross test of vision that can be also used. In non-intubated patients, testing for tongue protrusion symmetry (CN XII) and gag reflex (CN IX, X) are important for potential aspiration risk. A quick check of facial symmetry can be done with smile, eyebrow raise, and/or puffing the cheeks (CN VII) and of hearing by rubbing the fingers together or snapping the fingers near each ear (CN VIII). CN VII and VIII are often directly injured in the setting of basilar skull fracture. Attempts at facial nerve assessment early are warranted to help differentiate direct nerve injury or laceration (in which case function is immediately impaired) from nerve edema (in which case onset can be gradual). Having the patient shrug the shoulders and

turn the head against resistance tests CN XI but this is often not necessary on primary survey. It is usually very difficult to test smell in the trauma bay as this requires a degree of cooperativity and access to an odorant; therefore, this is typically foregone. Facial sensation (CN V) is also typically not tested in the trauma bay setting, unless patients are responsive and non-emergent. Since the corneal reflex is subserved by CN V, this reflex represents a quick test of function of this nerve.

It is critical to obtain as many details of the mechanism of injury as possible, as well as the time of injury and potential secondary insults occurring prior to arrival. These details will inform the degree of suspicion for various injury patterns and aid in the assessment of prognostic factors. If the traumatic event was witnessed, as many details should be gleaned as possible regarding the event, such as vehicles involved, trajectory, speed, use of restraints, and the status of other victims in the case of motor vehicle-related injuries. In cases of personal assault, the objects used, the caliber of weapon if a firearm was used, and the time last seen for those "found down" should be noted. For falls, height is critical and if it is possible to ascertain, whether the fall resulted from a mechanical issue or a neurological event. Prognostic factors include time from injury to potential intervention, degree and duration of hypothermia, estimated volume of blood loss, and the occurrence of any episodes of hypoxia, hypotension, or seizure, among others. Queries should be made regarding medications and fluids administered in the field, events requiring intervention, and trends in breathing, blood pressure, and responsiveness.

It is also important to identify the most relevant aspects of the patient's medical history and obtain facts quickly from family members or friends for those patients in coma or who have been intubated. These individuals are often not available at the time of presentation so this may need to be done during the secondary, tertiary, or quaternary surveys. However, the patient's personal effects can initially be checked for documentation of medications, allergies, diabetes mellitus, hemophilia, medical implants, anticoagulation medications, or other commonly documented conditions. These identifications may be in the form of wallet card inserts or medical bracelets/jewelry. When looking for such information, care should be taken to avoid injury from broken glass, metal, needles, and other sharps or even weapons that may be obscured in clothing.

In the current clinical scenario, information about the mechanism of injury and details regarding the scene were gleaned from communication with EMS providers. No family was available at presentation to provide details regarding the patient's past medical history or medications. The presence of extensive soft tissue injury, as well as obvious deformity of the right leg, suggests multisystem trauma. The neurologic exam, as described, suggests severe traumatic brain injury. Lateralizing findings such as pupillary and motor asymmetry raise concern for a space-occupying intracranial lesion. The presence of a large scalp laceration should raise concern for the possibility of open skull fracture with underlying intracranial pathology. The presence of blood at the nares and ear canals might suggest a skull base fracture. Once the ABCs have been satisfied and any life-threatening bleeding contained, further investigation of this patient's neurologic injury should take priority.

1.2 Differential Diagnosis

The differential diagnosis of altered consciousness or coma in a polytrauma patient such as this one includes impairment from drugs (alcohol, prescription medications, illicit drugs) and toxins. A combination of other findings points to traumatic brain injury or a compressive lesion as the cause of coma, namely, motor asymmetry, pupillary asymmetry, localizing or focal neurological deficits, and the presence of external trauma. Even so, serum and urine testing for alcohol and drug levels remains a mandatory portion of the workup, since central nervous system acting agents can mask neurological changes, can mimic the effects of TBI and cerebral edema, and can lower the seizure threshold. Hypothermia can occur even in relatively warm exterior temperatures if patients are exposed or unconscious for a significant period of time, and this can cause global depression of cerebral function as well.

A lucid interval in which there is no or minimal neurological impairment followed by a rapid decline with signs of transtentorial herniation is a "classical" presentation of an epidural hematoma. When coupled with external signs of temporal region trauma, this is the likely diagnosis, as temporal fracture associated with laceration of the middle meningeal artery can lead to a rapidly expanding epidural hematoma causing transtentorial or uncal herniation. Lucid intervals can be seen in other scenarios of brain trauma, including a rapidly expanding arterial subdural hematoma. While most subdural hematomas are venous in origin, cerebral arteries can be injured even in blunt trauma and result in SDH and rapid decline.

EDH can be seen in more posterior regions with occipital or suboccipital trauma. Common clinical scenarios include falling or jumping out of a moving car or truck bed, falling backwards off of a stool or falling backwards from a standing/walking position (such as in slipping on ice or being struck in the face during an assault). Swelling and bruising on the occiput coupled with one of these mechanisms should raise the index of suspicion for an occipital or posterior fossa extra-axial hematoma (EDH or SDH). These can arise from sheared draining cortical veins or direct trauma to the posterior draining cerebral venous sinuses, with or without skull fracture.

While both EDH and SDH may occur in isolation, without significant underlying brain injury, subdural hematomas are far more commonly associated with significant underlying brain parenchymal injuries and edema [6]. Therefore, signs of global cerebral dysfunction, multiple deficits, and bilateral posturing should raise suspicion of primary TBI with or without SDH.

Again, blunt vascular injury can mimic a unilateral extra-axial hematoma by causing hemispheric cerebral ischemia and infarction. Occasionally, BVI and TBI co-occur, obscuring the physical differential diagnosis even further.

1.3 Diagnostic Evaluation

The trauma care team should first ensure adequate oxygenation and blood pressure, and if hypothermia is present, employ a safe strategy for rewarming in order to gain the most reliable neurological examination. Serum and urine drug and alcohol tests should be done, as well as basic laboratory tests for electrolyte or glucose abnormalities that could contribute to coma, seizures, or altered sensorium. Routine tests for comatose trauma patients include arterial blood gases, comprehensive metabolic profile, complete blood count, coagulation studies, urinalysis, serum alcohol level, and urine drug toxicology tests at a minimum.

The mainstay of traumatic brain injury diagnostic imaging is computed tomography (CT) of the head without contrast. Rapid stabilization and transport to the CT scanner are a routine part of management of the comatose trauma patient. If polytrauma is obvious or the mechanism of injury suggests polytrauma, then chest, abdomen, and pelvis CTs are employed in addition to head CT. Cervical, thoracic, and lumbar spine CTs are routinely done in comatose trauma patients due to the high propensity for concurrent spinal trauma in such cases [5, 7, 8]. In isolated cranial injuries, cervical studies should be done at a minimum. Facial CTs may be required. If signs that are high-risk for BVI are present (major craniofacial fracture, neck soft tissue trauma, lateralizing examination without cause noted on brain CT, etc.), a screening CT-angiogram (CTA) of the head and neck arteries may also be done at the same time or subsequently.

EDH and SDH are hyperdense compared to brain on CT (i.e., bright white compared to gray). EDHs are typically lentiform or biconvex in shape, located near the common sources of bleeding (middle meningeal artery or venous sinuses), and usually do not cross cranial sutures due to the rigid attachment of the dura at the suture lines (Fig. 1.1). SDHs are typically crescent shaped as they follow the shape of the cranium and cerebral hemisphere, and they do cross suture lines (Fig. 1.2a–c). Supratentorial SDHs may be focal, hemispheric (layered over the surface of the hemisphere), tentorial (as blood layers onto the tentorium cerebelli), falcine (layering along one or both sides of the rigid falx cerebri), or a combination of any of these since the subdural space is essentially continuous. SDH can technically cross from the supratentorial and infratentorial space (a.k.a. posterior fossa) at the incisura of the tentorium cerebelli, but such occurrences are rare. They can also extend from the posterior fossa into the spinal canal. Isolated posterior fossa SDH can occur but is more unusual than supratentorial SDH.

Mixed density extra-axial hematomas can be seen with hyperacute and/or pulsatile bleeding into the hematoma. This is usually seen as an eddy-shaped, jet-shaped, or circular hypodensity in the center of a hyperdense hematoma. Mixed density SDH can also be seen in older patients who have had an acute hemorrhage into a subacute (isodense to brain) or chronic (hypodense to brain) subdural hematoma. In such instances, the SDH may be loculated due to the presence of multiple membranes (Fig. 1.3a, b).

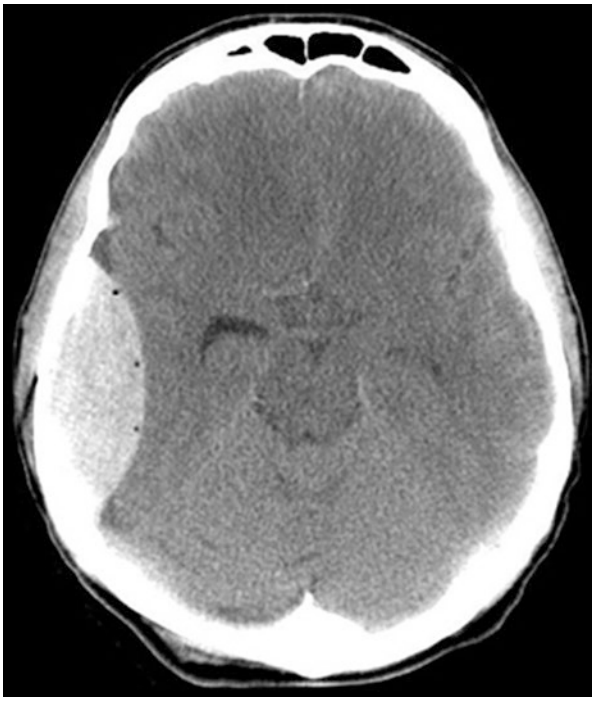

Fig. 1.1 Acute epidural hematomas are hyperdense on CT scan without contrast, are typically lentiform in shape, and do not usually cross cranial suture lines

Bone window interpretation is a key element of radiographic assessment of both TBI in general and in differentiating between EDH and SDH. Fractures involving the foramen spinosum and/or adjacent to the middle meningeal artery, or adjacent to any of the cerebral venous sinuses, or involving the orbital roof are commonly associated with the formation of EDH. Orbital roof fractures can result in more slowly developing and self-limited subfrontal EDH due to bleeding from bone fragments and bridging veins. Clival or other skull base fractures indicate significant force and are commonly associated with severe primary brain injury and SDH.

CT head without contrast for the patient in the current clinical scenario (Fig. 1.4a, b) reveals a left extra-axial hyperdense collection, associated with effacement of the local sulcal-gyral pattern, uncal herniation, dilatation of the contralateral temporal horn, effacement of the basal cisterns, and midline shift to the right that is disproportionate to the maximum thickness of the subdural hematoma.

1.4 Clinical Decision-Making and Next Steps

Clinical decision-making regarding extra-axial hematomas in the trauma bay centers on whether or not the patient needs to go to surgery for an emergent craniotomy. Clinical signs of herniation (transtentorial, uncal, or central/downward) and/or the presence of Cushing's triad, in conjunction with an identified causative lesion on

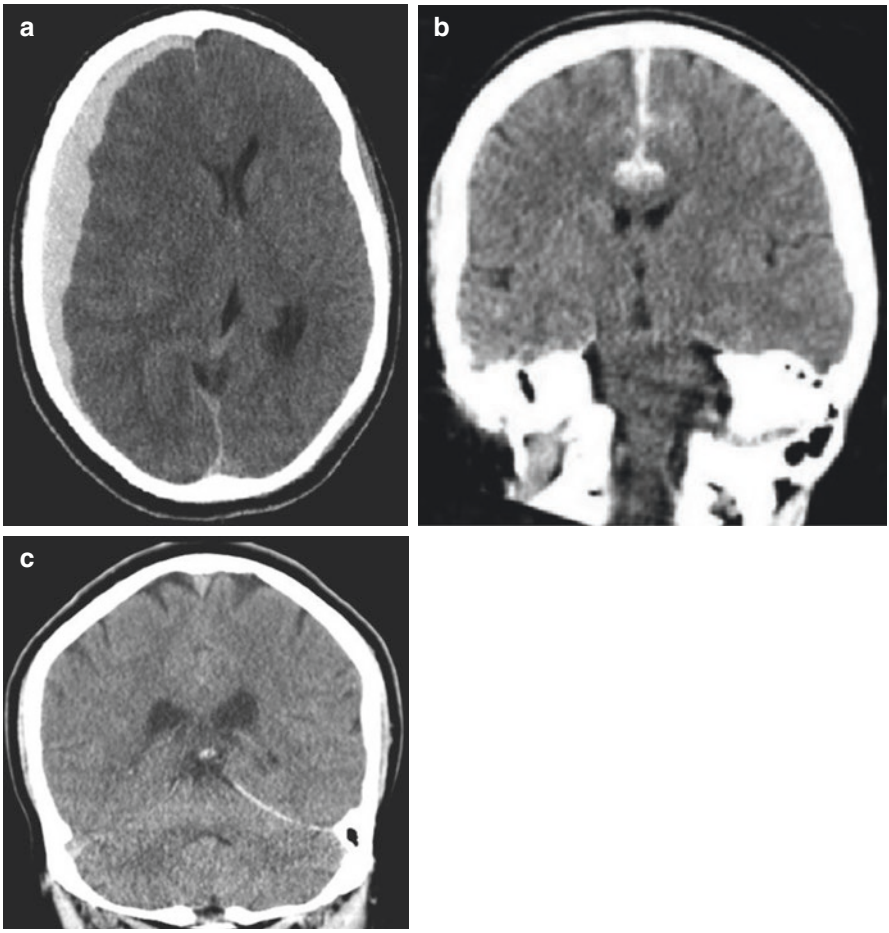

Fig. 1.2 (**a**) Acute SDH is hyperdense on CT without contrast, is typically crescent-shaped, and can cross suture lines. SDH can be located in any part of the subdural space. (**b**) Subdural blood along the anterior falx. (**c**) Subdural blood along the left tentorial leaflet

CT, mandate surgical evacuation of EDH or SDH if the patient's overall injuries appear to be survivable.

Absent signs of impending or actual herniation and death, there are several other indications for surgical evacuation. Surgical guidelines [9, 10] rely upon the key elements of hematoma size/volume and degree of mass effect attributed to the extra-axial lesion. The maximal thickness of EDH and SDH should always be measured, taking care to avoid apical measurements which can be overestimated because of tangential geometry. Midline shift should always be measured at the level of the anterior commissures. Notation of the appearance of the cisterns (patent, blood-filled, compressed, or absent/obliterated) should be made. Finally, estimates of the volume of extra-axial hematoma can be made using the $A \times B \times C/2$ method [11].

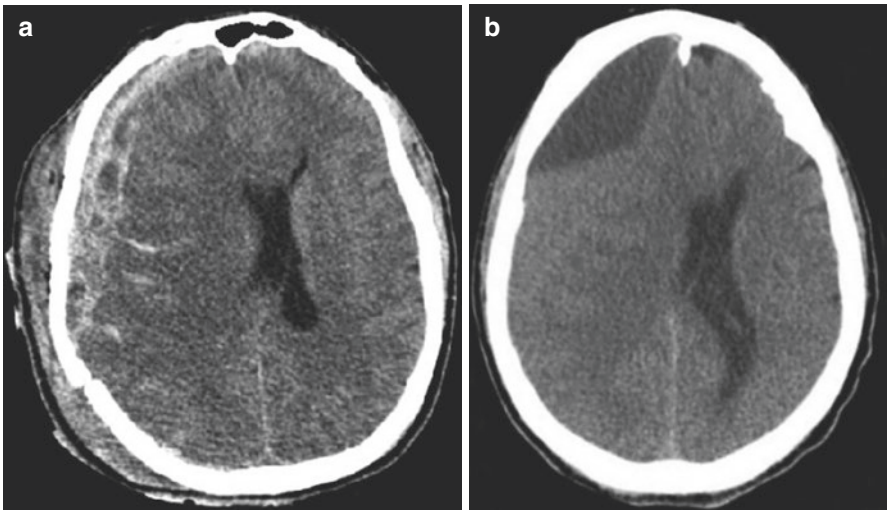

Fig. 1.3 (**a**) A hyperacute SDH is distinguished by a swirling appearance of hyper- and hypodense components within the subdural collection, whereas (**b**) an acute-on-chronic SDH may demonstrate a "hematocrit" effect reflecting the greater density of the dependent acute blood component

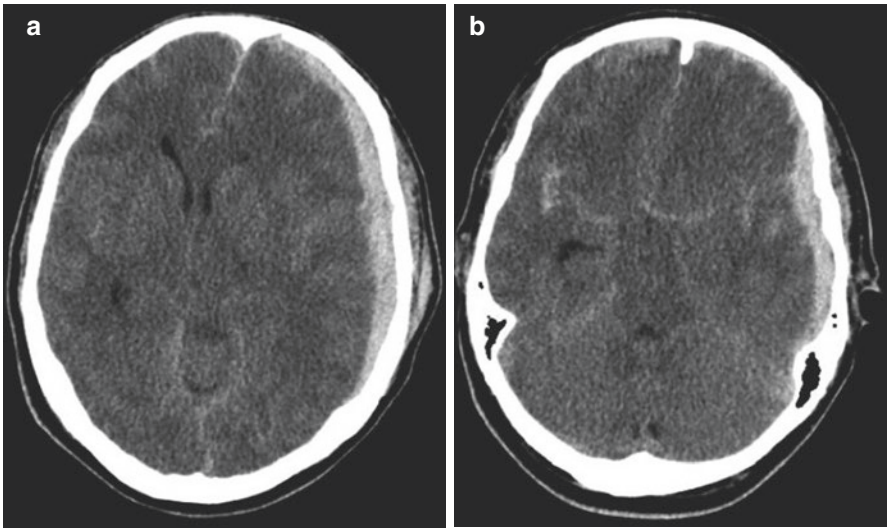

Fig. 1.4 (**a**, **b**) CT head reveals a left extra-axial hyperdense collection, associated with effacement of the local sulcal-gyral pattern, uncal herniation, effacement of the basal cisterns, and midline shift to the right that is disproportionate to the maximum thickness of the subdural hematoma. This constellation of radiographic signs, coupled with evidence of primary parenchymal injury such as contusion or edema, suggests the need for a decompressive hemicraniectomy (i.e., leaving the bone flap out) at the time of surgery

Indications for emergent evacuation of EDH via craniotomy are: (1) volume ≥30 cm^3, regardless of GCS and (2) anisocoria and coma (GCS ≤8), regardless of size. It is generally feasible to replace the bone flap after EDH evacuation.

Indications for evacuation of SDH are (1) ≥10 mm thickness OR ≥5 mm midline shift, regardless of GCS. (2) If a patient is in coma with GCS ≤8 AND the SDH maximal thickness is ≤10 mm AND midline shift is ≤5 mm, surgery may still be indicated. This is especially true if (a) the GCS has decreased by ≥2 points between injury and arrival, (b) the patient has anisocoria, (c) the patient has fixed and dilated pupils, or (d) the intracranial pressure (ICP) is >20 mmHg. When multiple types of lesions are present, these guidelines still apply, with the caveat that more aggressive action may be needed despite a smaller EDH or SDH in the face of multiple other mass lesions.

When the midline shift is proportional to the maximum thickness of the subdural hematoma, and there is relatively little parenchymal injury, the bone flap may be able to be replaced. However, if the initial CT shows that the midline shift is out of proportion (i.e., greater than) the maximum thickness of the SDH, the neurosurgeon should be prepared to perform a large hemicraniectomy incision and bone flap in anticipation of intraoperative cerebral edema outside the bounds of the cranium and the need to leave out the bone flap. Other radiographic signs suggesting this eventuality include compressed or absent cisterns, loss of sulci over the affected hemisphere, uncal herniation, or ipsilateral hemispheric contusions, hematomas, or edema, along with clinical signs of herniation or majorly elevated ICP if a monitor has been placed in the trauma bay. The patient in the current clinical scenario presents with most, if not all, of these ominous features (Fig. 1.4a, b). A primary decompressive craniectomy was performed, in conjunction with evacuation of the acute subdural hematoma.

ICP monitors (intraparenchymal or intraventricular) may be inserted emergently in the trauma bay in cases of delayed imaging due to ongoing resuscitation or CT unavailability. They can help guide surgical decision-making and medical therapeutics for cerebral edema and intracranial hypertension. For those patients whose EDH or SDH and/or clinical scenario does not meet the indications for emergent surgery, but who are in coma and harbor extra-axial lesions, ICP monitoring should be employed to provide a continuous physiological monitor of intracranial pressure and cerebral perfusion pressure (requires arterial line) that will (1) guide nonsurgical therapeutic measures for the primary brain injury, particularly in the setting of polytrauma and (2) provide an early warning of lesion expansion that would prompt surgical evacuation.

Rapid, detailed assessment of multiple history, examination, and diagnostic findings is necessary in the initial evaluation of the trauma patient suspected of harboring an extra-axial hematoma so that life- and function-saving surgery and medical management can be employed as quickly and efficiently as possible.

1.5 Clinical Pearls

- A lucid interval is often seen in the presentation of an epidural hematoma, followed by potential for rapid decline, herniation, and death.
- Contralateral motor weakness and ipsilateral third nerve palsy (evidenced by pupillary dilation) are localizing signs caused by mass effect from extra-axial hematomas.
- The Kernohan's notch phenomenon is a false localization sign; ipsilateral motor weakness is due to compression of the contralateral cerebral peduncle against the tentorium cerebelli.
- Acute subdural hematoma is frequently associated with significant underlying primary parenchymal injury.
- When the degree of midline shift is out of proportion to the thickness of an acute subdural hematoma, this is a sign of significant parenchymal injury and/or cerebral edema and decompressive hemicraniectomy may be indicated.

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Chapter 2
Chronic Subdural Hematoma

Andrew Ajisebutu and Gregory Hawryluk

Clinical Scenario

A 75-year-old man is brought to the Emergency Department (ED) by his daughter-in-law, who has noted a declined in his function. Over the past 3 weeks, he has exhibited memory lapses and gait impairment and has spent an increased amount of time sleeping. Today, his daughter-in-law noticed that he had some difficulty with word-finding.

2.1 History and Neurologic Exam

The first priority of any physician confronted with a patient with a suspected CSDH should be to obtain an accurate history, with special attention to some relevant questions:

- *Etiology*: Is there a history of blunt trauma? If so, what was the mechanism and its proximity to the current presentation? In elderly patients, an assessment of mobility and fall history is important. Recognize that even mild trauma can precipitate CSDH formation in older patients.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_2

- *Patient demographics*: Is this an elderly patient, with age-related atrophy predisposing to CSDH formation? In a younger patient, are there risk factors for subdural formation, such as alcohol use or prior brain injury?
- *Medications*: Is there a history of antiplatelet or anticoagulant use? If so, what is the indication and what are the potential consequences of withholding the agent(s) in question?
- *Presentation*: Is the onset of symptoms acute or more insidious? Do symptoms suggest subacute progression? Are symptoms consistent with focal or lateralizing deficits?

On review of systems, the patient denies headache, nausea/vomiting, and dizziness. He does endorse experiencing a mild "numbness" of his dominant right hand and, as a result, has had difficulty with fine motor tasks like fastening buttons. He lives at home with his spouse. Prior to this episode, he had been independent with all activities of daily living and ambulated without walking aids. He has a history of hypertension and diet-controlled type II diabetes. He takes aspirin 81 mg daily, which his family states is for "heart health." On physical exam, he is awake, alert, and oriented to self and place, but not to date. His speech is slow and, at times, halting. On motor exam, he has a slight right-sided pronator drift.

The clinical presentation of CSDH is heterogeneous; therefore, a high index of suspicion must be maintained for a structural pathology when approaching patients presenting to the emergency department—even when focal findings are not apparent. CSDH is a relatively common neurosurgical condition; the overall reported incidence ranges anywhere from 1.75 to 20/100,000 people/year [1–4]. CSDH is generally a disease of the elderly; a study that examined Japanese patients between 2005 and 2007 reported an overall incidence of 20.6/100,000; when stratified by age, the incidence rose to 76.5 in patients 70–90 years of age, and 127.1 in those over 80 [2]. As populations age, there appears to be an increase in the overall incidence, primarily due to the higher prevalence of falls and anticoagulant use in this population. One group in the United States (US) created a mathematical model based on US, Japanese, and Finnish data, estimating that by 2030 we may see an over two-fold increase in incidence as the population ages [5]. However, CSDH is not seen exclusively in elderly patients. Young or middle-aged patients may develop chronic subdural collections, typically after trauma, in the setting of an acute subdural hematoma that liquefies over time, or with certain risk factors that predispose to premature brain atrophy such as alcoholism—which, itself, can be associated with coagulopathy and thrombocytopenia. Patients with renal failure and secondary platelet dysfunction may also be predisposed to CSDH formation.

Historically, it was believed that a difference in osmolarity between CSDH fluid and cerebrospinal fluid (CSF) established an oncotic pressure gradient that, in turn, drove CSDH expansion; however, published evidence has served to disprove this theory [6]. The current proposed mechanism of CSDH growth is that, following the initial injury and maturation of the hematoma, a neomembrane forms on both the dural and arachnoid surfaces of the clot, leading to its encapsulation. Neomembrane

formation involves the formation of new, fragile blood vessels through the process of neovascularization. This process precipitates microhemorrhages, and, along with hyperactivation of the fibrinolytic system, is responsible for continued growth and expansion of the collection [7]. Of additional importance, CSDHs contain low concentrations of coagulation factors, such as fibrinogen and plasminogen, and relatively high concentrations of coagulation breakdown products, supporting the idea that CSDHs act as contained "disseminated intravascular coagulation chambers" [8].

Making the diagnosis of CSDH may be challenging at times, as the clinical manifestations can be diverse and non-specific. The most common presenting complaints include gait disturbance, confusion, and limb weakness. Over half of patients who present with CSDH requiring surgical intervention complain of gait disturbance and falls; a third will have unilateral hemiparesis, and many will present with confusion or mental deterioration [9]. Many assume headaches to be a universal symtom of CSDH, however they only occur in 20–30% of patients [9]. Most patients will present with some combination of these symptoms. Other symptoms, such as incontinence, vomiting, seizures, aphasia, anisocoria, and visual disturbances are less common but do occur in about 2–10% of patients. Most patients present with a Glasgow Coma Scale (GCS) score of 13–15, although a significant minority (approximately 20%) may present with a GCS below 13. Approximately, 5–7% of those patients will be comatose (GCS <8) at presentation [9, 10]. Another 20–30% with CSDH, however, will be completely asymptomatic. Table 2.1 illustrates common presenting symptoms, stratified by frequency of occurrence.

A careful, comprehensive history must be obtained from both the patient and family when evaluating patients with suspected CSDH. Trauma is the most common cause of CSDH; however, it is important to understand that the inciting event can be as trivial as a sneeze. The timing of the traumatic event with respect to presentation varies, but it is most commonly on the order of several weeks. It is also important to recognize that nearly 40% of patients deny a history of trauma [11]. A detailed neurological exam should be obtained for all patients with suspected CSDH, with careful attention paid to level of consciousness and the presence of lateralizing signs.

Certain risk factors predispose patients to the development of CSDH, and their identification on history can be important in making the diagnosis. Table 2.2 summarizes both fixed and potentially modifiable risk factors for development of CSDH:

Advanced age. By far the most commonly reported risk factor in the literature is older age. Many epidemiologic studies of CSDH report higher rates in older age cohorts—where advanced age generally is defined as 55 and older [12]. The contribution of age as a risk factor has multiple facets. It has been theorized that brain atrophy plays a major role in the pathophysiology of the development of CSDH; minor trauma leads to the tearing of bridging veins that traverse from the cortex to the dura—the point at which they are thinnest and most vulnerable [13]. This causes small hemorrhages that accumulate within the potential space between the dura and the arachnoid. Recurrent trauma, particularly in the

Table 2.1 Common symptoms associated with CSDH presentation

Presentation of CSDH	
Symptoms	Rate
Gait disturbance	~50%
Mental deterioration	~30%
Unilateral limb weakness	~30%
Headache	~20–30%
Drowsiness or coma	~10%
Speech impairment	~5–10%
Seizure	~<5%

Adapted from Santarius et al. [9]

Table 2.2 Fixed and variable risk factors for the development of CSDH

Fixed risk factors
• Advanced age
• Male sex
Variable risk factors
• Excessive alcohol consumption
• Coagulopathy
• Trauma

"frequent fallers" prevalent in this age group, compounds this risk [14]. Not only is the incidence of CSDH higher in patients with advanced age, but disease severity (in terms of the degree of neurological deficit) tends to be worse at the time of admission [2].

Male gender. Most epidemiologic studies identify a male predominance for the diagnosis of CSDH. The reason for this gender disparity is unclear; however, it has been theorized that other risk factors—such as trauma and alcohol use—are also more prevalent among men. Hematoma recurrence is similarly affected; one review of over 300 cases in South Korea quoted a recurrence rate of 10.2% among males, yet only 3.1% among females.

Alcohol consumption. Excessive alcohol consumption is often quoted as a risk factor for CSDH formation. Its effect is related to a number of factors—it increases the rates of trauma, fall, and acute subdural formation; it promotes brain atrophy; and it can be associated with coagulopathy or thrombocytopenia [15, 16].

Coagulopathy. The most pertinent modifiable risk factor for the development of CSDH is the use of anticoagulation or antiplatelet therapy. Elderly patients have much higher rates of atrial fibrillation, coronary artery disease, and stroke, and as such, frequently have indications for blood-thinning medications [17, 18]. However, this also increases the risk of developing CSDH. One review of national insurance databases in Australia showed that patients anticoagulated with warfarin had a 40 times higher risk of CSDH development [19]. It is difficult to ascertain whether anticoagulation/antiplatelet use increases the likelihood of developing a CSDH, increases the severity of an existing CSDH, or both. At least one study found that the average time interval between trauma and the first operation for CSDH was significantly shorter for patients who had received antiplatelet/anticoagulant medications than for those who had not, suggesting that these medications do have an effect on disease severity and clinical presentation [19]. A careful history of anticoagulation use should be obtained, as it impacts both the likelihood of the diagnosis and the subsequent treatment. Similarly, significant medical comorbidities—such as severe hepatic failure or renal failure—may be accompanied by coagulopathy and/or thrombocytopenia that may predispose to CSDH formation and affect its course [15].

2.2 Differential Diagnosis

Our elderly patient on antiplatelet therapy has presented with a gradual, subacute decline in his cognitive function. His physical exam demonstrates speech arrest and lateralizing symptoms. At this point, the differential diagnosis remains broad. However, the presence of lateralizing complaints may increase the likelihood of a structural brain etiology. We should consider both likely and less likely diagnoses, as well as the investigations needed to narrow our differential diagnosis.

Given the often vague history and variation in presentations, CSDH has been referred to as the "great imitator" [20]. Patients harboring a CSDH may present with a constellation of neurologic symptomatology: sensorimotor changes, dysphasia, and neuropsychiatric changes. It is important that clinicians maintain a broad differential diagnosis incorporating structural pathology when confronted with these patients, both when CSDH is suspected and when it is not.

For any patient presenting to the emergency department with decreased level of consciousness, lateralizing symptoms, and speech changes, stroke must be near the top of the differential. Though CSDH—by definition—develops gradually, patients may present with acute neurologic symptoms mimicking stroke. Prompt neurologic

assessment and imaging are essential to exclude an acute stroke that may require urgent intervention. More generally, CSDH can present like any intracranial space-occupying lesion, such as a tumor or intracerebral hemorrhage. This possibility, likewise, would prompt an urgent neurological assessment and neuroimaging.

It may also happen that a patient presents initially to a primary care provider, rather than to the emergency department, with subacute symptoms of gradual confusion and memory or mood changes—more suggestive of dementia than bleed. It is important to remember that the age groups and demographics of these two conditions may overlap. In such cases, a detailed neurologic exam may demonstrate lateralizing findings—making CSDH somewhat more likely—or at least prompt further investigation with neuroimaging. When lateralizing symptoms are not present, a structural cause still remains a possibility. Time course of symptom onset may be revealing. While one would expect CSDH-related symptoms to evolve over a period of weeks, a time line of several months to years would be more typical for dementia. One would also expect expansion of the hematoma to result in more rapid progression of symptoms as compared with dementia. Patients (particularly, elderly) presenting with confusion should be screened for other conditions, such as urinary tract infections or pneumonia, that may present with altered mental status.

The diagnosis of CSDH is usually evident by non-contrast CT imaging. However, a particularly important diagnosis that should be ruled out is subdural empyema. Presentation with a history of recent neurosurgical intervention, fever, constitutional symptoms, an elevated white blood cell count, immunosuppression, or intracranial mass effect disproportionate to the size of the extra-axial collection should prompt concern for this entity. Subdural empyema must be quickly identified, as prompt surgical intervention is often indicated. Magnetic resonance imaging (MRI) can be used to more clearly differentiate a CSDH from a subdural empyema.

An additional entity to consider in the setting of a hypodense extra-axial collection is subdural hygroma, which is a collection of CSF in the subdural space. Hygromas occur spontaneously, and are believed to form due to the splitting of the arachnoid and the dura at points of tension, allowing CSF to fill this otherwise potential space [21]. Subdural hygroma is generally a benign condition that does not require intervention, although it is possible to have acute bleeding into these fluid collections, which may, in turn, warrant surgical evacuation depending on the clinical context.

2.3 Diagnostic Evaluation

Non-contrast CT head is the best first step in the diagnostic evaluation for potential CSDH. CSDHs appear as crescentic collections that spread out within the extra-axial space between the dura and underlying brain. The density of the collections, measured in Hounsfield units (HU), provides an idea of the chronicity of the lesion: truly chronic collections appear hypodense (<30 HU), while those with a subacute component may appear more isodense (HU of 30–60), so much so that even

experienced physicians may overlook them if they do not review the images thoroughly [22]. In such cases, a post-contrast study may be helpful; enhancement of the cortical vessels more clearly defines the adjacent extra-axial space and its contents as distinct from brain.

The radiographic appearance of CSDH does have some clinical relevance to both treatment and recurrence rate. Some authors have attempted to characterize CSDHs into distinct subtypes, based on CT appearance: *homogenous*, wherein the CSDH retains the same HU throughout; *laminar*, in which a high-density component (thought to consist of fresh blood) runs along the inner membrane; *separated*, wherein a gradient is formed between the thin components and the thicker components of the CSDH; and finally, *trabecular*, in which the hematoma appears to be loculated, with a mix of isodense and hypodense components (Fig. 2.1a–d). Nakaguchi et al. hypothesized that these differing configurations represent distinct stages of the disease process and potentially impact recurrence rates. Recurrence rates among the separated subtype were high (36%), while those among the trabecular subtype were near zero. Homogenous and laminar subtypes were intermediate in behavior, with reported recurrence rates of 15% and 19%, respectively. In our experience, collections that are isodense or darker with respect to the brain are liquid and readily amenable to drainage.

The diagnosis of CSDH can be made solely on the basis of a non-contrast CT scan. If there is a clinical suspicion for subdural empyema, MRI brain pre- and post-gadolinium may provide additional detail to permit differentiation from simple hematoma. The post-gadolinium T1 sequence may demonstrate peripheral enhancement of the collection. A collection of infectious origin should demonstrate restricted diffusion (i.e., appear bright) on the diffusion-weighted imaging (DWI) sequence, whereas simple hematoma should not. This distinction is relevant both to surgical and medical management. A craniotomy is necessary in the case of suspected empyema, where organized phlegmon is unlikely to be amenable to burr hole drainage. Likewise, empiric broad-spectrum antimicrobial therapy would be appropriate in the setting of suspected infection.

For this particular patient, screening blood studies were unremarkable. Non-contrast CT scan of the head revealed a 1 cm thick, crescent-shaped, hypodense collection on the left side, associated with 0.25 cm of midline shift—consistent with a chronic subdural hematoma (Fig. 2.2).

2.4 Clinical Decision-Making and Next Steps

In this case, CT imaging identified the presence of a left-side CSDH with associated mass effect. How should this symptomatic (confusion, aphasia) elderly patient receiving antiplatelet therapy best be managed? What should be done with his antiplatelet agent? Is operative or nonoperative intervention appropriate? If operative, what type of procedure should be performed? What adjuncts are available, and are they necessary (or advisable)?

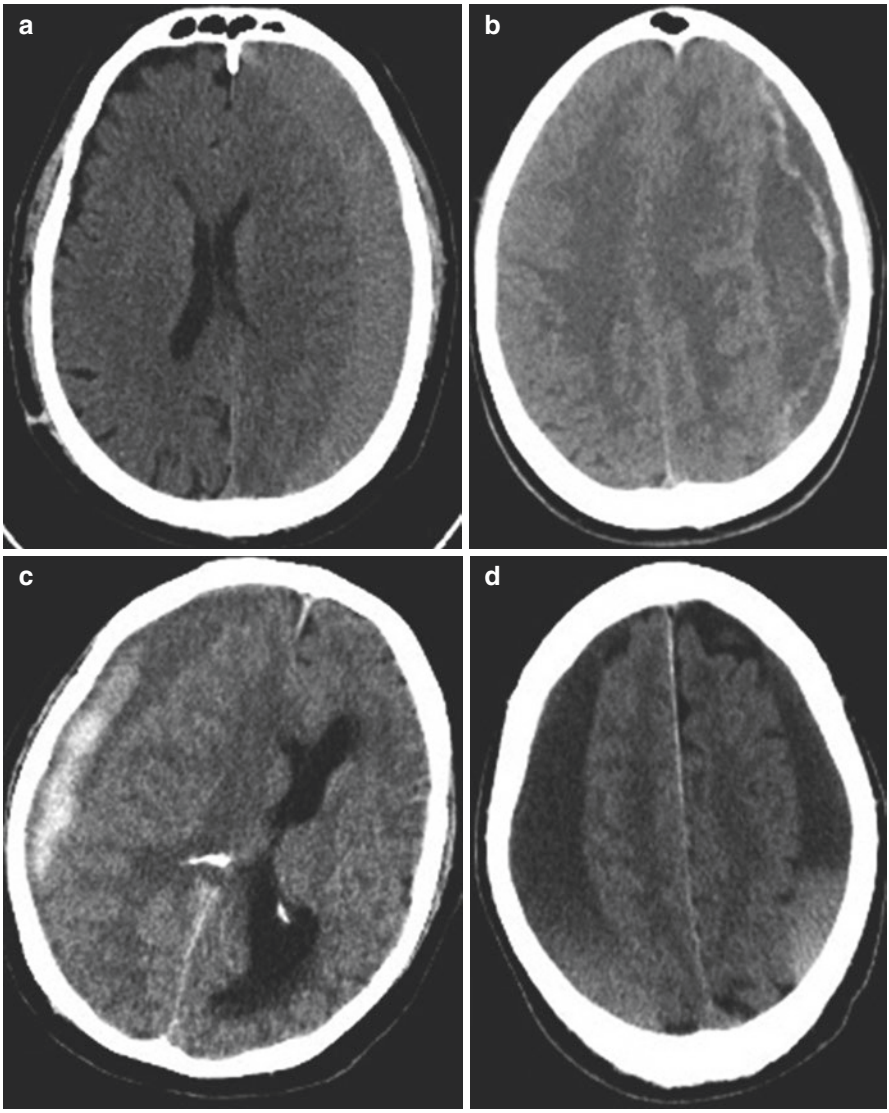

Fig. 2.1 (**a**–**d**) CSDH subtypes on CT scans. Proposed subtyping of CSDH by Nakaguchi et al. (J Neurosurg, 2001). (**a**) Homogenous—the CSDH general maintains the same HU throughout. (**b**) Trabeculated—the CSDH has a septated, mixed appearance with iso- and hypodense components. (**c**) Laminar—the CSDH has high-density components along its inner membrane. (**d**) Separated—the CSDH forms a gradient, representing its thinner and thicker components

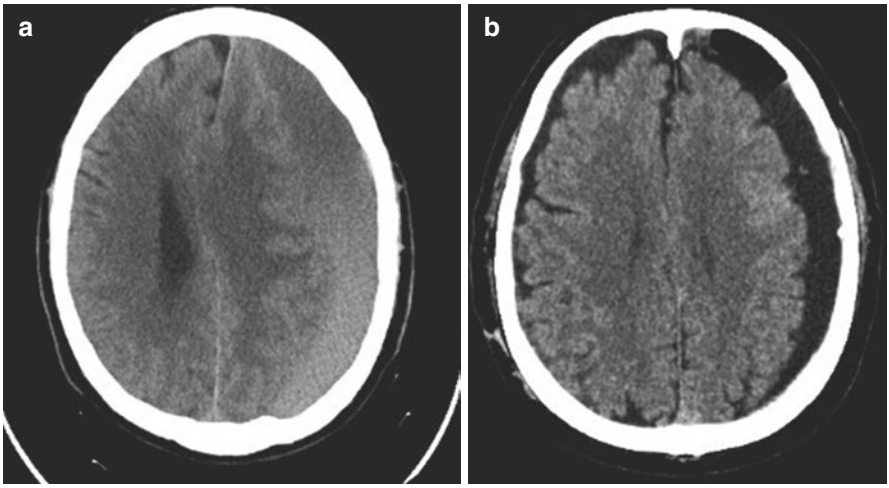

Fig. 2.2 (**a**) CT scan demonstrating a mixed iso- and hyperdense extra-axial collection, consistent with a chronic subdural hematoma. There is significant sulcal effacement and midline shift present. (**b**) Post-operative CT scan demonstrating single bur hole placement for evacuation of the CSDH. The subdural collection was thoroughly irrigated with saline; there is some evidence of post-operative pneumocephalus, common after these procedures. The midline shift and sulcal effacement have resolved, and a subdural drain has been placed (see arrow)

After arriving at the proper diagnosis, clinicians must decide on the appropriate course of treatment. The first step is to decide whether invasive or conservative therapy is indicated. What these two pathways share is medical optimization. Many patients, particularly elderly patients, have significant medical comorbidities, such as hypertension, congestive heart failure, renal or hepatic diseases that must be addressed and optimized prior to any intervention. Moreover, it is not uncommon for patients to present on anticoagulation or antiplatelet therapy. These agents should be held, and correction may be considered depending on the agent, indication, and planned intervention. Both anticoagulation and antiplatelet therapy have negative impacts on outcome: patients presenting on these medications have longer stays in hospital, higher rates of recurrence, and higher rates of mortality [23–26].

The method of reversal relies heavily on the mechanism of the coagulopathy. Patients on vitamin K antagonists, such as warfarin, may be reversed with a combination of vitamin K and prothrombin complex concentrate (PCC) or fresh frozen plasma (FFP), with a goal of reducing the International Normalized Ratio (INR) to <1.4. PCC helps to avoid fluid overload, as was typically seen when FFP was administered to these patients in the past. For direct oral anticoagulants, such as dabigatran and rivaroxaban, reversal agents do exist (idarucizumab and andexanet alpha, respectively); however, they are costly and not universally available. These agents

should be held, and when possible, surgical intervention should be delayed for 24–48 h. Reversal with PCC in emergent situations may show some benefit [27].

In the setting of antiplatelet therapy, operative intervention should be delayed to up to 7–10 days, if possible, to allow for replenishment of functional platelets. There is little to no evidence that platelet transfusions are beneficial in this setting and may, in fact, be harmful. Desmopressin (DDAVP) has been proposed as an agent that could be utilized in the setting of platelet dysfunction due to its ability to increase plasma von Willebrand factor, as well as to promote platelet adhesion. Currently, the Neurocritical Care Society and Society of Critical Care Medicine support the use of DDAVP in intracranial hemorrhage in patients exposed to antiplatelet agents although their utility in the setting of CSDH is less clear [28]. The timing for resumption of antiplatelet and anticoagulant agents is somewhat controversial—published studies suggest re-introduction variously at 5–7 days, 2 weeks, or 1 month after a bleed and/or invasive intervention [29]. Certainly, the correct answer depends on the indication for these medications, and risk stratification can be done using standardized scoring tools, such as the CHADSVASC score [30]. An individualized approach is recommended.

The mainstay of treatment for CSDH remains surgical. Patients with symptomatic CSDH benefit from surgical intervention: 70–80% of patients report a favorable outcome, though recurrence is seen in as many as 30%. There are a variety of surgical techniques that can be utilized, including twist-drill craniotomy (TDC) or craniostomy, burr hole craniotomy (BHC), and mini craniotomy. These techniques vary with respect to the size of the bony opening for access, where the procedure is performed (either in a sterile operating theater or bedside), and the drainage system utilized afterwards, if any. Surgery is generally safe; a meta-analysis published by Ducruet et al. quoted a complication rate of 2.5%, 3.9%, and 9.3% for craniostomy, craniotomy, and burr hole, respectively. They found a mortality rate higher for craniotomy (12.2%), when compared to TDC (5.1%) or BHC (3.8%). The rates of recurrence were as follows: BHC 11.7%, craniotomy 19.4%, and TDC 28.1% [26]. This particular meta-analysis gives a somewhat varied picture and suggests that no one technique is superior to another. Surgeons should exercise clinical judgment to ascertain which treatment is optimal for which patient. In patients with multiple comorbidities, a single burr hole may be best, as the procedure can be completed under local, with modest sedation, and is associated with a lower complication rate than mini craniotomy. Craniotomy is generally reserved for patients failing one or more attempts at burr hole drainage, those with a significant acute component, or those with problematic septations.

Each surgical option is imbued with certain technical nuances that may influence outcomes. For BHC, some advocate for two burr holes over simply one. Systematic reviews on the subject have not demonstrated clear evidence to support one versus the other [31, 32]. When performing craniotomies, an inner membranectomy can be performed, with the thought that this may facilitate brain re-expansion, along with the reabsorption of CSDH components by cortical and dural glymphatic/lymphatic pathways [33]. However, it is a common belief that this benefit must be balanced against the risk of seizures inherent to membranes stripping. The choice of

anesthesia, either using generalized anesthetic or local with sedation, is also a topic for debate; general anesthetics may pose some risk, particularly for patients with significant medical comorbidities. However, because these patients often present with confusion and agitation, it may be ill-advised to proceed without adequate sedation given the risk of patient movement during the procedure. The use of conscious sedation is, however, a good option for patients who carry a high risk with generalized anesthetic, but who may not tolerate the use of local anesthetic alone. Prospective randomized trials currently underway aim to assess the risk and benefits of general anesthesia (the NEURANESTH and GAS trials). The use of subdural drains has been investigated via a randomized control trial conducted by Santarius et al.; this study demonstrated a clear reduction in recurrence with the use of a drain [9]. Since that time, subperiosteal and subgaleal drains have been studied; published data suggest at least noninferiority of these techniques compared to subdural drain placement [34, 35]. It is the authors' preference to evacuate CSDH using a single burr hole, coupled with a high volume of intraoperative irrigation through a subdural drain—until the effluence runs clear. If there is concern about the ability to safely place a drain in the subdural location, the authors will leave one in the subgaleal space, given the recent supportive literature for that approach.

There are many situations in which surgical intervention may not be appropriate as first-line intervention. Nonoperative management should be reserved for patients for whom the benefits of surgery are felt to be outweighed by the risks; this may be true of patients with multiple comorbidities and poor baseline functioning. In those patients, a careful, patient-centered approach that includes other services (such as geriatric or palliative care medicine) should be undertaken, including detailed conversations with family members surrounding goals of care. For patients with small, asymptomatic collections, nonoperative management is often appropriate. Close follow-up with repeat imaging can be considered; generally, a CT scan at 1–2 weeks is performed to ensure stability of the subdural, followed by another at a 3-month interval. Spontaneous resolution of CSDH is possible and has been reported in the literature [36].

The non-surgical management of CSDH is an expanding field. Middle meningeal artery (MMA) embolization is a relatively new treatment modality for CSDH (Fig. 2.3a–d); the rationale for this approach is based on the concept that recurrent hemorrhage from the CSDH membrane is responsible for its evolution and that blood flow to the membrane originates from the MMA. This blood flow can be disrupted through embolization of this artery. Embolization versus conventional treatment was compared in a trial performed by Ban et al. Patients were prospectively enrolled in the study and underwent MMA embolization. Asymptomatic patients received MMA embolization alone, while those with symptoms also underwent surgery. This cohort was compared against a retrospective group treated in the conventional manner. The authors demonstrated significantly lower rates of treatment failure in patients who underwent embolization (1.4% vs %27.5) and a low rate of surgical rescue among those asymptomatic patients who underwent embolization as the sole modality of treatment (1.4% vs 18.8%) [37].

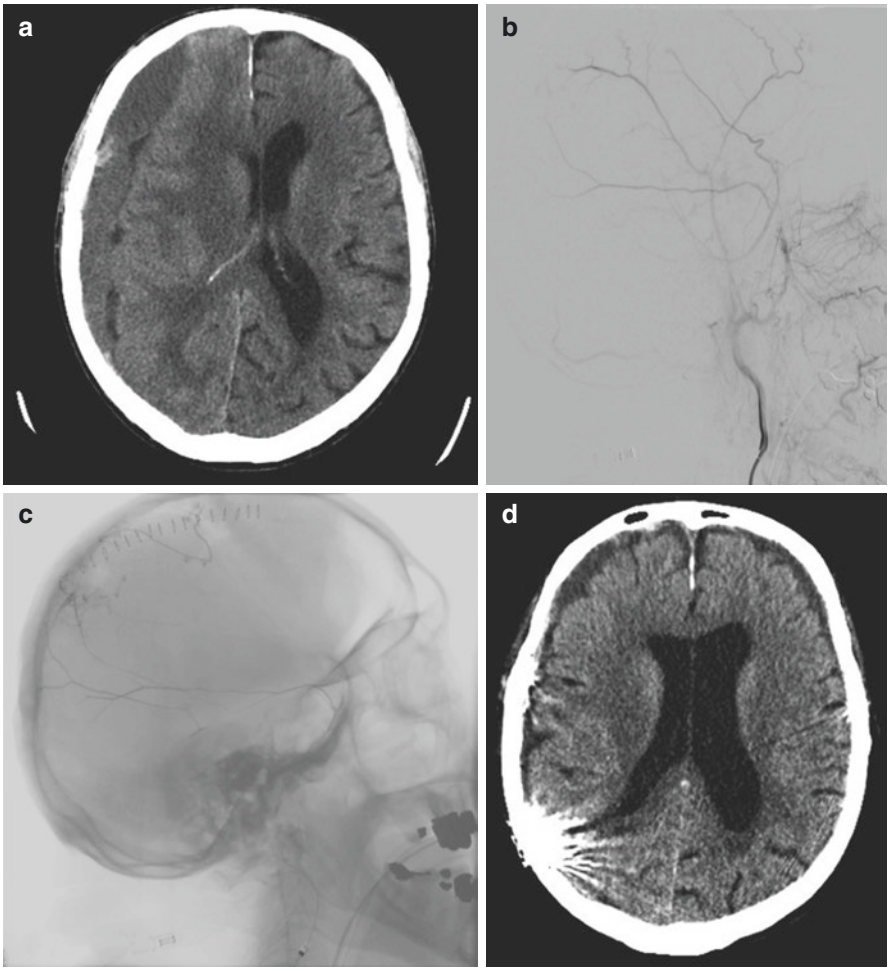

Fig. 2.3 (**a**–**d**) The use of MMA embolization in CSDH management. (**a**) CT scan demonstrating a mixed iso- and hyperdense extra-axial collection, consistent with a chronic subdural hematoma. There is significant sulcal effacement and midline shift present. (**b**) External carotid injection utilized for road mapping during the injection of non-adhesive liquid embolic agent (SQUID) material for MMA embolization. (**c**) Post embolization of the middle meningeal artery. Evidence of a mini craniotomy performed prior to embolization can be appreciated. (**d**) One month follow-up CT scan revealing resolved CSDH with hyperintense artifact representing the embolic material

A larger, multicentered clinical prospective study of MMA embolization as primary or rescue treatment has been performed. In this trial, surgical treatment options were left to the discretion of the attending physicians; surgery was offered to patients deemed clinically symptomatic (those with weakness grade 4/5 or worse and/or midline shift over 5 mm), and MMA embolization was utilized as an adjunct. The authors reported a 6.5% recurrence rate within 90 days, and a 9.4% complication rate, which included asymptomatic and symptomatic recurrence (2.2% and 5.1%,

respectively), asymptomatic MMA rupture (0.7%), post op seizure (0.7%), and facial droop (0.7%) [38]. Other published trials have been predominantly comprised of small case series that appear to support the use of MMA embolization in conjunction with surgical intervention for the reduction of recurrence [39, 40]. This may be a promising avenue for treatment for both asymptomatic patients and patients with recurrent CSDH; however, larger randomized trials must be completed and are currently underway. At this time, it is the preference of the senior author to reserve MMA embolization for recurrent hemorrhage.

Other adjuvant therapies may also be considered. The role of steroids in CSDH management is somewhat controversial. Existing retrospective and prospective studies do suggest that there may be role for steroids as an adjunct to reduce recurrence rates [41, 42]. However, a recent multicenter, randomized trial conducted in the United Kingdom compared oral dexamethasone treatment to placebo. The majority of patients in this study underwent surgical evacuation in addition to steroid treatment. They found that although patients treated with dexamethasone demonstrated lower rates of recurrence, they also had fewer favorable outcomes and more adverse events at 6 months [43]. This result may reflect the older population in which CSDH is most prevalent and which also tends to have higher rates of frailty and comorbidities; the results of this trial suggest that caution must be employed when considering steroids in the management of CSDH. Other agents, such as tranexamic acid, angiotensin-converting enzyme inhibitors, and platelet-activating factor receptor antagonists (such as etizolam), have been proposed [44–46]. Although they have yet to be become common place treatments, they remain active areas of research. Anecdotal evidence from our institution suggests that steroids may be more efficacious when instituted for CSDH believed present for only a short period of time—prior to the formation of membranes. Considering published evidence and personal experience, the senior author will consider offering dexamethasone therapy to select patients judged to have poor operative risk when a structurally complex CSDH is not evident and membranes are not suggested on imaging.

The use of prophylactic antiepileptic drugs (AEDs) lacks general consensus, and there remains a relative paucity of evidence to support their use [47]. On the one hand, that rate of seizures among patients with CSDH may be between 2% and 19% [48]. However, AEDs have been associated with increased incidence of falls in patients above the age of 65, and therefore, are not without risk [49]. The authors prefer to administer a 7-day course of AED prophylaxis to patients undergoing surgical drainage of CSDH, especially if membrane stripping is performed.

In this case, based on discussions with the patient and his family, operative intervention was chosen. The patient was admitted to hospital, and his aspirin was held. A pre-operative consultation with the anesthesiologist was arranged to optimize comorbidities and select the modality of anesthesia. Given the presence of aphasia and agitation, it was decided that this would not be an ideal case for a bedside craniostomy or awake burr hole, and so the patient was brought to the operating room for a generalized anesthetic. We opted for single burr hole drainage, coupled with high-volume intraoperative irrigation through a subdural drain. The patient

tolerated the procedure well. Post-operative CT scan revealed near total resolution of the CSDH. The drain was removed the next day. The patient's speech deficits and weakness resolved. He was discharged on post-operative day #3 after being clearing by our physiotherapy, occupational therapy, and speech language pathology teams. He continued to do well in follow-up, and, to date, has had no clinical recurrence.

2.5 Clinical Pearls

- CSDH may present with a constellation of neurological and neuropsychiatric symptoms and should be suspected in any patient—particularly if elderly—with a subacute decline.
- Many patients presenting with CSDH deny a history of trauma or point to an event that seemed trivial at the time.
- Surgical intervention—whether by burr holes or mini craniotomy—remains the mainstay of treatment for symptomatic CSDHs.
- There is growing evidence that middle meningeal artery embolization may provide a viable option for adjuvant or sole therapy in select CSDH patients.

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Chapter 3
Contusion and Diffuse Injury

Anthony DiGiorgio and Geoffrey Manley

Clinical Scenario

A 25-year-old female presents after a pedestrian versus auto collision in which she struck the back of her head. Her Glasgow Coma Scale (GCS) score was 13 (E3V4M6) both in the field and in the emergency room. It is unknown whether she had loss of consciousness (LOC). She cannot remember the incident, indicating post-traumatic amnesia (PTA).

3.1 History and Neurologic Exam

On clinical examination, our patient is alert but only oriented to her name. She moves all extremities equally. She has clear signs of trauma, including abrasions and an occipital subgaleal hematoma.

Cerebral contusion and diffuse traumatic brain injury describe a spectrum of traumatic brain injury (TBI) that initially presents without a space-occupying mass lesion. Contusions can evolve to become space-occupying lesions, causing increased intracranial pressure and mass effect. Pure diffuse axonal injury (DAI) does not typically follow this course. DAI is associated with contusions, as the force required to generate a contusion usually leads to some degree of diffuse injury as well. This has been confirmed when examining TBI patients with MRI [1].

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_3

A diffuse traumatic brain injury is to be suspected in any patient with altered mental status after a traumatic event. If the event is witnessed, the presence of LOC, PTA, alteration of consciousness (AOC), or seizures should be determined. These clinical "biomarkers" help the physician establish the severity of the injury. Additionally, the clinician should determine what the GCS was for the first responders in the field, as well as on arrival to the emergency department. A worsening GCS could portend an expanding mass lesion that requires emergent neurosurgical intervention. A low GCS—out of proportion to imaging findings—should raise concerns for DAI. If witnesses are able to describe the mechanism of trauma or even the site of impact to the head, this information can prove valuable.

In the patient with suspected but unwitnessed trauma (the "found down" patient), physical examination and imaging findings can help clue the examiner in to the presence of a diffuse traumatic brain injury. External signs of trauma out of proportion to what might be expected for a ground level fall point to trauma as an etiology rather than a syncopal event. Regardless of whether the event was witnessed, patients with diffuse traumatic brain injury often present with a degree of altered mental status that makes reliable history taking impossible. Instead, history must be obtained by speaking with relatives or caregivers and investigating any available medical records.

Relevant factors beyond the acute injury to be investigated include:

- *Use of medications that could increase bleeding risk (antiplatelets or anticoagulants) or history of a bleeding disorder*. This can include chronic liver or kidney disease. The reason for the antiplatelet or anticoagulant use must also be ascertained, as holding or reversing these medications also entails risk.
- *History of conditions which may preclude a patient from having a "normal" GCS at baseline*. For example, a patient with a history of stroke or spinal cord injury may have focal neurologic deficits at baseline, while a patient with dementia, mild cognitive impairment, or schizophrenia might have baseline confusion (GCS14, E4V4M6).
- *Drug or alcohol dependence*. Withdrawal from certain toxic substances, notably alcohol and methamphetamine, can mimic a neurologic decline from a mass lesion. This is especially relevant in the TBI population, which has a high rate of drug and alcohol use [2].
- *Systemic conditions that may complicate mechanical ventilation or fluid resuscitation*. These include congestive heart failure, kidney failure, and interstitial lung disease.
- *Advanced directive or durable power of attorney documentation*. It is important to provide patient-centric care, respecting any previously articulated wishes a patient may have. Obtaining an advanced directive or speaking with a designated decision maker can help guide clinical interventions.

The presence of polytrauma can alter intervention priorities. Other injuries may be acutely life threatening and influence treatment options for TBI. For example, hypotension from another injury is a contraindication for the administration of mannitol. A patient needing emergency surgery for an extracranial injury would likely

need intracranial pressure monitoring since the neurologic examination cannot be used to monitor for an enlarging mass lesion while under general anesthesia.

Neurologic examination should include evaluation of the distinct components of the GCS. This includes the best motor, verbal and eye-opening response. In an obtunded patient, the clinician should examine the pupillary response to light (ideally using a pupillometer) along with the corneal, cough, and gag reflexes. The examiner should attempt to assess any facial asymmetry and any gross differences in limb strength. If the patient can follow commands, a pronator drift can be assessed. Lastly, the clinician should examine the head for external signs of trauma, such as abrasions, subgaleal hematomas, scalp lacerations, otorrhea, rhinorrhea, raccoon's eyes, and Battle's sign. Signs of trauma to the posterior scalp could clue the examiner in to the presence of the classic frontotemporal *contrecoup* cerebral contusions.

3.2 Differential Diagnosis

The differential diagnosis for our patient would include diffuse traumatic brain injury, such as DAI, contusions, subarachnoid hemorrhage, and intraventricular hemorrhage. Concern for a mass lesion, such as a subdural or epidural hematoma, is also high.

In a patient with a witnessed trauma, the diagnosis is typically clear. However, the case can occasionally be murky, especially when a patient is found down. Even if the trauma is witnessed, it is possible that another event precipitated the trauma, especially in the case of a patient who fell. A syncopal event could cause a patient to fall. If a patient suffers one of these events while operating a motor vehicle, it would likely result in a crash. Thus, the pathogenesis of the patient's altered mental status could be from the underlying event alone, or in combination with the resultant traumatic brain injury. History here is important, as a patient who was seen acting inappropriately prior to the trauma is likely to have had a precipitating event.

Differentiating between a diffuse injury and an extra-axial hematoma is difficult on clinical exam. They often occur together. Lateralizing signs could suggest an extra-axial mass lesion, but this is nonspecific. For a patient with a declining GCS, worsening somnolence or unilaterally decreasing pupil reactivity to light could be signs of an enlarging mass lesion needing emergent surgical intervention.

Post-traumatic seizures can also be a cause of neurologic decline after traumatic brain injury. If an expanding mass lesion has been ruled out by CT scan, seizures should be considered. Rhythmic movements, eye deviation, and vital sign changes could signify seizures, but EEG must be performed to confirm this suspicion.

Toxic-metabolic encephalopathy can also mimic a diffuse brain injury. Again, history is important. A patient who fell or was found down may be suffering from acute intoxication. Knowing if the patient has a history of substance use disorder, takes medications with sedating side effects, or has a severe metabolic disorder would help make this diagnosis.

3.3 Diagnostic Evaluation

Our patient's initial labs are unremarkable, aside from a sodium of 135. A noncontrast CT of the head shows extensive bifrontal contusions, bitemporal contusions, and diffuse subarachnoid blood, along with a nondisplaced occipital bone fracture (Fig. 3.1a, b).

Noncontrast CT head will be the primary diagnostic modality to determine the nature and extent of injury in the acute setting and will facilitate rapid triage for pathology potentially requiring emergent intervention. Diffuse traumatic brain injury findings on CT include contusions, subarachnoid blood, intraventricular hemorrhage, as well as petechial hemorrhages at the gray-white matter junction and along the white matter tracts (corpus callosum, corona radiata, and/or brainstem).

CT is often negative in cases of diffuse injury. MRI, while not appropriate for first-line investigation in the acute setting, is more sensitive, especially for microhemorrhages [1, 3, 4]. Sequences that detect extravascular blood, such as gradient echo, are most sensitive for diffuse injury and DAI. MRI should only be pursued once the patient has been stabilized. A trauma survey CT scan should also be performed to rule out other injuries.

Diagnostic evaluation will be the primary which should include an examination of laboratory results. A basic metabolic panel (BMP), complete blood count (CBC), and coagulation studies (PT, PTT, INR) should be reviewed. Abnormal sodium or creatinine levels may help guide hyperosmolar therapy. While platelet count and coagulation studies are mainstays in the workup of any trauma patient, thromboelastography should also be strongly considered. Antiplatelet agents and newer anticoagulant agents will not always result in abnormal coagulation studies, but these can be detected on thromboelastography [5]. Additionally, traumatic brain injury

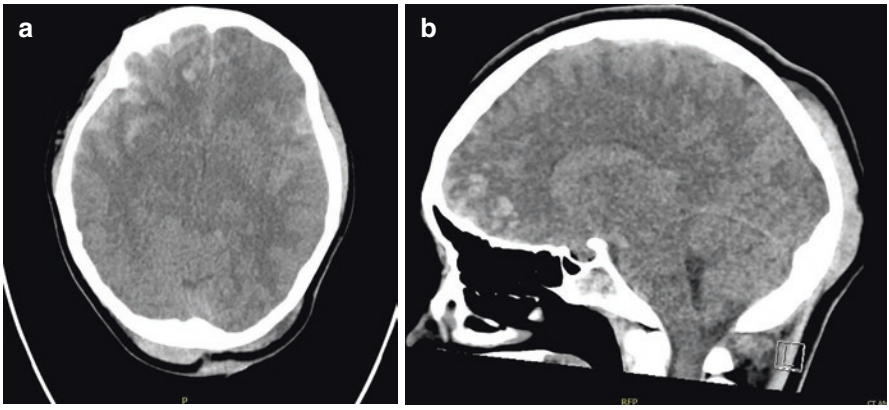

Fig. 3.1 Noncontrast CT head (**a**) axial and (**b**) sagittal images demonstrating the array of findings that might be associated with diffuse brain injury, including bilateral inferior frontal and temporal contusions, as well as traumatic subarachnoid blood. The occipital bone fracture is not well visualized on the brain tissue window

itself can result in a unique coagulopathy which is better characterized by thromboelastography [6]. Blood alcohol level and toxicology screening (both blood and urine) should also be performed in all traumatic brain injury patients [7].

3.4 Clinical Decision-Making and Next Steps

Initial clinical decision-making is guided by principles of Advanced Trauma Life Support (ATLS). Patients with diffuse brain injury may decline rapidly, so clinicians must ensure close monitoring of airway and breathing, even after initial stabilization. Hypotension should be avoided, and adequate fluid resuscitation continued.

The patient in the current clinical scenario was admitted to the neurocritical care unit with hourly neurologic checks, including pupillometer assessment. Antiepileptic drug (AED) prophylaxis was administered, and her sodium was corrected with normal saline fluid resuscitation. Thromboelastography was also obtained and was normal. Her follow-up CT scan showed significant blossoming of her contusions (Fig. 3.2a, b).

Coagulopathy should be corrected. However, for minor injuries and if a compelling indication for anticoagulant or antiplatelet use exists, full reversal need not be performed in every patient. The risks of anticoagulant or antiplatelet reversal must be weighed against the risk of intracranial lesion progression. If the patient requires an invasive procedure, be it surgery or insertion of intracranial monitors, anticoagulant or antiplatelet drugs should be reversed. Clinicians should also consider the potency and half-life of the antiplatelet or anticoagulant drug, including the time of the last dose.

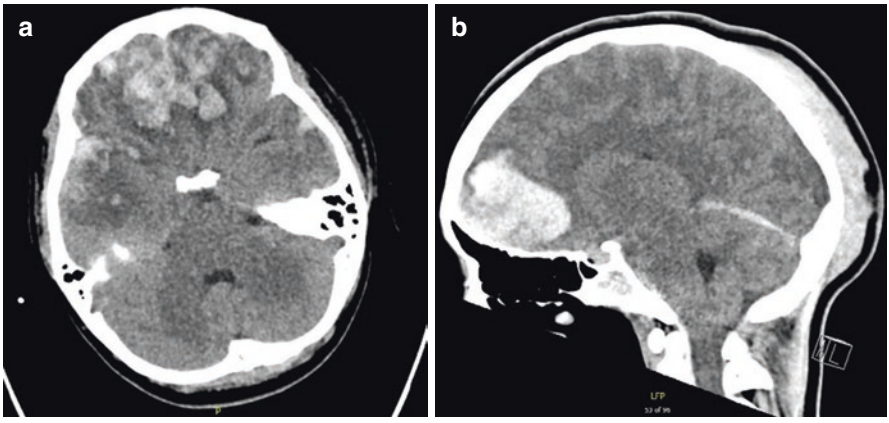

Fig. 3.2 Noncontrast CT head (**a**) axial and (**b**) sagittal images, performed at an interval of approximately 6–8 h from initial presentation, demonstrating generalized progression of the bilateral inferior frontal and temporal contusions, resulting in increased mass effect

All patients should undergo close neurologic monitoring with frequent neurologic checks and pupillometer assessment, along with repeat CT scan (typically 6–8 h after the initial scan). All patients with cerebral contusions or subdural hematoma should receive a loading dose of antiepileptic medications [8], followed by 7 days of administration. The head of bed should be elevated (30–45°). Adequate analgesia and sedation should be maintained in intubated patients. If there is expectation that vasopressors or hypertonic solutions will be administered, a central line should be placed. Arterial line monitoring should be established if cerebral perfusion pressure (CPP) will be monitored.

Much of the general treatment of TBI is outlined in the most recent guidelines released by the Brain Trauma Foundation (BTF) and the American College of Surgeons (ACS) TBI Best Practices Guidelines [9–19]. The BTF recommends intracranial pressure (ICP) monitoring to reduce in-hospital mortality after TBI while the ACS recommends monitoring patients with structural brain injury on CT and a GCS $\leq$8. This should include monitoring of cerebral perfusion pressure. The authors recommend the use of an external ventricular drain (EVD), as this offers the added therapeutic benefit of cerebrospinal fluid (CSF) drainage to lower elevated intracranial pressure [14]. The BTF guidelines recommend continuous CSF drainage for elevated ICP, and since an EVD must be clamped to monitor pressure, the authors also recommend placement of a parenchymal ICP monitor. A dual lumen bolt allows placement of both the parenchymal monitor and a brain tissue oxygenation monitor [20, 21].

Unless ICP is acutely elevated, hyperosmolar therapy is not recommended. Prophylactic use of mannitol or hypertonic saline should not be used [10]. Likewise, prophylactic hyperventilation and hypothermia are not recommended [11, 18]. The clinician should aim to achieve normonatremia, normothermia, and normocarbia.

Most patients with CT-positive diffuse traumatic brain injury will require hourly neurologic assessment, which typically necessitates an admission to an intensive care unit (ICU). While patients with TBI are treated in various ICU types (neuro, surgical, trauma, or medical ICUs), they require specialized nursing care with expertise in ICP monitoring, pupillometer use, and neurologic examination.

In the case of elevated intracranial pressure, a tiered strategy should be used and can be continued in the ICU [22]. Tier one includes ensuring venous return from the head must be unobstructed (neutral head position and removal of cervical collar if cleared). Analgesia and sedation can be increased, intermittent hyperosmolar therapy utilized and CSF drainage to maintain a minimum CPP of 60–70 mmHg.

For the acute patient in the trauma bay, escalation past the first tier of ICP control measures is rarely needed and, if required, would be an unfavorable sign Uncontrolled ICP would be indicative of a mass lesion requiring evacuation or a devastating injury with little chance of survival. However, if escalation beyond the first tier is needed, the second tier involves performing a cerebral autoregulatory challenge [22–24]. This is performed by elevating the mean arterial pressure (MAP) under direct physician supervision. If the ICP increases at a 1:1 ratio with the MAP, the patient is not able to autoregulate cerebral blood flow and future therapies should be directed at lowering ICP, rather than increasing CPP.

If autoregulation is intact, the second tier of ICP management includes using vasopressors or fluid boluses to increase CPP. Regardless of autoregulation status, other second tier interventions are a trial of neuromuscular paralysis and mild hypocapnia (32–35 mmHg). Tier three interventions are barbiturate coma and hypothermia to 35 °C.

It is rare that a diffuse injury, or even large contusions, will cause elevated ICP acutely. The intracranial hypertension typically develops over the next few days as the contusions blossom and the brain become edematous. However, a large contusion causing mass effect and midline shift may require surgical intervention. A declining neurologic exam, pupil asymmetry, or refractory elevated ICP are indications for surgery with a unilateral mass lesion. The operative approach is a large frontotemporoparietal decompressive hemicraniectomy no smaller than 12 × 15 cm. The contusion itself should not be evacuated, as this can lead to uncontrollable intraoperative hemorrhage. The surgical goal is bony decompression alone. Conversely, bifrontal decompressive craniectomy for intracranial hypertension secondary to diffuse injury without a focal mass lesion is not recommended based on the DECRA study [25].

Patients with a pure DAI without contusions rarely develop increased ICP, and monitoring can typically be discontinued after 2–3 days. We typically remove the parenchymal monitor after this trial, which allows the patient to undergo an MRI to help with prognosis. The EVD is MRI compatible and may be left for a few more days to ensure no ICP elevations develop. If the clinical and radiographic pictures indicate the patient will need an early tracheostomy and percutaneous gastronomy tube, keeping the EVD allows for continued ICP monitoring during these procedures.

The patient in the clinical scenario had a neurological exam remained stable. On the second night, her pupil reactivity index began trending downward. She responded to mannitol 50 g with a return to baseline. However, she progressed to develop a waxing and waning neurologic exam, prompting placement of triple monitoring (EVD/parenchymal monitor and brain tissue oxygen monitor). She had a prolonged ICU stay, with intermittent episodes of elevated ICP. These were treated with alternating CSF drainage and hyperosmolar therapy. She was eventually able to return to work 4 months after her accident.

3.5 Clinical Pearls

- Acute intracranial pathology is to be suspected in any patient presenting with altered mental status after trauma. Contusions and diffuse brain injury are typically apparent on initial imaging workup, but more advanced imaging, such as MRI, are required to show the full extent of the damage.
- ATLS protocols should guide initial management for an obtunded patient. Once stabilized. Invasive intracranial monitoring—preferably by external ventricular drain—should be initiated. Management of elevated ICP should follow a tiered protocol.

- Mass lesions causing elevated intracranial pressure should are candidates for surgical intervention. However, two large trials have failed to show improved outcomes with decompressive craniectomy in the setting of refractory ICP elevations.

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Chapter 4
Penetrating Brain Injury

Odette A. Harris and Daniel B. Herrick

Clinical Scenario

An otherwise healthy 21-year-old male in full protective gear was involved in a motorcycle accident travelling approximately 35 mph, whereby he crashed over an embankment and fell onto a tree. A tree branch penetrated his helmet visor and subsequently his cranial vault via the orbital cavity. Upon arrival to the Emergency Department (ED), he was found to have a large wood fragment penetrating his right orbit. On examination, he was awake, oriented, and following commands without focal neurological deficits.

4.1 History and Neurologic Exam

Traumatic brain injury (TBI) can be characterized by its severity (mild, moderate, severe) and mechanism (blunt versus penetrating). Penetrating brain injury (PBI) can be further classified as missile or non-missile, where missile PBI includes high velocity projectiles such as bullets and shrapnel, and non-missile PBI consists of penetration of the skull and brain with any low-velocity object such as a knife or, in this case, a piece of wood. Between 2000 and 2019, the Department of Defense estimates there were 5,388 penetrating brain injuries and 422,405 closed head injuries across all branches of the U.S. Military worldwide [1]. Approximately 10% (26,871) of 268,645 TBI patients in a 5-year retrospective study (2010–2014) using the Trauma Quality Improvement Program database were classified as having penetrating injuries [2]. A recent review of patients with craniocerebral gunshot

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_4

wounds—the most common mechanism of civilian PBI—found a mortality rate of 66–90% prior to hospital arrival; among those reaching medical care, 50% will survive [3, 4]. In one retrospective review of 119 patients admitted to the hospital with craniocerebral gunshot wound, mortality was 49% with 19% achieving a favorable outcome [5]. Conversely, analysis of the Brain Trauma Foundation TBI-trac® database of 2,513 patients who sustained severe non-penetrating TBI who had a GCS motor score >2 with at least one reactive pupil, 14-day mortality was 23% [6]. In the CRASH-3 study evaluating the use of tranexamic acid for patients with TBI and admission GCS <13 or CT evidence of any intracranial hemorrhage, mortality among patients with mild to moderate TBI (GCS 9–15) was 6.6% and mortality in the severe TBI group (GCS 3–8) was 39.8% 28 days after injury [7]. Overall, compared to closed head trauma, PBI is less prevalent and is associated with a significantly worse prognosis. Within PBI, there are often differences in clinical characteristics of patients presenting with missile versus non-missile injuries. However, current clinical data do not support dichotomizing the two injury mechanisms for the purposes of clinical management.

The most immediate consideration in this or any patient with PBI is management of airway, breathing, and circulation in the trauma bay. The patient should be deemed hemodynamically stable prior to initiation of cranial imaging. When possible, a basic neurological examination assessing mental status, cranial nerves, and gross motor strength will take place concurrent with hemodynamic stabilization and prior to administration of sedatives or paralytics, such as those required for intubation or severe agitation. Additionally, a focused medical history should be elicited from the patient, if possible, or a relative.

There are several pieces of patient history that must be elicited upon arrival for any patient with head trauma with known or suspected PBI:

- *Mechanism of injury*: Determine if the injury is missile or non-missile PBI. There is far greater kinetic energy in missile injury and thus more transfer of energy to and destruction of brain tissue. If the patient suffered a missile injury, especially a gunshot wound, the distance from which the patient was shot and the caliber of bullet can provide more information about the degree of kinetic energy transfer and associated underlying parenchymal injury.
- *Field examination and course*: The gross neurological examination in the field is important to obtain from the primary responder upon arrival to the ED. A change in neurological status such as a decrease in GCS score between the time of initial traumatic incident to arrival in the ED could signal a rapidly progressive space-occupying lesion such as a hematoma. Additionally, loss of consciousness and duration of such an episode should be relayed to the examining physician.
- *Past medical and surgical history*: Bleeding disorders and coagulopathies will require physicians to pay special attention to optimizing blood clotting in the setting of intracerebral hemorrhage.
- *Medications*: The most pertinent medication history to elicit is regarding the use of antiplatelets and anticoagulants, as use of these agents can exacerbate bleeding.
- *Drug or alcohol use*: Recent intoxication with drugs or alcohol can cloud the clinical examination. Routine drug screening is recommended, as elicit drug use and polypharmacy can cause altered mental status unrelated to brain injury.

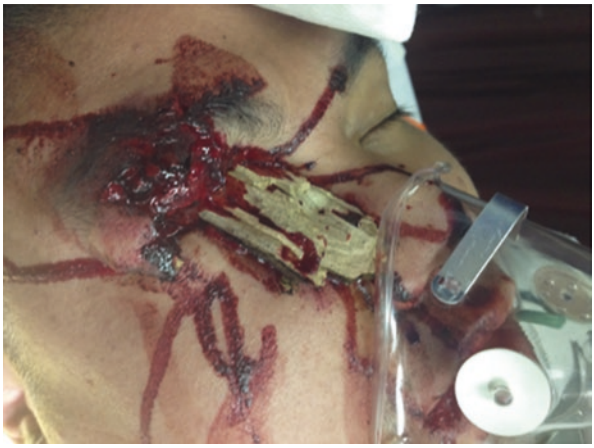

Fig. 4.1 The patient initially presented to the ED with a large wood fragment penetrating his right orbit and an abrasion above his right eye

Following the initial trauma evaluation and hemodynamic stabilization of the patient, a focused neurological examination should assess mental status, cranial nerve function, gross motor strength, sensation, and reflexes. Additionally, the primary neurosurgical concern to be evaluated in a patient with obvious or suspected PBI is underlying injury to the cranial vault and its contents. The integrity of the orbit, skull base, calvarial bone, and skin should be assessed, particularly at the site of cranial penetration. In the case of injury to the skull base, the clinician should thoroughly assess the patient for rhinorrhea and otorrhea. The entry site (and possibly a corresponding exit site) should be inspected carefully for blood, brain, and CSF and then cleaned thoroughly and covered with a sterile dressing to avoid communication between the atmosphere and the central nervous system. Involvement of the orbit or ear should prompt consultation of ophthalmology and otolaryngology, respectively.

In this particular case, the patient was found to be neurologically intact except for loss of vision in his right eye secondary to a tree branch completely obliterating the right globe with an unknown depth of penetration into the orbit and possibly the cranial vault (Fig. 4.1). The object was not moved or removed, and his right eye and protruding branch fragment were covered with a sterile dressing. The periorbital area was auscultated for a bruit, which, if found, would indicate a possible traumatic carotid-cavernous fistula. In addition to a full trauma evaluation in the ED, the ophthalmology service was consulted.

4.2 Differential Diagnosis

The diagnosis of PBI is self-evident at presentation and does not lend itself to the exercise of formulating a differential diagnosis. However, it is worthwhile to consider the range of injuries that are potentially associated with PBI, including direct injury to brain parenchyma along the tract of the object, extra-axial injury (SDH, EDH), intra-axial injury (tSAH, ICH, IVH), as well as vascular complication such

as traumatic aneurysms/pseudoaneurysms and arteriovenous fistulas. The incidence of traumatic aneurysms ranges from 3.2% to 60% among several small studies [8–10]. A retrospective review of 55 consecutive patients with missile (43 gunshot wounds) and non-missile (7 stab wounds, 4 nail gun accidents, 1 impaled by wooden piece) PBI and diagnostic subtraction angiography revealed the following risk factors associated with arterial injury: entry wound over the frontobasal-temporal regions, wound trajectory involving bilateral hemispheres, wound trajectory in proximity to the Circle of Willis (<2 cm), SAH, and IVH. Patients presenting with gunshot wounds with a trajectory proximal to the Circle of Willis were far more likely to have an arterial injury when compared with the PBI cohort as a whole (OR 6.8 for all PBI, OR 13.3 for gunshot wounds) [11].

4.3 Diagnostic Evaluation

4.3.1 Imaging Studies

4.3.1.1 CT

Initial diagnostic evaluation after the patient is hemodynamically stable is performed with a non-contrast head CT. This study will provide gross information about the extent and anatomical location of intracranial injury, as well as the location of the foreign body if still present in the cranial vault.

4.3.1.2 Cerebrovascular Imaging

A CT angiogram of the head and neck or digital subtraction angiography (DSA) of the head and neck is indicated in PBI, whether missile or non-missile, when the foreign body passes through or near a large named artery, passes near dural sinuses, or there is evidence of arterial bleeding that could be controlled with intervention. A retrospective review comparing CTA to DSA in 56 patients with both missile (48/56 gunshot wounds) and non-missile PBI who underwent both studies revealed the sensitivity and specificity of CTA to be 72% and 63%, respectively, when compared to the gold standard DSA for identifying penetrating cerebrovascular injuries [12].

4.3.1.3 Spine Imaging

If the injury is associated with a fall or traumatic whiplash injury of the cervical spine, a non-contrast CT of the cervical spine should be obtained to rule out acute fracture or subluxation.

4.3.1.4 MRI

An MRI study is both time-consuming and prohibited in patients with PBI involving metal. It is infrequently used in the initial diagnostic algorithm for workup of PBI. However, MRI can be used in the non-emergent setting for patients presenting with PBI by a wooden foreign body.

This particular patient's initial imaging consisted of a CT/CT angiogram head and neck and revealed the following: a linear foreign body object (measuring 7.1 cm × 1.7 cm) with intrinsic low density, penetrating the right orbit into the right frontal lobe; intraparenchymal hemorrhage in the right frontal lobe with associated vasogenic edema; displacement of the right globe inferiorly with herniation of the inferior rectus muscle and orbital fat into the right maxillary sinus; and multiple facial fractures, including a comminuted right superior orbital fracture, right orbital floor fracture, and right medial orbit fracture of the lamina papyracea with hemorrhage into the ethmoid air cells (Fig. 4.2). CTA showed patent anterior and posterior intracranial circulation, without evidence of flow-limiting stenosis or cerebral aneurysm. Dural venous sinuses were found to be patent. CT cervical spine was negative for acute fracture or subluxation. MRI was deferred, as the patient required emergent surgical intervention.

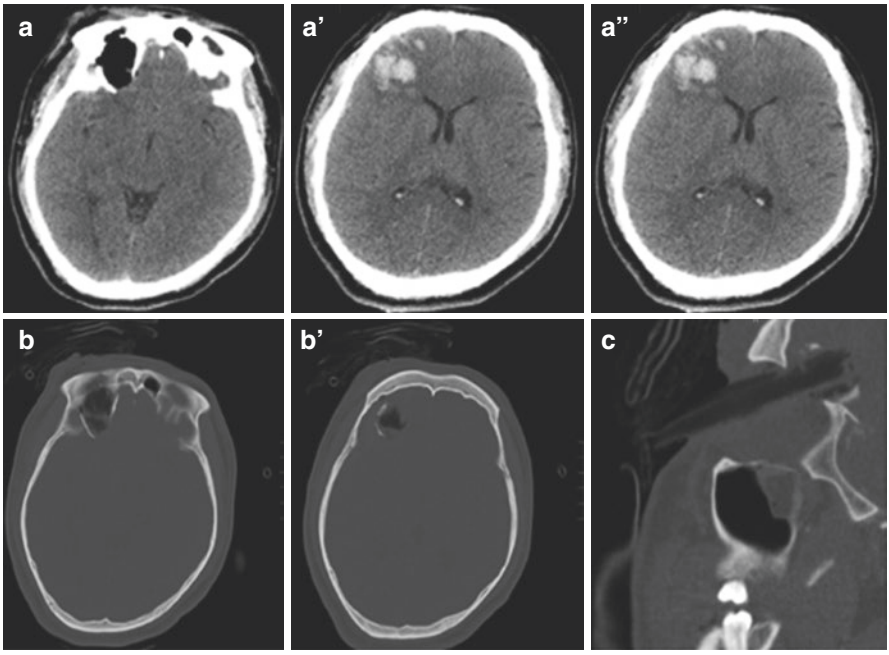

Fig. 4.2 CT findings upon arrival to the ED. (**a**–**a**″) Sequential axial non-contrast CT scan slices demonstrating a hypodense object penetrating the right orbit with associated hematoma. (**b**–**b**′) Corresponding CT bone windows demonstrating fractured bone fragment penetrating the brain parenchyma. (**c**) Sagittal view of the wood object penetrating the right orbit and brain parenchyma

4.3.2 Laboratory Studies

Laboratory studies should include a basic metabolic panel, complete blood count, coagulation studies, and a type and screen in the event the patient is hemodynamically unstable or requires surgical intervention. If the patient has increased urine output concerning for diabetes insipidus, a urine specific gravity and urine electrolytes should be obtained.

4.4 Clinical Decision-Making and Next Steps

4.4.1 Trauma Bay Management

4.4.1.1 ICP Management

There is a paucity of evidence evaluating the use of ICP monitoring in patients with PBI. When the Penetrating Brain Injury Guidelines were published in 2001, there were insufficient data to support treatment guidelines for monitoring ICP in this patient population [13]. However, the literature suggests that increased ICP is associated with worse outcomes, as is the case in blunt traumatic brain injury. Patients should be closely monitored for signs of increased ICP, and, without evidence for or against ICP monitoring in this population, we apply the Brain Trauma Foundation guidelines for ICP monitoring and management to the PBI population.

4.4.1.2 Seizure Prophylaxis

The use of anticonvulsants after PBI has not been systematically evaluated in large, controlled studies. Aarabi et al. retrospectively evaluated 489 patients from the Iran-Iraq War with PBI; 32% developed epilepsy during the study period [14]. Multivariate analysis revealed Glasgow Outcome Score and presence of a motor deficit to be significant predictors of late post-traumatic epilepsy. Patients with PBI disrupting brain cortex should be placed on a 7-day course of prophylactic anticonvulsants, consistent with the current Brain Trauma Foundation TBI guidelines.

4.4.1.3 Antibiotics

Use of prophylactic antibiotics in PBI varies significantly, as robust data supporting the use and type of agent is lacking. However, cephalosporins are the most preferred antibiotics among historical reviews addressing antibiotics in the last 30 years [15]. The British Society for Antimicrobial Chemotherapy performed an extensive review of the literature regarding antimicrobial use in penetrating craniocerebral injuries in

both civilian and military incidents and recommends that broad-spectrum antibiotic prophylaxis is necessary. They recommend IV cefuroxime 1.5 g, then 750 mg every 8 h with IV metronidazole 500 mg every 8 h. Administration should begin as soon as possible after injury and continue for 5 days [16].

4.4.1.4 Foreign Body Management

If the foreign body is still embedded in the patient and protruding from the head, careful planning is necessary to remove the object. The object should be stabilized during transport to imaging and the operating room. However, fragments of the penetrating object should not be surgically removed if it puts brain tissue at risk.

4.4.2 Operative Indications

There are no well-established guidelines for surgical intervention for patients suffering from missile or non-missile PBI. Several small studies have used criteria such as GCS, size of SDH/EDH/ICH, midline shift, and cranial nerve exam to determine when to consider surgery. When considering surgical intervention, there are two primary goals: manage malignant intracranial hypertension and isolate the CNS from the atmosphere at the site of penetration and exit, if one is present. To address the second goal, foreign objects that remain protruding from the skull must be removed or amputated to close the dura and skin. Additionally, if the dura does not close spontaneously or there is a large defect, operative intervention may be required to obtain a watertight dural seal to prevent infection and ongoing CSF leak.

In this particular case, the patient was administered 2 g ceftriaxone upon arrival in the ED. At that time, his neurological examination was reassuring, and there were no concerns for elevated ICP. Pain in his orbit was managed with IV fentanyl. He was taken to the operating room for a right frontal craniotomy for removal of foreign object, wound washout, repair of CSF leak and repair of right anterior cranial base with the assistance of ophthalmology. A piece of wood was sent for culture (Fig. 4.3). The patient did not require enucleation, as the globe was intact and displaced into the maxillary sinus.

The patient was admitted to the ICU for monitoring, loaded with levetiracetam (with a plan for a 7-day prophylactic course), and started on a 7-day course of vancomycin, cefepime, and metronidazole. He was transferred to the floor in stable condition, and the infectious disease team was consulted to assist with transitioning to oral antibiotics. The wood fragment sent for culture from the OR grew very rare *coagulase negative Staphylococcus*. Infectious diseases recommended 14 days of oral cephalexin and levofloxacin. The patient was discharged home on postoperative day 6. On postoperative day 10, ophthalmology performed a temporary right tarsorrhaphy.

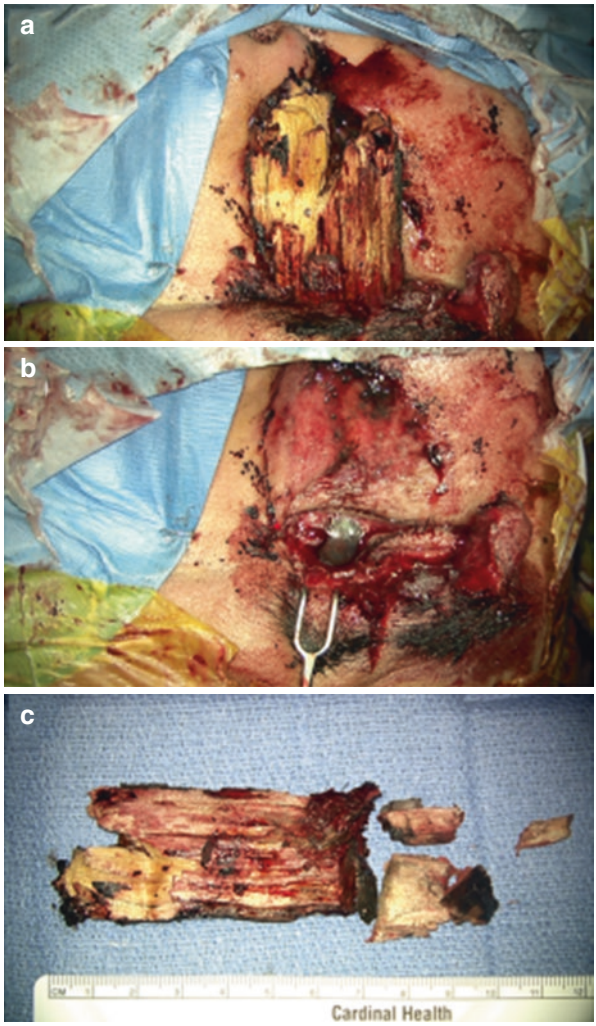

Fig. 4.3 Intraoperative images demonstrating the (**a**) the fragment in situ, (**b**) the orbit after fragment removal, and (**c**) the removed foreign body

4.4.3 Complications

4.4.3.1 CSF Leak

CSF leaks are common complications of PBI, and they have been reported to occur in as many as 28% of patients in one series of 163 consecutive military PBI cases [17]. They are associated with higher risk of infection [18, 19] and, in turn, mortality. As such, all CSF leaks—regardless of location (entry site, exit site, or sinus injury/temporal bone injury)—should be repaired primarily with a watertight closure if they do not close spontaneously or respond to lumbar drainage. The use of allograft for watertight closure should give the surgeon pause as the foreign body can become infected in a PBI wound considered to be contaminated.

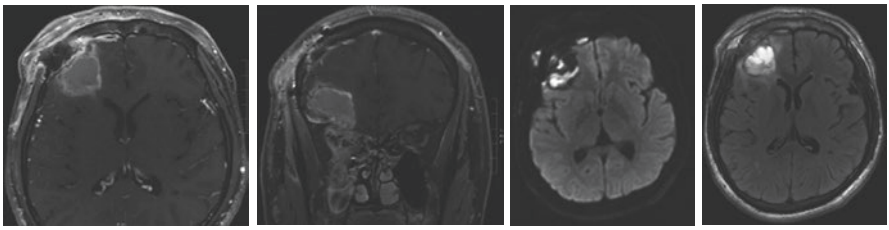

Fig. 4.4 Postoperative infection demonstrated on brain MRI with and without contrast. From left to right: axial T1 post-contrast, coronal T1 post-contrast, axial DWI, and axial flair series

4.4.3.2 Infection

Both CSF leak and retained foreign body put patients at risk of wound infection and abscess. In a prospective study of 192 patients with non-missile penetrating brain injury, 27 patients (14%) developed an infection. Infection was associated with delayed admission to the hospital more than 24 h, no antibiotic prophylaxis, and weapon/foreign object in situ. Multivariate analysis did not reveal surgical intervention to be independently associated with infection [20].

On postoperative day 18, the patient had a near syncopal episode and was brought to an outside hospital emergency department where he had a mild leukocytosis and was hypotensive. There was fluid draining from his right eye. He was transferred to our institution for concern of orbital cellulitis and possible sepsis. He was started on vancomycin, piperacillin-tazobactam, and fluconazole prior to transfer. Upon arrival, his antibiotic regimen was changed to vancomycin, cefepime, and metronidazole. MRI brain and orbit pre- and post-gadolinium were obtained, revealing an approximately 3 × 3 cm right frontal postsurgical cavity with significant restricted diffusion without a clear fluid-fluid level. There was peripheral enhancement—suspicious for cerebral abscess—with contiguous extension into the right orbit (Fig. 4.4). The original bone flap was removed, and a dural incision revealed granular and purulent material consistent with infected brain parenchyma/abscess. Contents of the surgical cavity were evacuated, cultures were sent, the area was irrigated, and a decision was made to perform a complete tarsorrhaphy to seal the orbit and thus the intracranial cavity from the atmosphere. His cultures did not grow bacterial or fungal colonies, and he was discharged on his intravenous antibiotic regimen. He recovered well and did not have recurrence of his abscess.

4.5 Clinical Pearls

- Initial management of PBI should be according to ACS and Brain Trauma Foundation guidelines.
- Vascular imaging may be necessary prior to considering neurosurgical intervention, especially when a foreign body passes near large named vasculature or

there is evidence of arterial bleeding that could be controlled with intervention. CTA and DSA are the imaging modalities of choice, with DSA being the gold standard to establish parenchymal and vascular injury secondary to PBI.
- The optimal medical management of PBI, including ICP monitoring and seizure prophylaxis, has not been well-studied in large trials and currently reflects the well-established Brain Trauma Foundation guidelines for TBI.
- Surgical management should focus on removing foreign objects protruding from the skull, while avoiding unnecessary debridement and retrieval of deep retained fragments, which could cause further parenchymal injury.
- CSF leaks and infections are common complications associated with PBI and should be monitored closely.

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Chapter 5
Concussion

Arjang Ahmadpour, Valentina Vasenina, Vimal Patel, and Julian E. Bailes Jr

Clinical Scenario

A 14-year-old male presents to the Emergency Department (ED) following injury during a football game. He made helmet-to-helmet contact with an opponent on the other team, while running at full speed. Immediately after the collision, he reports seeing a flash of white light and is amnestic to the events after that point. The patient's coach, who is at bedside, reports brief loss of consciousness lasting approximately 30 s. A neurological exam performed immediately after the patient regained consciousness showed no focal deficits; GCS was recorded as 14, with one point deducted for confusion. Noncontrast CT head and neck done on arrival to ED was normal. Labs were all within normal limits.

The patient reports mild diffuse headache, sleepiness, nausea without emesis, and difficulty concentrating. He denies vision changes, neck pain, weakness, and numbness.

All other review of systems were negative.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_5

5.1 History and Neurological Exam

Diagnosing concussion requires a thorough history and neurological exam. In the clinical scenario above, the key components of history include the patient's neurological status prior to the time of injury and that the patient experienced a high velocity helmet-to-helmet impact with resultant loss of consciousness and confusion upon awakening. Diagnosis is based on assessment of a range of domains which includes physical signs, cognitive impairment, clinical symptoms, neurobehavioral features, and sleep disturbance [1]. If even one of these symptoms is present, concussion should be suspected, and the proper management strategy should be implemented [1]. Diagnosis requires a focused clinical examination, paired with an awareness of multiple symptoms that may be present with concussive injury. On-site assessment tools may aid the provider in the diagnosis of concussion. Adjuncts to the clinical assessment, such as advanced neuropsychological testing, neuroimaging techniques, and blood-based biomarkers of injury can also be used to aid in identifying injury and secure the diagnosis of concussion. Although these new technologies are not required or recommended for routine clinical care, they show promise as investigative tools to advance our understanding of the pathophysiology of concussion and recovery. Through advanced imaging techniques and analysis of biomarkers that are released following injury, research has conceded that considering concussion as only a functional entity is an inappropriate underestimate.

There is a wide range of variability in the quality of training and experience of health care professionals diagnosing and caring for concussed athletes. This contributes to uncertainty and inconsistency in the various aspects of concussion diagnosis, prognostication, and treatment in affected athletes. In 2013, The Guideline Development Subcommittee of the American Academy of Neurology (AAN) published the "Evidence-based Guideline Update: Evaluation and Management of Concussion in Sports" [2]. This comprehensive publication reviews evidence in children, adolescents, and adults from 1955 through 2012.

The 2016 Consensus Statement on Concussion in Sport from the 5th International Conference on Concussion in Sport states [1]:

> *When a player shows any symptoms or signs of a sports-related concussion (SRC):*
>
> *a. The player should be evaluated by a physician or other licensed healthcare provider on site using standard emergency management principles, and particular attention should be given to excluding a cervical spine injury.*
>
> *b. The appropriate disposition of the player must be determined by the treating healthcare provider in a timely manner. If no healthcare provider is available, the player should be safely removed from practice or play and urgent referral to a physician arranged.*
>
> *c. Once the first aid issues are addressed, an assessment of the concussive injury should be made using the SCAT5 or other sideline assessment tools.*
>
> *d. The player should not be left alone after the injury, and serial monitoring for deterioration is essential over the initial few hours after injury.*
>
> *e. A player with diagnosed SRC should not be allowed to return to play on the day of injury.*

Signs and symptoms that are of particular concern include severe or progressively worsening headaches, positive findings on neurological examination, emesis, or rapid decline in mental status. These findings may indicate a more life-threatening injury (e.g., epidural or subdural hematoma, intraparenchymal hemorrhage) and necessitate immediate transfer to the ED. See Table 5.1 for a summary of commonly reported signs and symptoms of concussion.

Although standardized sideline assessment tools may be useful in the acute evaluation of concussion, several points must be kept in mind. These tools are designed for rapid screening of concussion by the wider spectrum of practitioner types and should not be used to replace comprehensive neuropsychologic testing by a trained neuropsychologist [1]. Furthermore, no sideline assessment tool should be used for the ongoing management of sports-related concussions [1]. A standardized clinical evaluation of concussion is useful, but should not substitute for clinician's judgment.

Given the wide range of variability in the experience of health care professionals diagnosing concussed athletes, it is important to obtain a detailed history. Pertinent topics of inquiry are discussed below.

Table 5.1 Common signs and symptoms of concussion

Signs of injury
Loss of consciousness
Retrograde amnesia (forgetting events that happened before the concussion)
Anterograde or posttraumatic amnesia
"Dazed" look
Confusion about injury events or details
Disorientation to person, place, or time
Emotional lability
Inappropriate emotions
Behavior or personality changes
Symptoms of injury
Headache
Dizziness
Balance difficulties
Fatigue
Visual changes (double or blurry vision are the most common)
Insomnia
Drowsiness
Attention dysfunction
Short-term memory and learning problems
Difficulty multitasking
Phonophobia
Photophobia
Bradyphrenia
Feeling mentally "foggy"
Emotional changes

5.1.1 Constitutional Symptoms

The clinical manifestations of concussion affect one or more of the domains of somatic, cognitive, behavioral, emotional, vestibular, cervical, autonomic, and sleep/wake. Common signs and symptoms of concussion are headache, fatigue, dizziness, amnesia, irritability, anxiety, poor concentration, photophobia/phonophobia, disorientation, and postural instability. In the clinical scenario presented above, the athlete experienced disorientation immediately following the impact from the helmet-to-helmet collision. He also endorses mild diffuse headache, sleepiness, nausea without emesis, and difficulty concentrating. These signs and symptoms are sometimes associated with other conditions in athletes, such as dehydration, exertional migraines, heat related illness, and sleep disorders. Thus, it is important to establish a relationship between mechanism of injury and the onset or worsening of symptoms [3–7]. Physicians, and others caring for athletes, must remember that although symptoms typically begin immediately following the inciting trauma, some patients may not.

5.1.2 Neurological Symptoms

Headache is the most common reported symptom of concussion—present in 83–86% patients [8]. The headache characteristics experienced after concussion or mTBI may include tension-type, cluster-like, tension-type, migraine-type, and mixed [9]. It is important to establish a timeline of when headaches first start, to permit clear correlation with the time of injury, as demonstrated in the scenario presented above.

It is important to obtain a detailed history regarding any complaints of headache with special focus on the quality, frequency, and duration of each episode. Next, determine whether there are conditions that exacerbate or relieve the headaches. Investigate other symptoms that might accompany headache episodes such as vision changes, dizziness, nausea, and emesis. Also give special consideration to seizures, asking whether there have been witnessed episodes of seizure-like activity, since patients might be amnestic to these types of events. Inquire regarding any new weakness or numbness that might be suggestive of spinal cord or nerve injury requiring further work-up.

The mechanism for headache following head injury is not well understood. Both migraine and concussion have common pathophysiologic effects, including increase in intracellular sodium, calcium, chloride, and extracellular potassium [9]. Both conditions have been linked to increased release of excitatory amino acids such as glutamate [10].

Post-concussion headache may be associated with slowed reaction time, memory impairment, on-field anterograde amnesia, and increased overall symptoms [11]. Patients with migrainous headache after concussion scored lower on several

neurocognitive measures (processing speed, verbal and visual memory, and reaction time) than those with nonmigrainous headaches or no headache after concussion [12]. Patients with migrainous headache also reported more or worse symptoms relative to the other two groups [12].

Mental status changes and subtle neurocognitive deficits are also quite common with concussion. Confusion has been a long-standing hallmark of concussion. Confusion may also include a disturbance of vigilance with heightened distractibility, inability to maintain a coherent stream of thought, or the inability to carry out a sequence of goal-directed movements. Although disorientation may be present during a concussion, more subtle changes—as described previously—are more common and should be sought during examination of the patient or athlete [13–15]. One study highlighted that concussed athletes exhibiting "fogginess" have demonstrated poor performance on memory, reaction time, processing speed measures, and an overall higher total symptom score [16].

Loss of consciousness (LOC) was previously viewed as a requisite for concussion, whereas the literature shows that more than 90% of concussions occur without LOC. Concussions of higher severity, with corresponding signs and symptoms, may occur with no LOC [17]. LOC occurs in 8–19% of sports-related concussions, with most LOC lasting less than 1 min [18]. The duration of LOC is not correlated to injury severity in concussion studies [19]. This is contrary to what is reported in moderate and severe TBI studies.

Post-traumatic amnesia can occur immediately or several minutes after concussive injury in athletes [20]. Both retrograde and anterograde amnesia may be associated with neurocognitive deficits and more reported symptoms in the days immediately following concussion [21]. The presence or absence of post-concussive amnesia as a predictor of long-term outcome is not currently established in the literature [1]. Decreased postural control after concussion is well established [22]. Assessing for this may be carried out by having the patient stand upright with the eyes closed. Eliminating visual referencing with eye closure accentuates postural control deficit that is associated with an inability to process altered sensory information [22]. Decreased postural stability symptoms typically persist up to 3 days following injury [23]. It is important to recognize that a variety of immediate post-concussive motor phenomena, such as convulsive movements and tonic posturing, may accompany a concussion. These clinical features are typically benign and do not require specific management [1].

5.1.3 Previous Concussion

Given a history of previous concussion(s), asking questions that gauge the previous type and severity of symptoms is useful for comparison to current symptoms. Each patient is unique with respect to the type and severity of the various possible concussive symptoms. Determining whether an athlete has a history of previous concussion(s) is important when a clinician is determining a return to play timeline.

Not doing so may result in an athlete returning to play too soon, which increases risk for further injury.

The taking of a detailed history should be followed by a comprehensive neurologic exam to assess mental status, cranial nerve, motor, sensory, and cerebellar function. For the athlete on the field, there exist a number of tools that might be applied for initial assessment and acute decision-making about return to play. These are described further in Sect. 5.4.

5.2 Differential Diagnosis

It is important to note that symptoms associated with concussion may also be associated with various other conditions. Differentiating among etiologies can prove to be difficult. For example, comparison of the diagnostic criteria for post-traumatic stress disorder (PTSD), major depressive disorder, acute stress disorder, anxiety disorders, and post-concussion syndrome (PCS) shows considerable overlap [24]. The differential diagnosis also can include vestibular dysfunction, visual dysfunction, cervical injury, somatization, chronic fatigue and pain, or combination of these in some form [25, 26]. When clinical recovery extends outside the expected window, management by a multidisciplinary team with experience in concussion management should be undertaken [1].

In this particular clinical scenario, the patient has a clear mechanism of injury, with resultant loss of consciousness, and subsequent mild diffuse headache, sleepiness, nausea without emesis, and difficulty concentrating. Mild diffuse headache may be attributed to a multitude of other factors (mentioned earlier in Sect. 5.2.1) such as dehydration, preexisting migraines, stress, etc. Thus, it is crucial to correlate the patient's history, mechanism of injury, new symptoms, and neurological exam when making a diagnosis of concussion.

In addition, the provider should recognize a number of concussion-associated syndromes that might follow from the initial diagnosis:

5.2.1 Post-Concussion Syndrome

Post-concussion complications include acute symptoms, post-concussion syndrome (PCS), persistent or prolonged PCS (PPCS), mild cognitive impairment, chronic traumatic encephalopathy (CTE), and dementia pugilistica. The WHO's *International Statistical Classification of Diseases and Related Health Problems,* 10th revision (ICD-10) defines PCS as a diagnosis requiring the presence of three or more of the following symptoms: headache, dizziness, fatigue, irritability, insomnia, concentration difficulty, and memory difficulty. It is unclear which patients will continue to experience PCS spectrum symptoms far beyond their injury, but certain variables may increase the risk. These clinical variables may include prior

concussions, female sex, a history of cognitive dysfunction, and the presence of affective disorders, such as depression and anxiety [26, 27]. The average time of normalization to pre-concussion baseline on neurocognitive testing has been reported as 10–14 days in high school students, 5–7 days in collegiate athletes, and 2–5 days in professional athletes [28]. There is no universally agreed upon time frame for symptom duration that constitutes the aforementioned syndromes; however, the persistence of symptoms for between 6 weeks and 3 months is generally consistent with PCS, and the presence of any symptom for longer than 3 months is consistent with PPCS.

5.2.2 Second Impact Syndrome

The short- and long-term sequela of repetitive concussion have gained increased focus in the media and medical community over the last several years. The biggest short-term fear regarding repetitive head injury is that of "second impact syndrome." This is defined as the quick deterioration and death of an athlete who experiences a second mild head injury following return to play subsequent to the first injury. Interestingly, most case reports describing this phenomenon are not associated with space-occupying lesions. Rapid decline and death, rather, were associated with severe and rapid cerebral edema [29]. This condition has been reported primarily in adolescent and young adult athletes. Proponents of this syndrome believe that following initial mild TBI in younger patients, there exists an increased underlying risk for development of impaired autoregulation and catecholamine release that may result in diffuse cerebral edema and possibly death after even a mild secondary impact [30]. The pathophysiology leading to the severe edema and small hematomas that are often encountered is not fully understood. Furthermore, it remains unclear whether the edema or hematomas are the result of one of the individual blows to the head rather than the proposed pathophysiologic mechanisms leading to severe disability or death [31].

5.2.3 Chronic Traumatic Encephalopathy

Suffering multiple concussions has been associated with increased risk for future concussion, cognitive deficit, delayed mild cognitive deficit, and sleep disruption. The association between suffering multiple concussions and Chronic Traumatic Encephalopathy (CTE) has gained increased attention in the media and the mainstream public [32]. First defined by Omalu et al. in 2005, CTE is defined as a progressive neurodegenerative syndrome caused by repetitive and episodic blunt force impact to the head that imparts acceleration-deceleration forces to the brain [33]. A systematic review by Manley et al. examined potential long-term sequelae of concussion by examining cognitive, mental health, neuroimaging, and neuropathological features of

CTE. This review demonstrated that despite reports with a small number of retired athletes who exhibited some mental health and cognitive problems, the majority of studies demonstrated these changes to be similar to the incidence in the general population [34]. While multiple concussions appear to be a risk factor for mental health problems and cognitive impairment in some individuals, more research is needed to better understand the prevalence of CTE and other neurological conditions and the degree to which they are related to concussions and sports-related repetitive neurotrauma [34].

5.3 Diagnostic Evaluation

The American Academy of Neurology (AAN) has evaluated tools that may be useful in identifying patients with concussion [35]. Despite the potential utility, it should be noted that no tool or diagnostic aid should substitute for a thorough medical, neurological, or neuropsychologic evaluation. The Standardized Assessment of Concussion (a component of SCAT5) is a sideline tool that assesses orientation, concentration immediate recall, and delayed recall. The Post-Concussion Symptom Scale (a component of SCAT5) and the Graded Symptom Checklist can aid in identifying concussion in athletes.

The guidelines set forth by the AAN also state that neuropsychologic testing, the Balance Error Scoring System (BESS), and the Sensory Organization Test (SOT) may help identify the presence of concussion with varying degrees of diagnostic accuracy. Although a combination of diagnostic tests may have better accuracy than an individual test, there is no sufficient data available to support an ideal combination.

5.3.1 Sports Concussion Assessment Tool (SCAT)

There are a variety of sideline assessment tools that gauge concussion-related symptoms, neuropsychologic function, and balance [36–40]. The most commonly used sideline assessment tool is the Sports Concussion Assessment Tool, 5th edition (SCAT5). This assessment includes a standardized evaluation of signs and symptoms, neurologic function, cognition, and balance [41]. The original SCAT was developed by the 2nd International Conference on Concussion in Sport [37, 42]. The SCAT5 is designed for use in athletes age 13 years or older, and combines aspects of several previously published concussion tools into multiple components (Table 5.2).

It is important to recognize that the SCAT5 cannot be performed properly if less than 10 min have passed since time of suspected concussion. In order to eliminate the possible confounding effects of fatigue from competitive play when testing for concussive symptoms, the athlete should be removed from play and be “in a resting

Table 5.2 Components of Sports Concussion Assessment Tool (SCAT), 5th edition

On field assessment
Red flags
Observable signs
Maddocks score (recent memory)
Glasgow Coma Scale score
Cervical spine assessment
Office or off field assessment
Athlete background
Symptom evaluation
Cognitive assessment/Standardized Assessment of Concussion (SAC)
Neurological screen • Cranial nerves • Neck examination • Balance examination (tandem gait and modified Balance Error Scoring System [BESS])
SAC delayed recall

state" before testing is performed [1]. This typically necessitates at least 10 min or more, which gives time for the athlete's heart rate to return to the resting state. A preseason baseline evaluation can provide tremendous benefit. Possessing a baseline "scorecard" for reference facilitates serial tracking of a concussion over time, should injury occur during competitive regular season events. This may be helpful given reports regarding the variability in baseline testing, as well as test reliability for earlier SCAT versions. One study reported baseline values for 260 collegiate athletes utilizing the original SCAT [43]. This study demonstrated gender differences in baseline values. A history of previous concussion in athletes also accounted for differences in baseline scores. Another study investigating representative baseline values on the SCAT2 reported differences in scores associated with age, gender, and self-reported concussion. This further highlights the benefit of baseline testing of athletes before initiation of competitive events during the regular season [44]. Scores for the SCAT5 are not "pass/fail" scores, but rather, the tool is used by the healthcare professional to assist in the diagnosis of concussion, to determine overall injury severity, and to guide management of concussion.

Current literature supports balance testing (which includes balance assessed with tandem gait), particularly in the first few days, as a sensitive component of the diagnosis of concussion [23, 45–47]. This influenced the inclusion of the BESS in the SCAT5. The examiner should follow this with a more detailed evaluation of cervical range of motion (ROM). Range of motion testing should assess flexion, extension, and rotation in all directions, both passively and actively. This should be followed with formal assessment of motor strength testing in all muscle groups. The athlete should be withheld from participation (even in the absence of deficits on previous portions of the concussion assessment) for further evaluation, because limitations in these areas may place the athlete at risk for further injury by restricting the athlete's ability to protect the head and anticipate impacts from oncoming opponents [48].

For athletes who have performed at or above baseline for all other aspects of the assessment, functional testing marks the final step in the concussion evaluation. The goal of functional testing is to elicit symptoms that may be exhibited with the physical and cognitive demands the athlete may experience upon return to play [48]. Simple tasks such as push-ups, sit-ups, and Valsalva maneuver should be performed first [48]. Next, physical activity may be advanced by having the athlete jog. This may be followed by more strenuous aerobic activity such as interval sprinting exercises. Successful completion of the progression culminates with sport-specific activities (e.g., dribbling/shooting a basketball, passing drills with a soccer ball, throwing/catching a football, shooting a hockey puck etc.) performed at a similar intensity level necessary for safe return to play [48]. With each step, the practitioner should ask the athlete whether any concussion-related symptoms have been elicited before moving on to an increase in activity level. If, at any time, an athlete reports symptoms that result from the exertion, the player should not be permitted to return to play (or progressed to the next step). If no symptoms are elicited through these functional tests and all other assessments demonstrate normal findings, the athlete has not likely sustained a concussion and may be considered for return to play.

Although standardized sideline assessment tools may be useful in the evaluation of concussion, several points must be kept in mind. These tools are designed for rapid screening of concussion by the wider spectrum of practitioner types and should not be used to replace comprehensive neuropsychologic testing by a trained neuropsychologist [1]. Furthermore, no sideline assessment tool should be used for the ongoing management of sports-related concussions [1]. A standardized clinical evaluation of concussion is useful, but should not substitute for clinician's judgment.

5.3.2 Computed Tomography

Computed tomography (CT) scanning is not useful for concussion diagnosis. However, CT should be considered to rule out more serious TBI in patients with LOC, focal neurological deficit, persistently altered mental status, posttraumatic amnesia, or signs of clinical deterioration.

5.3.3 Magnetic Resonance Imaging (MRI) and Advanced Neuroimaging Techniques

Conventional computed tomography (CT) and magnetic resonance imaging (MRI) studies are typically normal in concussion. CT and MRI of the brain are utilized when there is concern for intracerebral hemorrhage or a structural lesion is suspected in the setting of focal neurological deficit, prolonged loss of consciousness, or progressive worsening of symptoms. Several advanced neuroimaging techniques

such as diffusion tensor imaging (DTI), functional MRI (fMRI), magnetic resonance spectroscopy (MRS), high-definition fiber tracking (HDFT), and positron emission tomography (PET) might possibly increase the sensitivity of neuroimaging to detect both structural and functional abnormalities associated with concussion—both in the acute setting and subsequently, in the subacute and chronic phases of recovery.

Acute MRI findings include changes in white matter integrity on diffusion imaging, changes in cerebral blood flow on arterial spin labeling (ASL), altered functional connectivity on resting state functional MRI (rs-fMRI), and appearance of microhemorrhage on perfusion imaging.

Several studies have evaluated and discussed fMRI findings in sports-related concussion [49, 50]. Brain activation has been shown to be more widespread following concussion than before injury (baseline fMRI used for comparison) [51]. The mid-dorsolateral prefrontal cortex (DLPC) is an area associated with working memory. Less task-related activation in the DLPC was observed in subjects with persistent post-concussion symptoms 1–14 months following concussion. Some studies have also demonstrated a correlation between fMRI abnormalities and cognitive test results. Athletes with post-injury fMRI findings that demonstrated hyperactivation experienced a more prolonged clinical recovery when compared to those without hyperactivation [52].

Magnetic resonance spectroscopy (MRS) measures concentrations of compounds in the brain within a sampled region. It is a tool that is commonly used in the evaluation of brain lesions [50]. TBI is associated with specific metabolites that may include choline, a marker of membrane damage and turnover; lactate, an indirect marker for ischemia and hypoxia; *N*-acetyl aspartate (NAA), a marker of neuronal integrity; creatine (Cr), a cellular energy marker for adenosine triphosphate (ATP) resynthesis; and myoinositol, a glial marker [47].

Reduced NAA:Cr ratios have been observed 3 days after concussion, with normalization of the NAA:Cr ratio 30 days post-injury [53]. This suggests that metabolic normalization differ from symptom recovery. Reduction in NAA and other metabolic derangements in post-concussion patients is supported by various studies comparing athletes with and without concussion [54].

HDFT and DTI, both techniques that are capable of providing information regarding fiber tract integrity and white matter microstructure, have been increasingly utilized following concussion and concussion. Many DTI studies have shown a correlation between concussion and widespread structural changes in cortical white matter tracts [55]. These studies report abnormalities in various regions of the brain, including the corona radiata, corpus callosum, uncinate fasciculus, inferior and superior longitudinal fasciculus, cingulum bundle, inferior fronto-occipital fasciculus, internal capsule, as well as the acoustic and posterior thalamic radiations [56]. Correlation between DTI and injury severity with symptoms, as well as functional deficits measured by neuropsychologic testing and other behavioral measures, has been reported in various studies [57].

HDFT provides high-resolution details of axonal pathways and projection fields that allow detection of the specific location and degree of damage [58]. HDFT was used in one study to identify a specific lesion of the corona radiata corticospinal pathway that was associated with left-sided weakness in a patient 4 months after injury [58]. HDFT may overcome some of the shortcomings of DTI, but routine use of either modality for concussion is premature [58]. The results of initial studies using HDFT are preliminary and must be validated in larger studies, but emerging data are encouraging.

PET measures certain components of cerebral metabolism, including blood flow and cerebral metabolic oxygen consumption. Some limitations of PET include expense, exposure to radiolabeled tracers, and the time required to complete the study. Despite these limitations, studies have demonstrated interesting findings when PET is performed after concussion. Umile et al. observed adults after concussion who exhibited persistent post-concussive symptoms. This study found the subjects to have significantly reduced metabolism in the medial temporal lobe [59]. Chen et al., demonstrated differences in cerebral metabolism during a visual-spatial working memory task in adult subjects with persistent symptoms following concussion [60].

5.3.4 Cerebrospinal Fluid (CSF) and Serum-Based Biomarkers of Injury

There has been an uptrend in research of both cerebrospinal fluid (CSF) and serum biomarkers for neuronal, axonal, and astroglial injury with a goal of improving diagnosis and helping predict the clinical course after concussion and mTBI. Despite these efforts, there is a lack of sufficient evidence to justify their routine clinical use [1]. Changes in common TBI biomarkers after SRC show evidence of neuronal cell body damage, axonal injury, and neuroinflammatory response to injury [61]. Serum may seem to be an attractive biofluid for analysis given its lower cost and lower associated risk of acquisition, but extensive studies with sampling of both biofluids suggest otherwise. Trauma to areas outside of the brain, as well as non-trauma related athletic exertion, are associated with increased levels of certain biomarkers that may give a false representation of levels in the brain. For example, S100 calcium-binding protein (S100B) and glial fibrillary acidic protein (GFAP), both markers of astroglial injury, have been shown to be elevated in the serum of mTBI patients [62]. Other biomarkers, such as myelin basic protein (MBP), tau protein, and neuron-specific enolase (NSE) are being actively studied. Immunoassay technique sensitivity, validity, clinical assays for quantification, and the amount of longitudinal data in concussion need to improve before these biomarkers can be routinely used [63].

5.4 Clinical Decision-Making and Next Steps

The mainstays in concussion management have been both physical and cognitive rest. The Berlin consensus statement states:

> *There is currently insufficient evidence that prescribing complete rest achieves these objectives. After a brief period of rest during the acute phase (24–48 hours) after injury, patients can be encouraged to become gradually and progressively more active while staying below their cognitive and physical symptom-exacerbation thresholds (i.e., activity level should not bring on or worsen their symptoms). It is reasonable for athletes to avoid vigorous exertion while they are recovering. The exact amount and duration of rest is not yet well defined in the literature and require further study.*

Most concussive symptoms resolve relatively shortly over the course of several days following injury allowing the patient to gradually return to social and academic activities. A stepwise program is generally accepted with regard to return to athletic play [1]. This program begins with a period of no activity followed by light aerobic exercise. This is followed by sport-specific exercise, noncontact training drills, full-contact practice, and finally return to play. Each of these levels is performed over a 24-h period. The program may be initiated when the athlete is asymptomatic at rest. If the athlete exhibits any post-concussion symptoms at any of these steps, another 24-h period of rest is completed, and the athlete reverts back to the previous step in the program. Same-day RTP should not be permitted on the day of injury. This is due to evidence that RTP on the day of injury may be associated with prolonged neuropsychological deficits with delayed onset.

It is uncommon for post-concussion symptoms to persist beyond 10 days, but it is possible in a subset of patients. This may prompt clinicians to consider pharmacologic treatments for management of symptoms. If this option is to be employed, the patient and clinician should come to a mutual agreement that benefit of treatment outweighs any possible adverse effect of a medication under consideration [64]. There are no clinically validated treatments that have demonstrated benefit with regard to expedited recovery or amelioration of deficits attributed to TBI. However, patients with post-concussion syndrome or prolonged post-concussion syndrome may experience some benefit from symptomatic medical treatment during the recovery phase [65].

The treatment of concussion should be specific to patient symptoms, which are grouped into the following four categories: cognitive, emotional, somatic complaints, and sleep disturbance [1]. However, it should be noted that alleviating one symptom may improve upon others. A concise review of selected agents studied in mTBI or concussion for the management of various symptoms is provided below.

Patients with post-concussion syndrome or prolonged post-concussion syndrome may experience some benefit from symptomatic medical treatment during the recovery phase [66]. Medications that lower seizure threshold, or those that contribute to fatigue, cognitive slowing, or daytime drowsiness should be avoided. Medical therapies should be initiated at the lowest effective dose, with a slow dose titration

according to patient tolerability, clinical response, and side effects. In order to prevent adverse interactions, special care should be taken to review all medications and over the counter supplements the patient is currently using [67].

Patients with persistent post-concussion headaches most commonly develop migraine-like or tension-type headaches. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) are typically avoided in the acute period following concussion. Therefore, acetaminophen is a reasonable choice for post-concussion headache treatment in the acute period. A majority of patients experience spontaneous resolution of the headache; patients with persistent headaches may require further treatment. Amitriptyline (an antidepressant) has shown efficacy in the treatment of post-concussion headaches. Data is currently limited regarding other treatments, such as triptans, dihydroergotamine (DHE), anticonvulsants (valproic acid, gabapentin, and topiramate, and gabapentin), calcium channel blockers, and beta clockers [68, 69].

5.5 Clinical Pearls

- Concussion typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, signs and symptoms evolve over a number of minutes to hours.
- Concussion results in a range of clinical signs and symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive features typically follows a sequential course.
- The clinical signs and symptoms of concussion cannot be explained by drug, alcohol, or medication use, other injuries (such as cervical injuries, peripheral vestibular dysfunction, etc.) or other comorbidities. These other conditions should all be ruled out before a diagnosis of concussion is made.
- Concussion may result in neuropathological changes, but acute clinical signs and symptoms largely reflect a functional disturbance rather than a structural injury.
- Duration of loss of consciousness does not correlate to severity of concussion.

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Chapter 6
Traumatic Arterial and Venous Injuries

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Clinical Scenario

A 28-year-old male suffered a stab wound to the left posterior neck and left shoulder. He was hemodynamically stable in transit, but on arrival to the trauma bay his blood pressure was 70/40s. Patient was lethargic but answering questions. His Glasgow Coma Scale (GCS) score was 14 (E3 V5 M6). After the patient was stabilized with a massive transfusion protocol, a computed tomography angiogram (CTA) of the neck was obtained. It showed active contrast extravasation adjacent to the left vertebral artery. The patient was developing a large anterior cervical hematoma as a result. The patient was intubated due to concern for airway compromise, and the neurointerventional team was consulted regarding possible left vertebral artery transection.

6.1 History and Neurologic Exam

The initial evaluation of this patient in the trauma bay should follow the ATLS guidelines. The primary evaluation and resuscitation occur simultaneously. Focus should be placed on securing the airway with either endotracheal intubation or, in

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_6

the setting of neck trauma, an emergent cricothyrotomy or tracheotomy. Intravenous (IV) access with two large-bore IVs should be started for fluid resuscitation, and arterial access should be obtained for invasive hemodynamic monitoring. A massive transfusion protocol was initiated for the active hemorrhage from the left neck. Initial packing and bandaging of the neck wound provided temporary cessation of the hemorrhage. However, given the penetrating injury's proximity to the thoracic cavity, urgent evaluation for tension pneumothorax and cardiac tamponade is imperative with quick auscultation of the pulmonary and cardiac windows. In addition, bedside ultrasound is a key imaging modality to identify and diagnose these life-threatening injuries. Once these are ruled out then attention turns to the penetrating neck wound to evaluate the source of hemorrhage.

There are certain physical exam findings that may suggest the source of hemorrhage. The amount and appearance of the hemorrhage may suggest an arterial versus venous source. A rapidly expanding hematoma that is difficult to compress, with obvious tracheal deviation, will mostly likely be from an arterial source, as compared to the slow, compressible bleeding from a venous injury. Unilateral loss of the carotid pulse suggests a significant carotid artery injury. Injury to the common carotid or local sympathetic chain may reveal a Horner's syndrome, characterized by ipsilateral ptosis, miosis, and anhidrosis. Horner's syndrome may be difficult to elucidate during the organized chaos of a trauma and the bright lights of the trauma bay. The miotic pupil is best visualized in a dark room. The V1 segment of the vertebral artery also runs in proximity to the sympathetic chain, so the presence of a Horner's syndrome cannot be used to distinguish between carotid and vertebral artery injury.

The phrenic nerve is located inferiorly within the posterior triangle, and injury to this nerve will cause paralysis of the hemidiaphragm. This finding can be appreciated on a chest X-ray demonstrating elevation of the affected hemidiaphragm or by diminished breath sounds on auscultation. The vertebral artery is in close proximity to the phrenic nerve. The phrenic nerve runs on top of the anterior scalene muscle, and the vertebral artery runs just medial and deep to the muscle.

The brachial plexus emanates from between the anterior and middle scalene muscles. The presence of an upper extremity paresis suggests penetration in close proximity to the spinal canal and should lead to further examination for a spinal cord injury. The typical spinal cord injury pattern seen in unilateral penetrating injuries is the Brown-Sequard syndrome. This is a hemicord injury characterized by ipsilateral hemiparesis and contralateral loss of pain and temperature. More common in posterior triangle penetrating injuries is ipsilateral shoulder weakness resulting from injury to the spinal accessory nerve as it travels along the posterior border of the sternocleidomastoid. Lymphatic channels are also present in this region and may present in a delayed fashion. Injury to the right lymphatic duct or left thoracic duct may produce a lymphocele or chylothorax but typically present with concomitant neurovascular injuries.

If there is air within the mediastinum, then injury to the trachea and/or esophagus should be considered. If the airway is secured, then tracheoesophageal injury can be evaluated at a later time—once the active hemorrhage has been identified and

treated. Spinal precautions should be maintained until a full neurologic exam or diagnostic imaging can rule out spinal canal penetration or cervical spine fractures.

The secondary survey revealed a second stab wound over the left shoulder, but no signs of ongoing bleeding. He had bilateral symmetric and reactive pupils and no other obvious cranial nerve deficits. There was no motor function in the left arm, but there was intact two-point discrimination and good distal perfusion. He had full strength and sensation in the right upper extremity and bilateral lower extremities. Rectal tone was normal. This brief neurologic exam should identify any gross neurologic deficits. Once stabilized, a more detailed neurologic exam and neuroimaging can help differentiate a spinal cord injury from a peripheral nerve injury.

A review of the patient's AMPLE history—allergies, medications, brief past medical history, last meal, and events surrounding injury—was unrevealing. Review of the patient's medications is important as it may reveal antiplatelet or anticoagulant use that could be corrected with blood products or reversal agents. Thromboelastography (TEG) can help identify underlying coagulopathies and guide blood product administration. TEG may not be available at all institutions and requires a technically trained perfusionist to perform the analysis. Further review of the patients medical, social, and family history can be completed during the secondary and tertiary survey after the patient has been stabilized.

6.2 Differential Diagnosis

The active hemorrhage from the neck stab wound appears to be the obvious cause for the patient's shock presentation and is certainly a contributor to his hemodynamic instability.

Penetrating neck injuries are classified according to the anatomical location of the entrance wound. In 1969, Monson published the current anatomic zone-based classification: zone 1 injuries involve the clavicle to the cricoid; zone 2 from the cricoid to the angle of the mandible; and zone 3 from the mandible to the skull base [1]. However, there has been a trend toward a "no-zone" approach that tailors management strategies to injuries based on physical exam and CT/CTA, thereby reducing the number of mandatory neck explorations [2].

Our patient's stab wound is located in zone I and specifically, within the posterior triangle of the neck. The posterior triangle is bordered anteriorly by the sternocleidomastoid, posteriorly by the trapezius, and inferiorly by the clavicle. The posterior triangle is further subdivided by the inferior belly of the omohyoid. Above the omohyoid is the occipital triangle and below is the subclavian triangle. There are many neurovascular structures that can be injured, but the main vascular concerns at this time include the common carotid artery, external and internal jugular vein, subclavian artery, and vertebral artery. Once the patient is resuscitated, a CTA will confirm and identify the source of hemorrhage, and in conjunction with the neurologic exam, suggest a spinal cord or peripheral nerve injury. An MRI C-spine should also be obtained once stabilized to evaluate the spinal cord and brachial plexus given his unilateral arm paralysis.

6.3 Diagnostic Evaluation

After the patient's airway is secured with either endotracheal intubation or tracheotomy, a **chest X-ray** will be obtained. The chest X-ray should be evaluated for pneumothorax, hemothorax, hemidiaphragm, mediastinal air, widened cardiac silhouette, and tracheal deviation.

If the hemorrhage can be controlled and the patient adequately resuscitated, then a **CT/CTA neck** must be obtained expeditiously to determine if operative intervention is required. The CTA will show contrast extravasation if the vessel has been transected. If the artery has not been transected, a dissection and/or pseudoaneurysm may be apparent. A dissection or intimal flap will show a crescentic filling defect within the lumen of the vessel on axial imaging and a string sign in the sagittal or coronal plane. The Denver criteria is a grading scheme for blunt cerebrovascular injuries that helps guide treatment decisions based on CTA findings and is sometimes used to classify traumatic or penetrating vessel injuries as well. Grade 1 has luminal narrowing less than 25%, grade 2 has greater than 25% narrowing or intraluminal/mural thrombus, grade 3 has a pseudoaneurysm, grade 4 has complete occlusion, and grade 5 has transection with active extravasation [3].

The **trajectory** of the stab wound can be approximated by the entrance wound and point of vessel injury. In addition, air may track along the penetration trajectory. Knowing the trajectory is important for surgical planning and exposure so you know what you may encounter and plan accordingly. Any air within the spinal canal indicates canal penetration and the patient should be treated as a spinal cord injury. If the CTA is nondiagnostic or there is active contrast extravasation, then a diagnostic angiogram should be performed with the intention of possible vessel sacrifice. The CTA may be nondiagnostic for a number of reasons, including poor contrast timing or metallic streak artifact.

A **diagnostic angiogram** should be performed for all penetrating head and neck injuries—either acutely for possible treatment or in a delayed manner to evaluate for pseudoaneurysm or arterio-venous fistula development. Typically, femoral artery access will be obtained for the angiogram rather than radial access in case there is a subclavian artery injury that limits the ability to access the supra-aortic vessels. A six-vessel angiogram should be completed, including bilateral vertebral arteries (VA), common carotid arteries (CCA), and internal carotid arteries (ICA). Common angiographic findings in penetrating injuries include vessel transection with active contrast extravasation on injection, pseudoaneurysm formation, arterio-venous fistula, and dissection with or without flow-limiting stenosis. Prolonged runs will reveal venous injuries that appear as contrast extravasation or acute venous cut offs with filling of collateral venous channels. If the vertebral artery is injured, the contralateral vertebral artery should be injected to document collateral flow and filling of the basilar artery. If the contralateral vertebral artery ends in the posterior inferior cerebellar artery (PICA) and does not fill the basilar trunk, then the anterior circulation needs to be injected prior to treatment with vertebral artery sacrifice in order to evaluate for and document patent posterior communicating arteries and retrograde

filling of the vertebrobasilar circulation via the anterior circulation. If the dominant vertebral artery is injured and there is no filling of the vertebrobasilar trunk, then vessel reconstruction may be considered to avoid a posterior circulation stroke.

6.4 Clinical Decision-Making and Next Steps

Our patient presents with multiple stab wounds of the left neck and shoulder and is in hemorrhagic shock on admission. The patient was emergently intubated for airway protection and decreasing level of consciousness. There was active arterial hemorrhage from the left neck stab wound located in zone I of the posterior triangle of the neck. The primary survey did not reveal any additional sites of active hemorrhage. The patient had bilateral breath sounds and no obvious intrathoracic or intraabdominal blood on ultrasound. Intravenous and arterial access were obtained to aid in the massive transfusion protocol. He received five units packed red blood cells and two units of fresh frozen plasma. Pressure was applied to the neck but did not stop the hemorrhage; therefore, the trauma surgeon inserted and inflated a 16-F Foley balloon catheter into the wound (Fig. 6.1). This temporized the patient enough

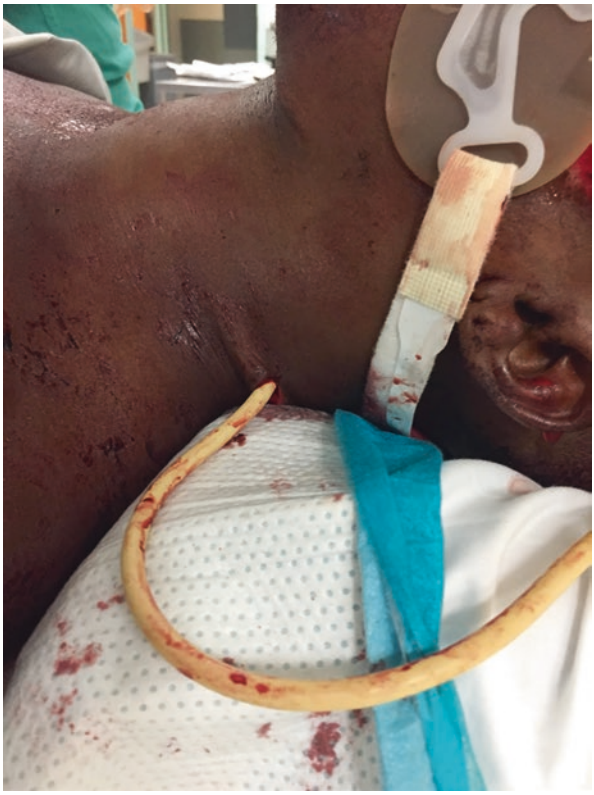

Fig. 6.1 A 16-F Foley catheter inserted into the entrance wound within the posterior triangle. This provided enough tamponade to obtain the CTA to identify the hemorrhage source

to be able to transport to the CT scanner for a CT/CTA of the head and neck. CTA demonstrated active contrast extravasation within the left neck adjacent to the left V1 segment of the vertebral artery as it was entering the C6 transverse foramen.

At this point, it is obvious that the vertebral artery needs to be inspected and either occluded to prevent ongoing hemorrhage or reconstructed to preserve flow. This can be accomplished through open surgical exploration in the operating room (OR) or under biplane fluoroscopy in the interventional angiography suite. Zone II injuries are easily accessible through open surgical exploration, whereas zone I and III are more challenging from a surgical exposure standpoint. Zone I injuries may require cardiothoracic surgeons to perform a sternotomy or thoracotomy to obtain proximal control of bleeding, and zone III injuries extending to the skull base require extensive dissection, place the lower cranial nerves at risk, and are constrained by the mandible.

If proceeding to the operating room for surgical exposure, one should be prepared for both vessel sacrifice and reconstruction. Interposition grafts for vertebral artery injuries are not usually required because of the robust collateral flow to the posterior circulation through the contralateral vertebral artery and the posterior communicating arteries. However, if there are no collaterals on CTA or angiography and there is flow-limiting stenosis not amenable to endovascular techniques, then open surgical exploration with vessel reconstruction should be considered. Surgical exposure of the vertebral artery requires different approaches depending on the segment involved. The V1 segment extends from the subclavian origin to the C6 transverse foramen, the V2 segment from the C6 transverse foramen to the C2 foramen, V3 from the C2 foramen to the intradural transition, and V4 from the intradural transition to the vertebrobasilar junction. V3 and 4 segment exposures require midline posterior and far lateral approaches. V2 segment exposure requires surgical access through the anterior triangle, dissecting through the longus colli muscle and drilling out the artery from the transverse foramen.

More common is the V1 segment exposure for proximal control. A vertical incision is made along the anterior border of the sternocleidomastoid, and the sternal attachment of the SCM is cut to mobilize the SCM lateral. The carotid sheath is identified, and the retrojugular fat pad is identified lateral to the sheath. The retrojugular fat pad is then dissected to identify the anterior scalene muscle and the overlying phrenic nerve. The sympathetic trunk will be overlying the longus colli muscle which, itself, is deep and medial to the anterior scalene muscle. The vertebral artery is identified underneath the longus colli muscle. The vertebral artery is followed superiorly as it enters the C6 transverse foramen.

If the origin of the vertebral artery needs to be exposed, then the dissection is carried proximally. Careful dissection proximally will reveal the thoracic duct on the left and the lymphatic duct on the right. These lymphatic vessels are located medial to the thyrocervical trunk. The thoracic duct needs to be ligated as it enters the junction of the inferior jugular and subclavian vein to prevent avulsion and chylothorax or lymphocele formation [4]. If the vertebral artery needs to be preserved, there are a number of reconstruction options. If there is redundancy of the vertebral artery, then an end-to-end anastomosis after resection of the injured segment can be completed. If there is a long segment injury, then a radial artery interposition graft

can be used. If an interposition graft cannot be used, then an end-to-side anastomosis can be completed with the carotid artery. For carotid artery injuries, interposition grafts, such as saphenous vein or polytetrafluoroethylene (PTFE), are commonly used when there is segmental tissue loss. Venous injuries are typically ligated without any sequelae [5, 6].

At our institution, we have a dedicated neuro-angiography suite with 24-h neurointerventional coverage. We decided to proceed with angiography for possible vessel sacrifice, as this is often the quickest and most effective way of controlling the hemorrhage. In the event that this patient presented to a trauma center without neurointerventional radiology capabilities, then this patient would need to go to the OR with either neurosurgery or vascular surgery for open exploration.

The role for interventional radiology is twofold. First, diagnostic angiography is the gold standard for vessel visualization and will define the injury type. Second, vessel sacrifice, if required, is relatively straightforward and simple from an endovascular approach. Several methods for endovascular vessel sacrifice include coil embolization, microvascular plugs, and liquid embolic agents including Onyx (Medtronic) and glue. In this case, the right common femoral artery was accessed with a 6-F sheath. Bilateral CCA, external carotid artery (ECA), ICA, and left VA were injected to understand the anterior and posterior circulation prior to sacrificing the left vertebral artery. On the left VA injection, there was significant contrast extravasation from the V1 segment just prior to entering the left C6 transverse foramen (Fig. 6.2). There was no distal flow, indicating this was a complete transection

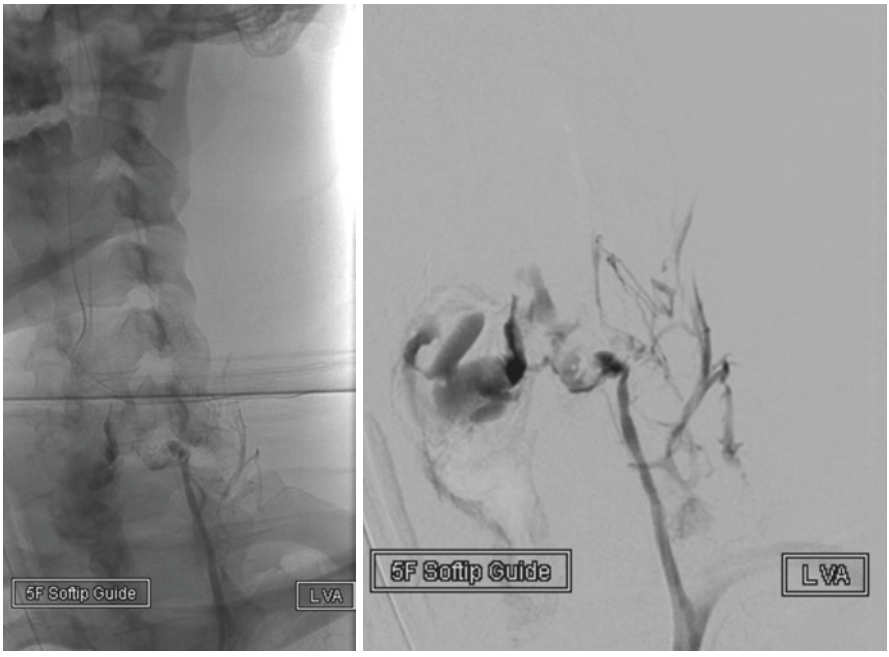

Fig. 6.2 Unsubtracted and subtracted oblique view of the left VA in the mid-arterial phase showing the contrast extravasation just prior to the C6 transverse foramen

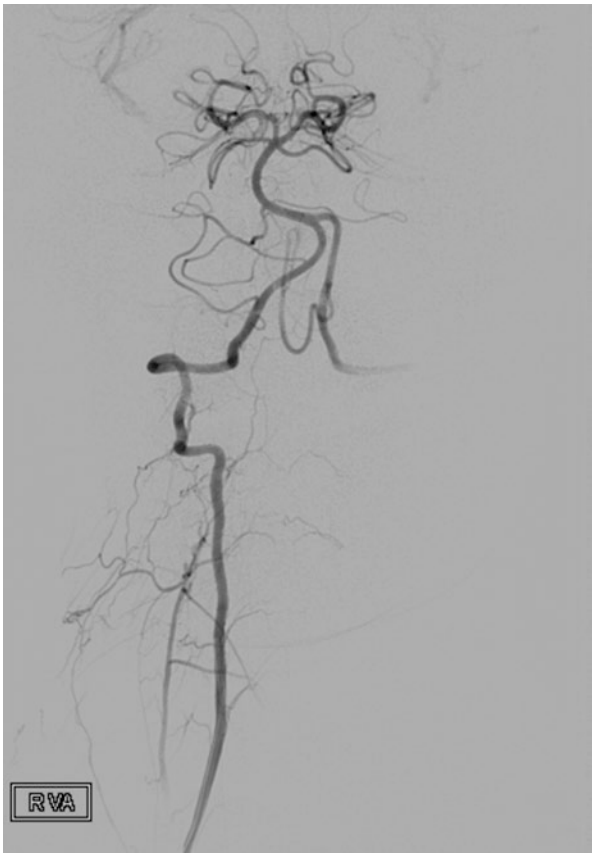

Fig. 6.3 Right VA AP injection showing the entire posterior circulation can be filled from the right VA

of the V1 segment. The patient had bilateral posterior communicating (PComm) arteries and the right vertebral artery filled the entire vertebrobasilar system, including retrograde filling of the left posterior inferior cerebellar artery (PICA), indicating the left VA could be safely sacrificed (Fig. 6.3).

As there was no possibility for vessel reconstruction and he had redundant posterior circulation flow through the right VA and bilateral Pcomms, the decision was made to proceed with a left VA sacrifice. A 5-F guide catheter was navigated to the proximal left VA and an 0.021 in microcatheter was advanced over an 0.014 microwire just proximal to the transected V1 segment. The left VA was occluded with a microvascular plug (MVP-3, Medtronic). A single microvascular plug occluded the VA, and post-procedure angiogram injections demonstrated proximal VA occlusion with no contrast extravasation (Fig. 6.4). A right VA injection was completed post-embolization to demonstrate flow within the posterior circulation (Fig. 6.5).

When the vessel is transected, as in this case, the treatment is straightforward. The treatment paradigm is complicated when there is distal flow through either a dissected artery or pseudoaneurysm. When there is distal flow, the decision to

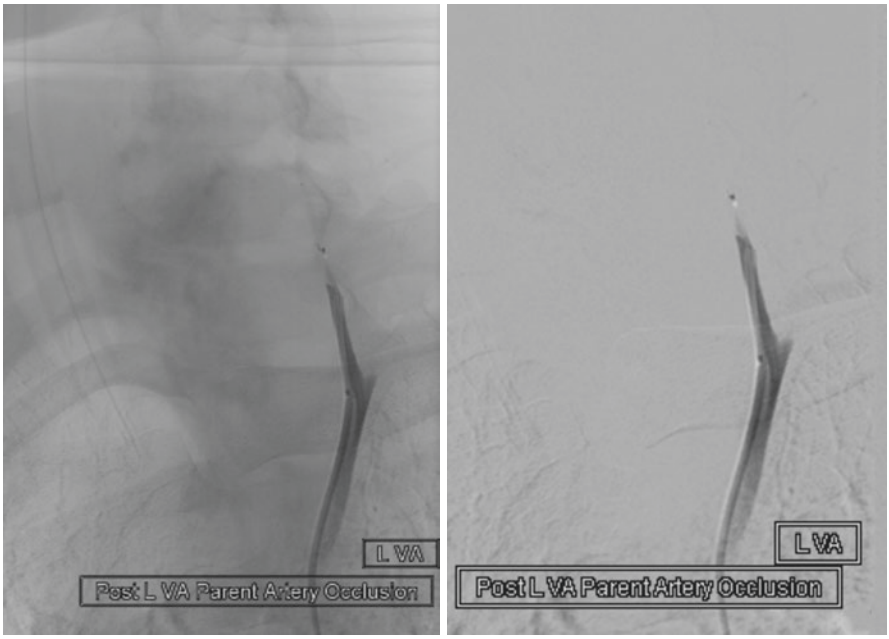

Fig. 6.4 Unsubtracted and subtracted left VA injection after deployment of a single microvascular plug. There is no further contrast extravasation

proceed with either a reconstructive or deconstructive treatment needs to be made based on the distal territory supplied and the presence of collateral blood supply. Medical management with antiplatelet or anticoagulation can be used if there is a small dissection with no flow limitation. The risk factors for stroke development after vessel injury may be different in spontaneous dissections versus traumatic dissections [7, 8]. Intimal flaps and multivessel dissections are more often seen in traumatic dissections [9]. In spontaneous dissections, there is a low stroke rate with either antiplatelet or anticoagulation use [7]. However, in traumatic dissections there are often multiple injuries, and the bleeding risk needs to be taken into account prior to initiating treatment. If the patient develops any stroke-like symptoms despite escalation of medical management, then endovascular and open surgical approaches for treatment need to be considered.

The treatment paradigm for blunt cerebrovascular injuries is similar with regard to screening, identification, and management. However, blunt injuries often involve high impact and, therefore, may be associated with additional accompanying injuries. Common mechanisms of injury include extreme cervical hyperextension and/or rotation as seen in high-speed motor vehicle collisions and hanging accidents. Other associated injuries include facial, basilar skull, and cervical spine fractures. As previously mentioned, the Denver criteria is a grading scheme for blunt cerebrovascular injuries with grades 1–5. Grades 1–4, if hemodynamically stable, may

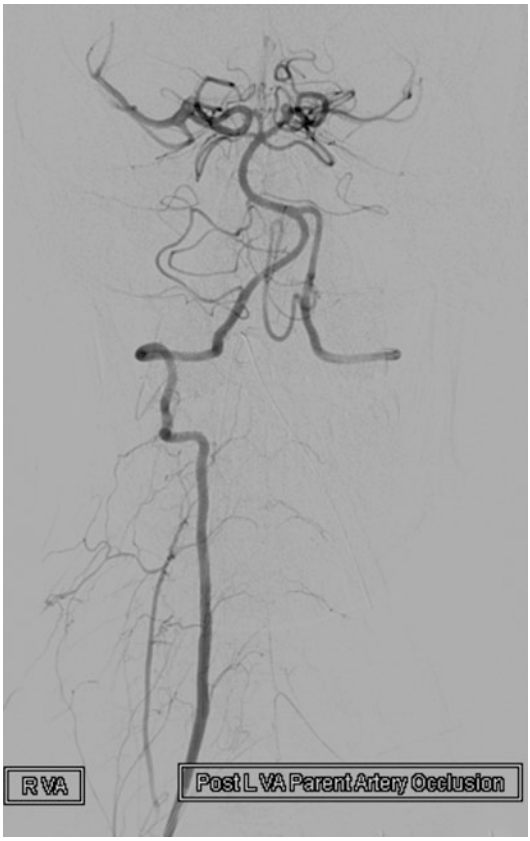

Fig. 6.5 Follow-up injection of the right VA demonstrating the filling of the posterior circulation after the left VA has been occluded

require acute heparinization, which reduces stroke incidence to <1%. Mono-antiplatelet therapy with aspirin 325 mg also reduces the stroke risk and may be a first-line treatment if there is no concern for ongoing bleeding. Grade 5 injuries require either open surgical exploration or endovascular treatment as previously described. Injuries are typically followed up with repeat CTA or angiography within 7–10 days to demonstrate resolution or stability. If there is progression despite medical management,then operative intervention may be required [3, 10].

An MRI and MRA of the head and neck were obtained after the patient was extubated and stabilized from the left VA sacrifice. There was no evidence of spinal cord edema or ischemia. A brachial plexus MRI did not show any nerve root transections or avulsions; however, there was significant edema within the anterior and middle scalene. His left arm weakness was due to a neuropraxic injury from the large cervical hematoma causing mass effect on the plexus. His weakness improved within months of the injury, but he continued to complain of dysesthesias of that left upper extremity.

6.5 Clinical Pearls

- With advancing endovascular techniques, there are many treatment options for intracranial and extracranial vascular injuries. The key is to identify the injured vessel, have a thorough understanding of the distal territory that vessel supplies, and determine whether a reconstructive or deconstructive solution is warranted.
- Endovascular occlusion is straightforward and often quicker than open surgery—without the potential for collateral damage of the surrounding structures.
- The primary goal is to stop the bleeding and stabilize the patient. Here, a Foley catheter was inserted into the wound to provide temporary relief by tamponade in order to evaluate the injury, initiate a massive transfusion protocol, and buy time before the vessel could be occluded by endovascular techniques.

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Chapter 7
Cerebrospinal Fluid Fistulae

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Clinical Scenario

A 27-year-old man presented to the Emergency Department (ED) following an assault. He was neurologically intact. He suffered extensive right periorbital swelling and underwent an emergent lateral canthotomy. Upon leaning forward, clear fluid leaked from the patient's right nostril.

7.1 History and Neurologic Exam

A thorough history is very important in determining the etiology of a cerebrospinal fluid (CSF) leak or fistula. A CSF fistula occurs when CSF drains via the paranasal sinuses, external ear, or a cutaneous tract. The terms are often used interchangeably [1]. The leak may also be occult.

7.1.1 Cranial CSF Leaks

Cranial CSF leaks may be divided into those of traumatic/iatrogenic and those of non-traumatic origin.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_7

7.1.1.1 Traumatic and Iatrogenic

Over 80% of CSF leaks and fistulae result from trauma, including falls and motor vehicle accidents that leave patients with basilar skull fractures [2, 3]. Skull fractures are identified in 6–12% of patients with head injuries [3]. About one fifth of these fractures involve the skull base, and 10–30% of patients with basilar skull fractures will develop a leak or fistula [3]. There is an increased risk of leak in patients with anterior cranial fossa skull fractures [3–5]. Anterior cranial fossa fractures usually result in rhinorrhea, and very rarely oculorrhea [5, 6]. Middle cranial fossa fractures can result in otorrhea or rhinorrhea, as the middle ear communicates with the nasopharynx via the Eustachian tube [5, 7]. Interestingly, there are reports of traumatic leaks following nasal swab testing for the novel coronavirus [8–10]. Sinus and cranial surgery are also risks for iatrogenic leaks.

In patients with a CSF leak following trauma, **perform primary and secondary surveys and rule out life-threatening injuries**. The patient's level of consciousness should be assessed immediately and monitored regularly, and the Glasgow Coma Scale (GCS) score should be recorded. These patients can have additional intracranial pathology, including hematomas, impacted foreign bodies, and depressed skull fractures requiring surgery, and can deteriorate quickly from these injuries [2, 3, 5]. A thorough cranial nerve examination is necessary to evaluate for concomitant olfactory, optic, oculomotor, trochlear, abducens, facial, and/or cochlear nerve injuries [2]. Patients may have obvious anosmia. Occasionally, urgent decompression of these nerves, especially the optic or facial nerve, is necessary [2]. Patients may suffer hearing loss, which can be conductive, central sensorineural, peripheral sensorineural, or a combination of these mechanisms [11]. Evaluate for hemotympanum and look for CSF in the external auditory canal [11].

Provocation maneuvers may also be helpful. Evaluate for headache and other symptoms with position change. In patients with a concern for CSF rhinorrhea, have the patient sit up and lean forward. Evaluate for leakage. Patients with CSF otorrhea may have worsening symptoms when moving the ipsilateral side down [12], and a formal otolaryngology evaluation is warranted.

7.1.1.2 Non-traumatic

Some skull base and ear malformations result in CSF leaks and meningitis in children. Occasionally, these are found after myringotomy/tube placement [13]. Patients with normal labyrinth anatomy can develop leaks from the petromastoid canal, a widened cochlear aqueduct, a persistent Hyrtl's fissure (this usually closes at 24 weeks' gestation), or the facial canal [14]. Spontaneous cranial leaks may be related to increased intracranial pressure (ICP). Evaluate for signs and symptoms of elevated ICP. Rule out idiopathic intracranial hypertension (IIH), which is often seen in young obese females [4]. If there is any concern for IIH, the patient should undergo formal ophthalmologic evaluation.

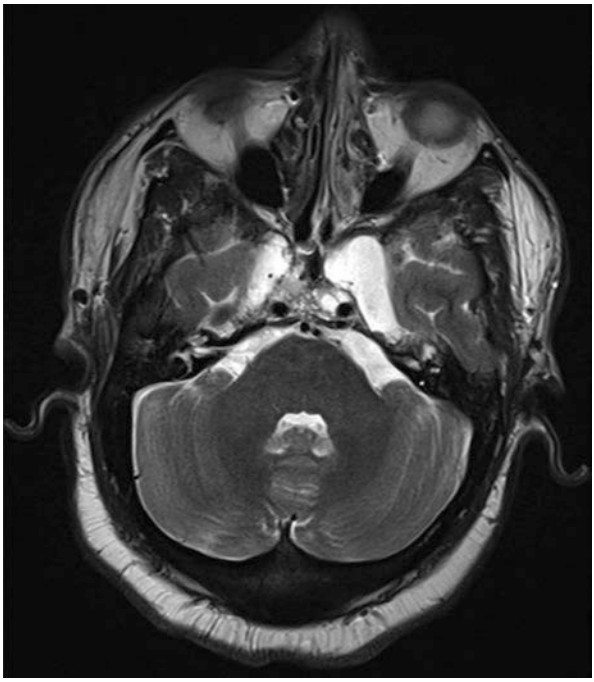

Fig. 7.1 T2-weighted MRI showing bilateral encephaloceles at the level of Meckel's cave

Symptoms of elevated ICP include headaches that are worse in the morning or while lying flat, nausea, vomiting, pulsatile tinnitus, and blurry vision [4]. Increased ICP can thin and erode the skull base, and the brain can herniate through small defects, forming encephaloceles and meningoencephaloceles [4]. The herniated brain tissue is often not functional and may pose a risk for intracranial infection [15]. Figure 7.1 shows the T2 MRI sequence of a patient with bilateral encephaloceles at the level of Meckel's cave.

7.1.2 Spinal CSF Leaks

Like their cranial counterparts, spinal CSF leaks can be spontaneous or traumatic/iatrogenic. However, **a spinal CSF leak usually presents differently than a cranial leak.** Regardless of the etiology, spinal CSF leaks often cause significant postural headaches that are worse with standing and relieved when lying flat. Occasionally, patients develop subdural hematomas from intracranial hypotension and may present with a rapid decline in mentation [1]. In alert patients with concern for a spinal CSF leak, have the patient move between the flat and upright positions. Assess for headache, nausea, and other symptoms. Altered patients with spinal CSF leaks may improve quickly after being placed flat or in the Trendelenburg position [16, 17].

Calcified disk herniations, usually in the thoracic spine, can cause ventral dural tears that allow CSF egress. Nerve root sleeve tears can also result in CSF leak, and patients can also develop CSF-venous fistulae [18–20]. Fistulae can also form between the spinal subarachnoid space and pleura or mediastinum after spinal surgery, cardiothoracic surgery, chest tube placement, or trauma [1, 21, 22]. Yoshor et al. used non-invasive, positive-pressure ventilation successfully to treat a persistent subarachnoid-pleural fistula. Their patient underwent surgery for an L1 burst fracture, developed the fistula, and failed treatment with a chest tube thoracostomy and lumbar drain prior to this intervention [23].

Ask patients about a personal or family history of connective tissue disorders. Schievink et al. found that there may be an association between spontaneous spinal CSF leak/intracranial hypotension and these disorders [16, 24]. These disorders can also complicate wound healing and the patient's postoperative recovery [25, 26].

7.1.3 Postoperative CSF Leaks

Evaluate the incisions of any postoperative patients with concern for CSF leak. Palpate for a soft collection and look for CSF egress. A contained pseudomeningocele may not pose problems, but persistent CSF leakage impairs wound healing and increases the risk of meningitis [17].

7.1.4 Delayed and Occult CSF Leaks

Most leaks present immediately, but delayed leaks can present weeks to months later with CSF rhinorrhea, otorrhea, or signs of a spinal leak [1]. Occasionally patients have recurrent bouts of meningitis before a diagnosis is made [7, 13, 27, 28]. Some patients are misdiagnosed with allergic rhinitis [29]. A history of trauma, recent or remote surgery, cancer diagnosis, nasopharyngeal swabbing, lumbar puncture, and/or signs and symptoms of a skull base tumor, cancer, or increased intracranial pressure can help elucidate the cause of CSF leak in patients without obvious trauma or risk factors.

The patient in the current clinical scenario presents with obvious signs of facial trauma. The patient should be evaluated for the presence of cranial neuropathies. He should be examined for signs associated with skull base fracture (Battle's sign, raccoon eyes, etc.), as well as for violation of the tympanic membranes. The observation of clear rhinorrhea should immediately raise concern for the presence of a skull base fracture, with clinical evidence of a CSF leak, and prompt further diagnostic evaluation.

7.2 Differential Diagnosis

The differential diagnosis for clear fluid egress or collection depends on anatomic location.

7.2.1 Cranial

Broadly, the differential for rhinorrhea includes allergic rhinitis, nonallergic perennial rhinitis, nonallergic rhinitis with eosinophilia, infectious rhinorrhea (bacterial or viral), and vasomotor rhinorrhea (like that seen in cluster headaches) [30]. The differential for otorrhea with temporal bone involvement includes otitis media, cholesteatoma, and tumors, including sarcomas and Langerhans cell histiocytosis [31].

7.2.2 Spinal

Pathologies presenting with postural headaches include postural orthostatic tachycardia syndrome (POTS), cervicogenic headaches, and other primary headache disorders [18].

7.2.3 Postoperative

Surgical incisions with clear drainage should be evaluated for infection, seroma, and fat necrosis, in addition to CSF leak.

A patient presenting with unilateral clear rhinorrhea in the setting of trauma—as in the current clinical scenario—should prompt further diagnostic evaluation, with a suspicion for an anterior skull base fracture. Other possible etiologies for rhinorrhea are much less likely given the clinical context provided.

7.3 Diagnostic Evaluation

Following a thorough history and physical examination, imaging can be very helpful to provide a structural anatomic correlate for clinical observation.

7.3.1 Cranial

Obtain a formal otolaryngology consultation when patients have CSF rhinorrhea or otorrhea. Nasal endoscopy, laryngoscopy, and otoscopy may be warranted. Imaging evaluation should start with a high-resolution, noncontrast head CT with soft tissue and bone windows [3]. Evaluate for fracture, congenital, or acquired bony anomalies/defects, air/fluid levels, and pneumocephalus [3, 11]. Also, look for signs of elevated ICP, like an empty sella, and for pneumatized bony sinuses [4]. The lateral recess of the sphenoid sinus, the ethmoid roof, and cribriform plate are common sources of spontaneous leaks [4]. CT cisternography may be helpful when the fistula site is unclear. This study requires a lumbar puncture, with intrathecal injection of an iodinated contrast agent. The patient is tilted with the head down [32]. Thereafter, a high-resolution CT scan is performed, as shown in Fig. 7.2, which demonstrates a CSF leak into the left sphenoid sinus. MR myelography is also feasible but requires off-label intrathecal gadolinium injection. An older method of fistula detection involves intrathecal injection of a radioactive tracer. Pledgets are placed in the nasal sinuses and then examined for radioactivity, with the goal of localizing the leak site [1, 19, 20, 32, 33].

Intrathecal fluorescein injection, first described by Kirchner and Proud in 1960, can be very helpful in the operating room [33]. Fluorescein turns bright green when it encounters CSF, allowing the surgeon to readily visualize the fistula. Figure 7.3 shows intraoperative use of fluorescein during an endoscopic, endonasal resection

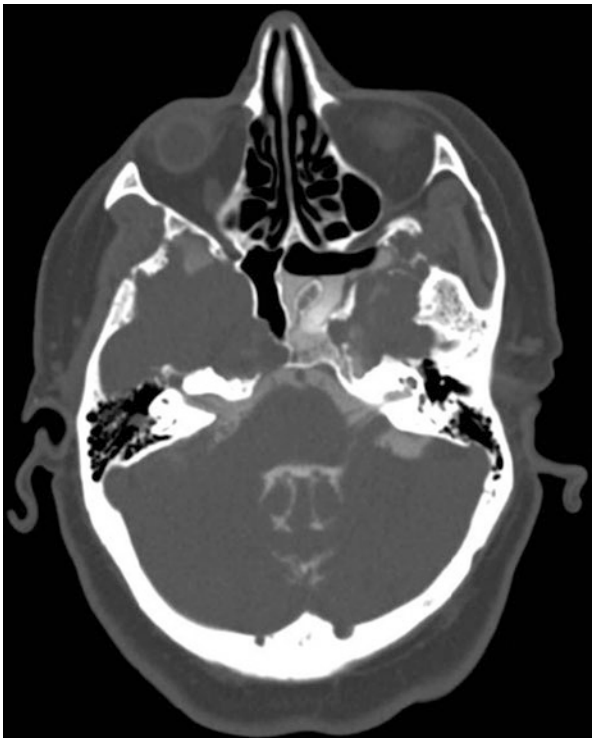

Fig. 7.2 CT cisternogram utilizing Omnipaque contrast demonstrates a CSF leak into the left sphenoid sinus

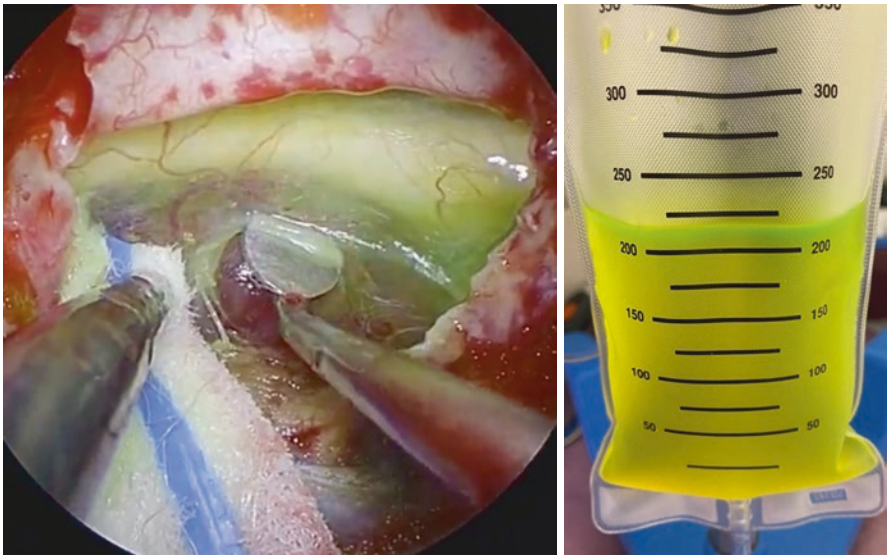

Fig. 7.3 Intraoperative use of fluorescein (left) showing green CSF circulating in the subarachnoid space during an endoscopic, endonasal approach to a craniopharyngioma, and bright green CSF in a lumbar drain system (right) after fluorescein use

of a craniopharyngioma, with green CSF circulating in the subarachnoid space during the procedure (left) and bright green CSF that has reacted with fluorescein in the lumbar drain collection bag (right).

Note that intrathecal use of fluorescein is off-label. Premedicate patients with a steroid (dexamethasone) and an antihistamine (diphenhydramine) [34]. Standard 10% fluorescein dye is diluted to 1% using preservative free saline. One milliliter (mL) of the diluted fluorescein is then mixed with 10 mL of the patient's CSF and slowly injected into the spinal subarachnoid space, usually via a lumbar drain [35]. Rare adverse effects with fluorescein administration include headaches, seizures, vomiting, paresthesias and radiculopathy, hemiparesis, transverse myelitis, and lower extremity weakness [3, 34, 35]. These effects may result from meningeal irritation; the combination of steroids and antihistamine may counter that [34]. Antihistamines also mitigate the increases in plasma histamine seen in patients receiving intravenous fluorescein [36]. Some surgeons apply the dye topically to reduce the risk of a systemic or intrathecal fluorescein injection and necessary lumbar drainage [37].

7.3.2 Spinal

Patients with spinal CSF leaks can be evaluated with noncontrast CT, MRI, myelography (CT or MRI), or newer techniques like digital subtraction myelography [19, 20, 38, 39]. Perform a noncontrast head CT to rule out an extra-axial collection—either subdural hematoma or hygroma. MRI may demonstrate findings associated

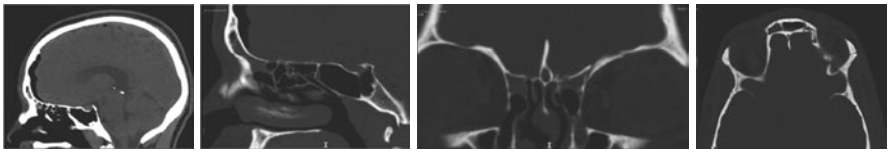

Fig. 7.4 Noncontrast CT head demonstrated pneumocephalus (left image) and skull base fractures (right three images) in a patient with CSF leak following assault

with intracranial hypotension, including diffuse dural enhancement, brain sagging, and venous sinus dilatation [18]. Diffuse dural enhancement is the most common abnormality [18–20]. On spinal imaging, a nerve sheath may dilate or appear irregular at the site of a dural tear and leak. Myelography can occasionally demonstrate contrast extravasation from the subarachnoid space into a vein in patients with CSF-venous fistulas [18, 20, 39].

7.3.3 Unclear Cases

Occasionally, it is unclear if expressed fluid from the nares, ear, or surgical site contains CSF. Two markers indicative of CSF are β2-transferrin and beta-trace protein (βTP). Patients with ocular trauma can have false positive β2-transferrin values, since the aqueous humor contains the substance, and βTP values may be unreliable in patients with bacterial meningitis or renal insufficiency [1, 5, 12]. The β2-transferrin values can take several days to result. βTP testing may be more helpful in some instances when the assay is available and can be performed readily.

For the patient in this case scenario—suspected to have a cranial CSF leak of traumatic origin—noncontrast CT head (Fig. 7.4) showed significant scattered pneumocephalus (left), and bone window revealed fractures of the bilateral orbits, cribriform plate, ethmoid bones, and frontal sinus (right).

7.4 Clinical Decision-Making and Next Steps

Cranial and spinal CSF fistulae can require different treatments.

7.4.1 Cranial

Initial treatment of a cranial CSF leak includes bedrest with the head elevated. It is important to minimize straining, coughing, sneezing, and nose blowing. Laxatives and cough suppressants may be helpful. Acetazolamide can reduce CSF pressure by

reducing CSF production; monitor for metabolic acidosis. Over 70% of traumatic CSF rhinorrhea cases and almost all CSF otorrhea cases resolve with these measures [1, 12]. Spontaneous leaks often require intervention [1, 3, 12]. While these patients are at risk for developing meningitis and brain abscess, prophylactic antibiotics are not recommended. A Cochrane review including five studies and 208 patients with CSF leaks from basilar skull fractures found no benefit of antibiotic administration [40].

Patients with cranial CSF leaks who fail to respond to conservative measures after 5–7 days can undergo lumbar puncture or lumbar drain placement [41]. Patients with lumbar drains must be monitored in the ICU, as overdrainage can lead to tentorial herniation and death [12, 41]. The goal of drainage is to lower the CSF pressure and let the fistula heal [1, 3, 15]. If the leak persists, additional workup and direct surgical repair may be needed. Also, consider surgery in patients with spontaneous leaks [1].

A range of surgical approaches are available for management of cranial origin CSF leaks; the choice of surgical procedure depends in part upon the anatomic localization of the leak and in part upon the comfort of the operative team with various techniques. The fistula site should be located with imaging preoperatively and/or fluorescein intraoperatively. Aid from otolaryngology can be helpful during endoscopic cases, when a CSF fistula involves the inner or middle ear, and in patients with bony anomalies [13, 27].

Extracranial approaches to the fistula, including endoscopic, endonasal surgeries, are often successful in patients with CSF rhinorrhea and anterior skull base pathology. Frontal sinus fractures can also be repaired through extracranial approaches, using a bicoronal, forehead (within a crease or existing laceration), or naso-orbital incision to allow exposure and repair of the frontal sinus [5]. Intradural approaches may be needed for large defects that cannot be closed through the endoscopic, endonasal route. Sometimes direct primary dural repair is feasible; pericranial flaps can reinforce the closure and seal off other defects. Fibrin glue is helpful in adhering the pericranium to the dura [3, 15].

Fat, fascia, dural substitutes, and fibrin glue can be used to plug and seal bony defects; a multilayer closure may be necessary and is most effective [1, 3, 13, 15, 27]. Nyquist et al. used a DuraGuard (Biovascular Corp, Minneapolis, MN, USA) inlay, fat, fascia lata, and fibrin glue in small leaks, and incorporated MedPor (Stryker Corporation, Kalamazoo, MI, USA), vomer bone, or titanium plates as needed in their series of endoscopically repaired leaks [15]. Vascularized grafts from the mucosa or turbinates and nasoseptal flaps can also be helpful [42, 43]. For large leaks, some surgeons use a "gasket seal" technique [15, 44]. A large soft tissue graft, like fascia lata, is placed in the defect, and then buttressed with a rigid graft like bone or MEDPOR® (Stryker, Kalamazoo, MI). The soft tissue graft should circumferentially surround the rigid graft. A vascularized flap and fibrin glue are used on top of the repair [15, 45].

CSF fistulas in the middle fossa can also be repaired using extracranial approaches, including transmastoid and transnasal approaches through the maxillary sinus [46]. Intracranial, intradural approaches risk injury to the vein of Labbe,

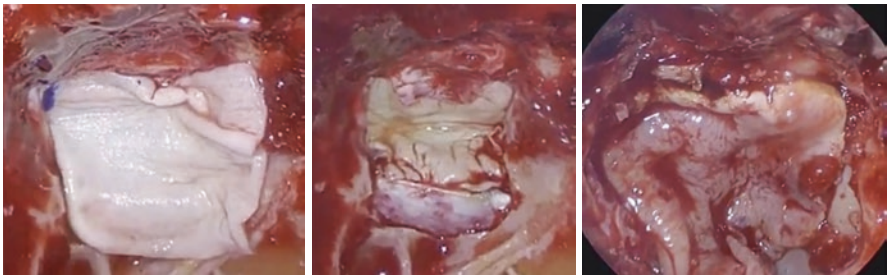

Fig. 7.5 CSF leak repair with a dural substitute (left) that is eventually tucked under the native dura (middle), covered with Surgicel® (not shown; Johnson & Johnson, New Brunswick, NJ, USA) and then sealed with a nasoseptal flap (right)

but extradural approaches may require traction on the facial nerve [3, 47]. Pericranial grafts are again helpful [3]. Prevent mucocele formation either by stripping away mucosa as needed (and "cranializing" the frontal sinus) or by ensuring that the mucosa has a safe pathway to drain its secretions [48]. The multilayer closure described above can be used during these operations [15, 45]. Figure 7.5 shows a dural substitute and nasoseptal flap used in skull base reconstruction after an endoscopic, endonasal tumor resection.

A lumbar or external ventricular drain can be used to minimize CSF pressure on the repair in the perioperative period. The patient should be monitored for the development of significant pneumocephalus after leak repair with CSF diversion [1, 12, 13, 15, 41]. If multiple surgeries fail to resolve a cranial or spinal leak, consider CSF diversion with a shunt. CSF diversion may also be needed in patients with increased intracranial pressure [15, 49]. These patients may not develop signs and symptoms of hydrocephalus until after fistula repair [1, 15, 38]. A classic example of this phenomenon is the postoperative Chiari decompression patient who returns with a CSF leak at the surgical site—ultimately determined to have occurred due to unrecognized, co-morbid hydrocephalus.

7.4.2 Spinal Leaks

CSF leaks and fistula from penetrating trauma generally require direct surgical repair. Often there will be other serious injuries to address, especially in penetrating trauma [2, 22, 48]. Iatrogenic CSF leaks are more common than their traumatic counterparts. Unfortunately, iatrogenic postoperative leaks can significantly impair patients' recovery, increase the risk of serious infection, and add to health care costs [50]. Durotomies that occur during minimally invasive, tubular procedures like microdiscectomies can be challenging to repair primarily. Faltings et al. present two cases in which patients undergoing microdiscectomies experienced CSF leaks [51]. Both had complete resolution of their symptoms following administration of an

epidural blood patch (EBP). Some patients also can be managed conservatively, and the incision can be oversewn as needed [1].

Woodruffe et al. advocate for primary repair, use of a fibrin glue, and consideration of lumbar drain placement at the index surgery [50]. In their series, delayed re-exploration was associated with longer hospital stay and increased infection risk. In general, patients with lumbar leaks should be flat for 24–48 h postoperatively to minimize pressure on the repair although there is some debate on this topic [17]. Patients with cervical and thoracic leaks should be positioned upright for a similar period to divert CSF away from the repair by gravity. Surgical drains should be used with caution; some argue that the suction generated by them can pull CSF, weaken the surgical repair, and impair fistula closure [17, 50]. Patients who undergo multiple unsuccessful attempts at repair should be considered for shunt placement [50].

7.4.3 Spontaneous Leaks

Conservative measures can be tried in patients with spontaneous intracranial hypotension and spinal CSF leak, but these may fail in upwards of 80% of patients [18]. Medical management includes hydration, caffeine, and bed rest [19]. The next line of treatment is an EBP. Multiple authors report success using EBP in patients with disc herniations or spontaneous nerve sheath tears [1, 18, 19]. Long-segment blood patch can be performed in patients when workup has failed to identify a specific leak source [19].

Subdural effusions may resolve after EBP alone. Therefore, patients who have brain MRI hallmarks of intracranial hypotension that include extra-axial collections should be considered for EBP [19]. Direct drainage may result in worsening of the extra-axial collections, risking neurological decline and a need for further surgery [16, 52]. Collections can also recur if the underlying leak is not addressed [52]. Figure 7.6 shows the noncontrast head CT of a patient who underwent a craniotomy for tumor resection, with an intraoperative lumbar drain. She was readmitted several days later with worsening positional headaches and an epidural fluid collection. Her symptoms resolved and scan improved after an EBP was placed. She was discharged approximately 24-h after the EBP and did not require additional treatment.

An EBP can also help patients with persistent headaches following lumbar puncture or drainage. If a blood patch fails, consider targeted fibrin glue injection [18, 19, 53]. If that also fails, consider surgery and direct repair of the fistula after successfully localizing the lesion [18, 20]. Surgery may require nerve root ligation since most leaks occur in the thoracic spine, this is generally tolerated [20].

Occasionally, patients treated for spontaneous intracranial hypotension (SIH) develop rebound intracranial hypertension. In a series of 113 patients, Schievink et al. found rebound high-pressure headaches in 27% [54]. These patients were more often female, younger, and had spinal extradural CSF collections. Some of the patients who developed intracranial hypertension also suffered from transverse sinus stenosis. These patients may require shunt placement [4, 15, 54].

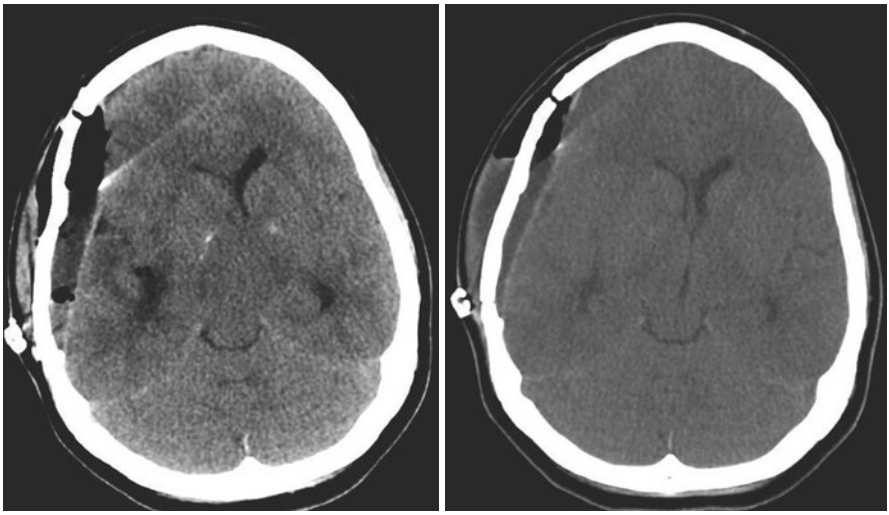

Fig. 7.6 Noncontrast CT head showing an epidural fluid collection and air following craniotomy with lumbar drain (left). Following epidural blood patch, the patient's postural headaches resolved completely, and a post-procedure CT head performed 18 h later showed decrease in the collection (right)

The patient in the current clinical scenario was admitted to the intensive care unit, placed on bedrest, and started on acetazolamide. The cerebrospinal fluid rhinorrhea persisted despite these measures. A lumbar drain was placed, with five milliliters of CSF drained hourly for 5 days. Serial X-rays were performed to monitor for pneumocephalus. The drain was clamped without return of rhinorrhea, and the patient was discharged home without further intervention.

7.5 Clinical Pearls

- All patients with head injuries, especially those with basal skull fractures, should be evaluated for CSF leak.
- Spinal injuries, fractures, and surgery can also cause CSF fistula formation.
- A fistula can go unrecognized for days, months, or even longer. Intermittent and slow leaks can be difficult to diagnose, and patients with spinal CSF leaks may be treated for headaches and other problems before a leak is considered.
- Various imaging modalities and dyes are useful for locating the fistula site and guiding repair.
- Treatments for CSF leaks depend on the location and etiology, and can include conservative management, blood patches, and surgery.
- Prophylactic antibiotics are not recommended.
- An untreated CSF leak or fistula can lead to meningitis, pneumocephalus, brain or spine abscess, hydrocephalus, and death.

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Chapter 8
Decompressive Craniectomy

Peter J. Hutchinson, John Hanrahan, and Tamara Tajsic

Clinical Scenario

A man in his twenties is brought to the emergency room. It was reported that he was the unrestrained driver of a vehicle involved in a high-speed, roll-over collision. On arrival of the pre-hospital medical crew, the patient was unconscious; he had a patent airway but was hypoxic and hypotensive with high clinical suspicion of respiratory compromise due to chest trauma and pneumothorax. He received rapid sequence induction and was intubated at the scene while maintaining spinal precautions; bilateral thoracostomies were performed. Pre-intubation Glasgow Coma Score (GCS) was 5 (E1V1M3). Both pupils were small, with preserved pupillary light reflex on examination. He received supplemental oxygen and fluid resuscitation correcting the hypoxia and hypotension. There was suspicion of left femur fracture, and his left lower limb was immobilized. He was transported emergently to the nearest trauma center with full spinal precautions.

8.1 History and Neurologic Exam

Traumatic brain injury (TBI) is a significant cause of preventable morbidity and mortality across the world, with the most prevalent causes of TBI being falls, assaults, and motor vehicle accidents [1]. Prompt recognition and institution of TBI management improves outcomes [2].

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_8

When attending to a trauma patient, the primary consideration is identification and management of immediately life-threatening injuries following the Advanced Trauma Life Support (ATLS) protocol, with multidisciplinary input [2]. Information from first responders and the pre-hospital medical team (who will often relay relevant information from bystanders) about the timing and circumstances of injury, followed by their clinical assessment of the patient at the scene and during transfer to hospital, will help the multidisciplinary trauma team to gauge the mechanism and potential impact and extent of injury, including the likelihood of TBI. Incorporating the information about the patient's level of consciousness and pupillary size and reactivity to light at the scene will then inform about the clinical severity of TBI.

8.1.1 History

TBI can be classified using different approaches, but the most frequently employed are mechanism of injury, clinical severity, and imaging findings. Obtaining information relevant to these elements informs the clinical picture at presentation and helps guide further interventions.

Different mechanisms of injury include closed, penetrating, crush, blast, and combination injuries—each resulting in characteristic pathological changes in the brain. Closed injuries involve cases where the cranium remains intact after injury. A major contribution of acceleration and deceleration forces would typically cause various degrees of diffuse axonal injury; this is often the case with road traffic accident. However, if there is an element of an impact in which the head hits a hard surface, either during a road traffic accident or as a consequence of a fall or a blow to the head, then this will typically result in focal contusional head injury and/or extra-axial hematoma [3, 4]. At the time of the impact, some of the dynamic forces are absorbed by the skull, which can result in skull fracture(s); depending on the magnitude of the impact, a varying degree of dynamic force will then be transferred onto the intracranial contents [3, 4]. In crush injuries, the dynamic forces are largely absorbed by the skull, causing skull injuries to be extensive and the TBI less severe. In penetrating head injuries, a projectile damages the brain tissue—on its way generating contusions and hematomas, with a high risk of vascular injury [3, 4].

The provider, therefore, should obtain as much information as possible about the circumstances of the injury. For a road traffic accident, the occurrence of blunt head trauma, the use of restraints, the rate of speed, the extent of damage to the vehicle(s), the deployment of airbags, and the severity of injury to other passengers may be relevant. Time to extrication is also important. For a fall, the height and point(s) of contact with the ground (or with other objects mid-fall) may be relevant.

Clinical severity of TBI is defined by patient's level of consciousness, which is assessed using the Glasgow Coma Scale (GCS) score [5]. Eye, verbal, and motor responses are recorded and added up to make the GCS score ranging from 3 to 15. Patients scoring 8 or less are classified as severe TBI, 9–12 as moderate, and 13–15 as mild [6]. The overall GCS score and the motor score are major predictors of

outcome in severe TBI [2]. It should be noted that GCS can change early after injury, following resuscitation or early recovery. Furthermore, it should be considered that GCS assessment can be confounded by prior alcohol or substance use, seizures (and post-ictal state), and hypoglycemia, as well as the use of sedation and paralysis in preparation for endotracheal intubation. It is thus paramount to record the GCS and its three components accurately before the patient is sedated and intubated.

Though not always feasible due to clinical condition at presentation and/or the absence of corroborating family members, information should be solicited regarding the patient's past medical and surgical history, as well as chronic medications—particular antiplatelet and/or anticoagulant agents—and social history.

8.1.2 Examination and Early Management

Primary survey of the trauma patient involves rapid identification of life-threatening extracranial injuries and rapid resuscitation. Adherence to Advanced Trauma Life Support (ATLS) guidelines ensures that assessment and treatment are provided thoroughly yet efficiently [2]. Hypotension and hypoxia, both pre-hospital and in-hospital, increase morbidity and mortality following severe TBI; therefore, the prevention or prompt correction of existing hypotension (aiming for a systolic blood pressure of at least 90 mmHg) and hypoxemia is of extreme importance [6]. However, if a lower blood pressure is required during the treatment of life-threatening extracranial hemorrhage, the duration of hypotension should be as short as possible, and other physiological parameters should be optimized to maximize cerebral oxygen delivery, such as avoiding hypoxia and hypocapnia [6].

Neurological examination will yield the patient's GCS score (unless already sedated), pupillary size, and reaction to light. Head-to-toe examination will reveal any external signs of head injury (lacerations with or without underlying skull fracture, abrasions, periorbital and soft tissue hematomas, mastoid bruising (i.e. Battle's sign), blood, or CSF otorrhea). In a comatose or sedated patient, pupillary size and reaction to light have significant diagnostic and prognostic weight. If there is unilateral or bilateral pupillary dilatation and loss of reaction to light, neuroprotective measures need to be adopted immediately—nursing the patient head up at 30° if possible, avoiding hypercapnia or even allowing a period of hyperventilation and hypocapnia, and using osmotic therapy as temporary measures until further diagnostic procedures have been completed and interventions can be performed [7].

In the current clinical scenario, the precipitating event is a road traffic accident, so the mechanism of injury is presumed to be a closed head injury. A GCS of 5 defines the TBI as severe. The motor score suggests a "best" response of flexion to stimulus. Pupils are small, equal, and reactive to light. Comorbid injuries are suspected. The presence of hypoxia and hypotension in the field raises concern for exacerbation of TBI. The patient's low GCS at presentation precludes interview to establish past medical history (Table 8.1).

Table 8.1 Key aspects of history and examination

History	– Injury mechanism (from bystanders/first responders) – Events at scene of trauma – Neurological status at scene (GCS, pupil size and reactivity, neurological deficits)
Examination	– ATLS protocol—identify immediate life-threatening injuries – Neurological status (GCS, pupil reactivity, pupil size, neurological deficits) – Head-to-toe survey for traumatic injuries – Avoid hypotension and hypoxia if possible

8.2 Differential Diagnosis

The patient in the current clinical scenario presents with a high-risk mechanism for traumatic brain injury. The presence of hypoxia and hypotension in the field suggests the likelihood of polytrauma. His presentation GCS of 5 defines him as *severe* TBI. A combination of intracranial traumatic pathology and the possibility of diffuse rather than focal injury should be presumed for patients presenting with a depressed level of consciousness. Neuroimaging will bring clarity to the array of possible intracranial findings, here summarized by involved anatomic compartment:

- *Extradural/epidural hematomas (EDHs)* occur in approximately 2% of all head injuries, are a result of direct impact, and usually present as isolated lesions without significant intraparenchymal swelling [8]. Typically, the source of bleeding is arterial, following a fracture in the region of the pterion with subsequent tearing of the middle meningeal artery and hematoma formation in the middle cranial fossa. Nevertheless, extradural hematomas may occur in other anatomical locations including in the frontal, occipital, and parafalcine regions—associated with injuries to the anterior ethmoidal artery, transverse or sigmoid sinuses, and superior sagittal sinus, respectively. EDHs originating from venous sources are thought to expand more slowly compared to their arterial counterparts (and, therefore, may present with a patient who "looks too good" for the size of the radiographic hematoma) [8, 9].
- *Acute subdural hematomas (ASDHs)* result from tearing of bridging veins that cross the subdural space to communicate with the venous sinuses or from disruption of superficial pial arteries on the brain surface. ASDHs can develop as a consequence of acceleration/deceleration injuries or direct impact or blow to the head. They are present in approximately a third of severe TBI patients and in two-thirds of patients undergoing surgery for TBI [10]. ASDHs are often associated with the presence of intraparenchymal contusions or hematomas and with a propensity for brain swelling [10–12].
- *Traumatic subarachnoid hemorrhage (tSAH)* is a frequent finding in closed head injuries, resulting from direct damage to cortical vessels. In patients with severe TBI, it is associated with other traumatic lesions and it may contribute to secondary injury (cerebral swelling and/or vasospasm) [4].

- *Intraventricular hemorrhage (IVH)* is found predominantly in severe TBI, in association with other extra-axial and intraparenchymal lesions. It results from damage to the septum pellucidum, choroid plexus, and subependymal veins in the fornix [4].
- *Cerebral contusions* result from forceful contact of the brain parenchyma with the internal bony prominences of the skull and occur in predictable locations, commonly on the antero-inferior aspect of the frontal lobes or at the temporal poles. Such injuries can be described as coup (same side of impact) or contrecoup (opposite side of impact). Initial CT imaging can underestimate their size, with ongoing bleeding occurring in the hours following the initial injury. Interval scanning can demonstrate blossoming of these injuries with hemorrhagic foci. They can contribute significantly to progressive brain swelling, intracranial hypertension, and secondary brain injury [4, 7].
- *Diffuse axonal injury (DAI)* results from shearing forces from rotational acceleration or deceleration that damages neuronal axons. Classically, DAI is defined as diffuse damage in the cerebral hemispheres, corpus callosum, brainstem, and cerebellum. Long-tract structures (axons and blood vessels) are especially at risk. It is more common with high energy injuries and often associated with other traumatic lesions such as a subdural hematoma. Signs of DAI may not be immediately visible on a CT in the acute phase. Brain MRI with diffusion weighted imaging and gradient echo sequences provides powerful tools to detect microbleeds and aid diagnosis of DAI [4].

8.3 Diagnostic Evaluation

Resuscitation and stabilization of the patient according to ATLS guidelines should succinctly be followed with diagnostic CT imaging. The dangerous injury mechanism and impaired consciousness are suggestive of intracranial pathology which necessitates neuroimaging [2].

Non-enhanced CT head remains the primary procedure for diagnostic imaging because of its sensitivity for detecting intracranial hematoma and the speed, availability, and safety of the examination [3]. It provides information about the morphology and extent of traumatic brain injury. In patients with moderate and, in particular, severe TBI, imaging is likely to show a combination of different lesions and diffuse rather than focal injury, as well as signs of increased intracranial pressure. In cases of penetrating head injury, cerebral angiography is recommended due to high risk of vascular injury. Computed tomography angiography (CTA) is an alternative, though interpretation may be limited by the presence of metallic streak artifact. There is no role for MRI in the initial clinical decision-making process, though MRI may play a role in further characterization of certain injuries (DAI, for example) once initial triage and acute management have been satisfied. MRI may not be feasible in the setting of retained metallic foreign bodies. CT imaging of the cervical spine, chest, and abdomen generally will be obtained by trauma staff in the course of evaluation for polytrauma.

In the current clinical scenario, CT head showed a thin left-sided acute subdural hematoma and left temporal intraparenchymal contusions, as well as contusions in both inferior frontal lobes; traumatic subarachnoid hemorrhage; and a small amount of intraventricular hemorrhage. There was left to right midline shift measuring 4 mm. There was no hydrocephalus (Fig. 8.1).

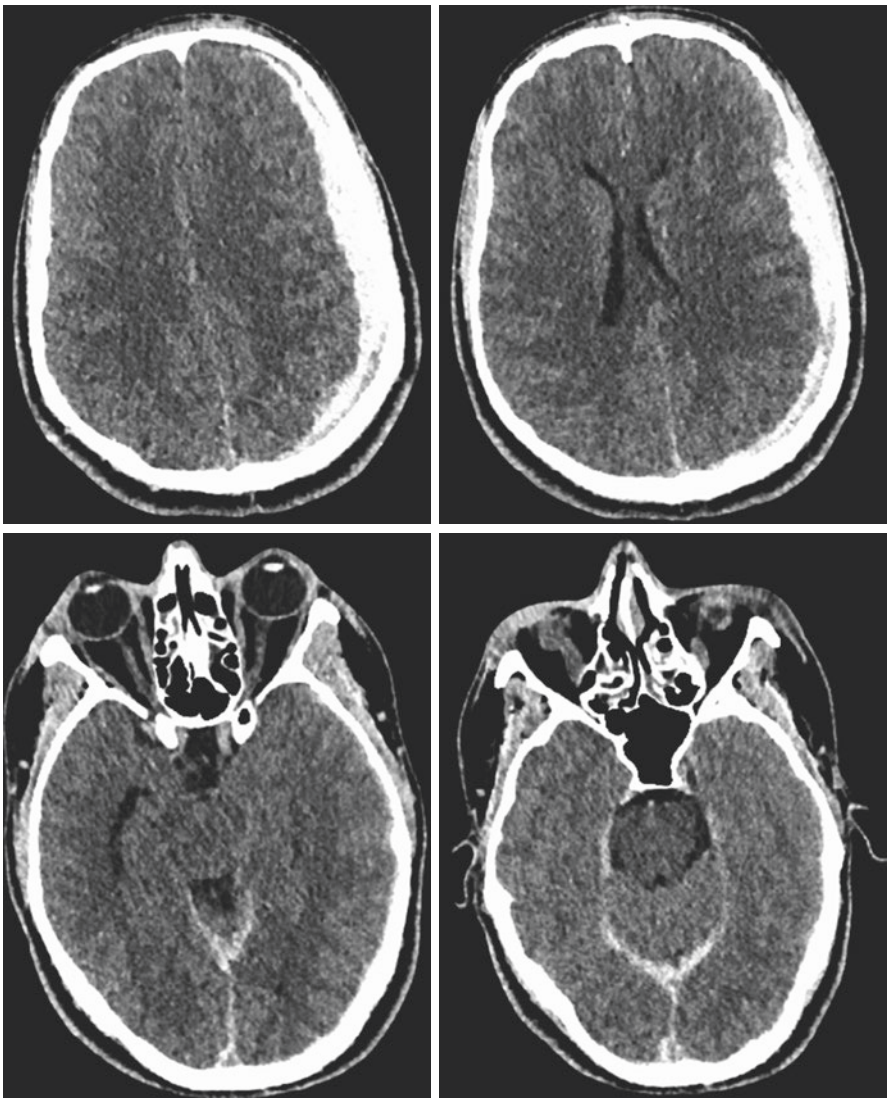

Fig. 8.1 CT head without contrast reveals a thin, left-sided acute subdural hematoma and left temporal intraparenchymal contusions, as well as contusions in both inferior frontal lobes; traumatic subarachnoid hemorrhage; and a small amount of intraventricular hemorrhage. There is left to right midline shift measuring 4 mm. There is no hydrocephalus

Basic laboratories—including BMP, CBC, PT/PTT, and a toxicology screen—should be performed coincident with initial clinical assessment. It is important to correct hypoglycemia, if present, as well as to identify and treat coagulopathy.

8.4 Clinical Decision-Making and Next Steps

The curious and disconcerting fact about TBI is that not all brain damage happens at the time of the traumatic event. Primary brain injury, which happens at the time of trauma, activates cellular and molecular cascades that mediate potentially reversible, secondary TBI in the ensuing hours and days. These events can lead to progressive brain swelling and increased intracranial pressure (ICP), thereby compromising cerebral perfusion pressure (CPP) and cerebral blood flow (CBF) and resulting in tissue ischemia, hypoxia, and cellular energy failure [7, 13, 14]. Management of TBI involves a combination of surgical procedures and medical measures. Clinical decision-making relies on the understanding of different TBI morphologies and their propensity to result in secondary brain injury and brain swelling and is helped by imaging and, where and when available, intracranial pressure monitoring.

Following initial assessment, a determination needs to be made as to whether the patient requires emergent cranial surgery. This decision must take into account the level of consciousness; pupillary size and reactivity; and review of imaging with attention to the presence and volume of extra-axial and/or intraparenchymal hematomas, as well as the degree of midline shift. Comorbid extracranial traumatic injuries—if deemed life-threatening and/or associated with hemodynamic instability—may take precedence in this setting. An ongoing dialogue with trauma staff (and possibly other subspecialist surgeons) may be necessary to coordinate the order of operations.

Surgical treatment would involve emergency craniotomy and evacuation of the hematoma, aiming to mitigate the injury caused by the space-occupying lesion and reduce intracranial pressure [15]. Decompressive craniectomy (DC) is a neurosurgical procedure that involves removal of a section of the skull ("bone flap") and opening of the underlying dura. From a physiological viewpoint, it provides additional space for the swollen brain to decompress, leading to reduction in ICP and maintained or improved cerebral compliance [15]. DC can be performed at the time of the initial craniotomy for removal of the traumatic extra-axial or intraparenchymal hematoma (**primary DC**), or as a treatment option for progressive and medically refractory secondary brain swelling (**secondary DC**) [15].

The decision whether to proceed to emergency surgery for a new TBI patient, as well as the choice of surgical technique (craniotomy versus primary decompressive craniectomy), will depend on the clinical severity of TBI, extent of injury, presence of a mass lesion amenable to evacuation, presence of brain swelling, degree of midline shift, and the propensity of the traumatic brain lesions for (further) swelling. Figure 8.2 reveals CT head findings for a patient with multifocal intracranial injury who underwent primary DC at the time of subdural hematoma evacuation. A decision about the need for post-procedural invasive intracranial pressure monitoring will also have to be made.

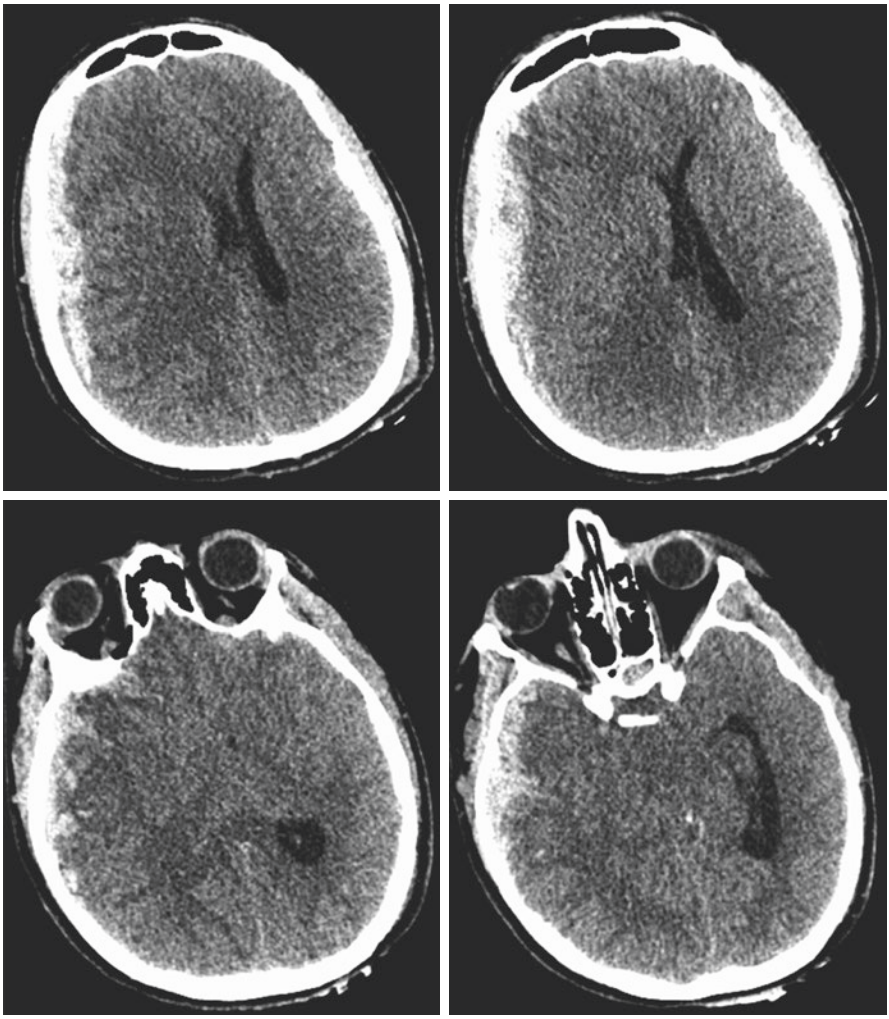

Fig. 8.2 CT head without contrast for a patient who underwent primary decompressive craniectomy. This 23-year-old female patient fell from a horse. Her GCS was 6 (E1V1M4) at the scene; the right pupil was dilated and the light reflex was lost. Imaging demonstrates a 13 mm right-sided acute subdural hematoma with multiple small contusions through the right frontal and temporal lobes, resulting in 9 mm midline shift and uncal herniation. The patient underwent emergency primary decompressive craniectomy and evacuation of subdural hematoma

If the imaging reveals an isolated extradural hematoma (EDH) , current guidelines recommend craniotomy and evacuation for all patients with an EDH volume of greater than 30 mL—regardless of GCS score—and in comatose patients (GCS 8 or less) with pupillary abnormalities [8]. Evidence on ICP trends following evacuation of isolated EDH shows that there is low risk of intracranial hypertension developing [16], suggesting that DC is not routinely required for treatment of isolated EDH [15, 16].

Acute subdural hematomas (ASDHs) , by contrast, are often accompanied by intraparenchymal contusions or hematomas and demonstrate a greater likelihood of secondary brain swelling [10–12]. Brain Trauma Foundation (BTF) guidelines recommend immediate operative intervention if ASDH thickness is more than 10 mm or midline shift is greater than 5 mm, regardless of the GCS score. Evacuation of ASDH is also recommended for severe TBI (sTBI) patients with hematoma thickness <10 mm and midline shift <5 mm if the GCS decreased by 2 points from injury to admission and/or if the patient presents with pupillary abnormalities and/or the ICP exceeds 20 mmHg [12].

There are variations in clinical practice around the world when it comes to ASDH evacuation, with some neurosurgeons performing primary DC more readily and more frequently than others. A recent consensus meeting on the role of DC in TBI recommends that primary DC should be performed following evacuation of the ASDH if the brain is bulging beyond the inner table of the skull intra-operatively; an ICP monitor may be placed, if available, for postoperative monitoring [15]. If the brain is relaxed following evacuation of ASDH and preoperative imaging is not in keeping with high risk of progressive brain swelling (such as for an elderly patient with involution brain changes and capacity to accommodate more brain swelling without a rise in ICP; or low energy mechanism of injury), the bone flap should be replaced [15]. Placement of an ICP wire intra-operatively for continuous ICP monitoring is recommended; in situations where continuous ICP monitoring is not available, serial CT imaging should be used to monitor progress [15]. For the intermediate category of ASDH patients (brain neither very relaxed nor bulging), surgeon judgment must be used to decide whether to leave the bone flap out or not. It is not clear if performing DC instead of replacing a bone flap in this clinical scenario provides any additional benefits for the patient; the results of the RESCUE-ASDH trial—a multicenter, pragmatic, parallel group randomized trial that aims to answer this question—are awaited [12, 15].

Intraparenchymal contusions and/or hematomas are often multiple and diffuse. The likelihood of perilesional cerebral edema is high. Current evidence and expert-based guidelines recommend operative intervention if hematoma volume is more than 50 mL, GCS score is 8 or less in a patient with a frontal or temporal hemorrhage more than 20 cm (>20 mL) with either midline shift of more than 5 mm and/or cisternal compression on CT scan [17]. The surgical approach may vary in this setting. We advocate craniotomy and evacuation of the hematoma or contusion(s). Others may elect to perform a decompression, without direct debridement of contusion. Primary DC is an option for comatose patients with diffuse contusions with signs of raised ICP on imaging if contusions are not being evacuated or, if following evacuation, the brain bulges beyond the inner table of the skull [15].

In cases of penetrating head injury, there are no clinical trials to date that specifically assess the role of DC. Practice is based on case series and has been driven by military experience. Brain swelling is often severe, and in these cases, intracranial hypertension can be relieved by a large DC [15].

The patient presented in our clinical scenario had severe TBI with a pre-intubation GCS score of 5. His pupils were small and reactive to light. His imaging showed diffuse head injury, but no lesions amenable to evacuation. There were no

indications for emergency cranial surgery; instead, an intracranial pressure monitor was inserted, and he embarked on a tiered intensive care TBI management (Table 8.2).

As mentioned earlier, secondary brain injury develops in the hours and days following primary brain injury and can lead to progressive and potentially dangerous brain swelling and intracranial hypertension. The burden of intracranial hypertension (the time spent with ICP above a defined threshold—usually 20–25 mmHg) is associated with excess mortality and worse functional outcomes [7, 13–15, 18].

ICP monitoring is performed ideally using an intraparenchymal microtransducer pressure probe inserted through a cranial access device or under direct vision at the time of craniotomy. Intraventricular catheters can be used; they allow therapeutic drainage of CSF, but are associated with a higher risk of complications, such as hematoma or infection, when compared to intraparenchymal probes [19]. In settings where invasive intracranial pressure monitoring is not available, non-invasive methods can be used according to available resources (for example, serial CT imaging) [15]. The goals of ICP control and preservation of CPP are pursued through the application of tier-based protocols employing neuroprotective measures such as sedation, controlled hyperventilation, therapeutic hypothermia, hyperosmolar therapies, barbiturate coma, and ventricular drainage [7]. Figure 8.3 illustrates the positioning of commonly employed invasive pressure monitoring devices.

Table 8.2 Key considerations in surgical decision-making

Factors necessitating consideration of emergency cranial surgery	– Neurological status (GCS, pupil size, and reactivity) – TBI morphology – Imaging findings (presence of lesions amenable to evacuation, midline shift, effacement of CSF spaces) – Presence and severity of extracranial injury
Factors influencing surgical approach (craniotomy vs primary decompressive craniectomy)	– TBI morphology—specifically, propensity for swelling of non-evacuated traumatic brain lesions – Intraoperative brain swelling

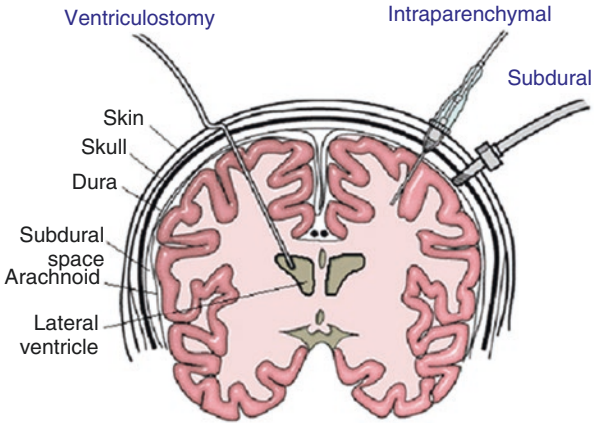

Fig. 8.3 ICP monitoring can be performed using subdural and intraparenchymal probes, as well external ventricular drains

A secondary DC can be undertaken as last-tier, life-saving therapy for patients with refractory intracranial hypertension (i.e., when all other measures have failed to reduce ICP) or as a second-tier therapy in patients with less pronounced elevation of ICP (i.e., as a neuroprotective measure) [7, 15]. DC is effective in reducing ICP and CPP, but the effects on functional outcomes are not straightforward [7, 15]. Two surgical techniques for DC are employed most commonly: bifrontal DC for diffuse injuries and unilateral frontotemporoparietal craniectomy (also termed hemi(spheric)-craniectomy or unilateral DC) for unilateral pathology with midline shift and swelling (e.g., ASDH with parenchymal injuries) [15].

Decompressive Craniectomy in Diffuse Brain Injury (DECRA)—an international, multicenter, randomized controlled trial—tested the utility of DC as an early neuroprotective measure [20]. Patients with severe, diffuse TBI were randomly assigned to either bifrontotemporoparietal DC or standard (medical) treatment if they developed intracranial hypertension—defined as ICP of more than 20 mmHg for more than 15 min in a 1-h period, refractory to first-tier therapies [20]. Patients in the DC group had better control of ICP and fewer days in the ICU. However, better ICP control did not translate into improved outcomes for the DC patients. Mortality was similar in the two treatment groups (19% in DC group and 18% in control group), and there was no improvement in functional outcomes in the DC group [20]. Therefore, current guidelines cannot recommend DC as an early neuroprotective measure. Rather, patients should be continued on the tiered intensive care TBI management [7, 15].

The Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intracranial Pressure (RESCUEicp) trial [21] aimed to examine the clinical and cost effectiveness of secondary DC (unilateral or bifrontal DC) as a last-tier therapy for severe TBI patients with refractory intracranial hypertension. Severe TBI patients with raised and refractory ICP (threshold 25 mmHg >1–12 h despite standard medical therapy) were randomized to ongoing medical therapy or secondary decompressive craniectomy. The results showed that decompressive craniectomy resulted in a marked reduction in mortality, with a concomitant increase in vegetative state, an increase in lower (dependent) and upper (independent at home for at least 8 h) severe disability, and similar rates of moderate disability and good recovery. Outcome improved between 6 and 12 months, with a significant proportion of patients in the surgical arm being upper severe disability or better [21].

A recent consensus meeting on the role of DC in the management of TBI has agreed that while secondary DC is a potentially useful operation, it should be applied selectively as there is uncertainty as to which severe TBI subgroups will truly benefit. It may decrease mortality but is associated with significant risk of complications and survival with severe disability; thus, frank discussions with family members/surrogates regarding the risks, benefits, alternatives, and potential prognosis are needed preoperatively. Both bifrontal and unilateral DC are options in the surgical treatment of diffuse TBI. The consensus group recommended a large DC (at least 12 × 15 cm) with durotomy to effectively reduce ICP and reduce incidence of secondary cortical injury from reduced venous drainage [15].

8.5 Clinical Pearls

- Primary DC involves removal of the bone flap at the time of initial evacuation of a mass lesion; the decision to leave the bone out depends upon intraoperative assessment of clinical findings and projected risk of intracranial hypertension.
- Secondary DC is usually employed as an end-stage measure when maximal medical management fails to control the ICP.
- DC is rarely indicated in the setting of EDH evacuation.
- DC carries a significant risk for morbidity.
- Clinical decision-making depends on the synthesis of several parameters (pathology, clinical examination, radiology findings, and ICP trends).

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Chapter 9
Cervical Spine Fractures/Acute Cervical Spinal Cord Injury

David O. Okonkwo and Harry M. Mushlin

Clinical Scenario

A 31-year-old male presented to the trauma bay after a motor vehicle collision. At the scene, the patient did not report any loss of consciousness. Glasgow Coma Scale (GCS) score was recorded as 15. Per EMS, the patient had no sensation or movement in his lower extremities at the scene and was hypotensive. The patient was also noted to have priapism and be incontinent of stool. On arrival to the trauma bay, the patient had a patent airway, systolic blood pressure >100 mmHg, and regular pulses. FAST (focused assessment with sonography in trauma) examination was negative. He was noted by the surgical trauma team to have antigravity movement of the proximal upper extremities and weakened handgrip, with no movement in the lower extremities. Radiographic assessment by cervical computed tomography (CT) scan demonstrated C6–7 bilateral facet fracture dislocation (jumped facets) and anterolisthesis >50% of C6 over C7 (Fig. 9.1a–c).

9.1 History and Neurologic Exam

The initial assessment of the trauma patient is based on Advanced Trauma Life Support protocols and includes primary assessment of the airway, breathing, and circulation (ABCs). It is of particular importance to address hypotension in the

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_9

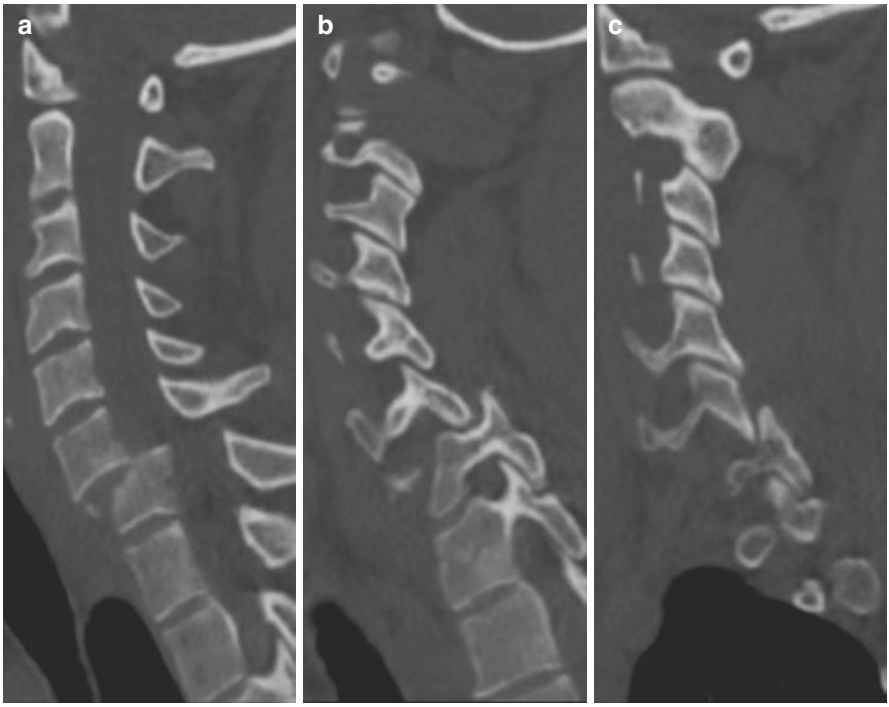

Fig. 9.1 (**a**–**c**) Cervical CT showing bilateral jumped facets. (**a**) Sagittal midline view showing anterolisthesis of C6 over C7; (**b**) sagittal view of left-sided jumped facet atC6/C7; (**c**) sagittal view of right-sided jumped facet at C6/C7

setting of spinal shock and loss of sympathetic tone [1]. Cervical injury patients can, less commonly, have autonomic dysreflexia with resultant hypertension [2]. Noxious stimuli such as an overdistended bladder can lead to a massive sympathetic response. An indwelling urinary catheter should be placed in all patients with suspected spinal cord injury to help prevent this phenomenon.

Once the patient is stabilized from a respiratory and hemodynamic perspective, a more detailed history and physical can be performed. Initial history should include an understanding of the mechanism of injury. Facet dislocations are usually found in the setting of a high-impact trauma, including motorcycle and car collisions and fall from heights [3, 4]. Medical history including medications should be obtained if possible from an awake, alert, and oriented patient. Relevant medications such as antiplatelet/coagulants should be known prior to any surgical planning and properly reversed. A detailed secondary survey including manual palpations for pain, step offs, tenderness, and spinous process gaps is important when evaluating for traumatic spinal injuries.

Patients with cervical facet dislocation can present with a wide range of symptoms from no clinical sequelae to radiculopathy and neck pain to incomplete or complete spinal cord injury [5]. A formal neurologic exam will document motor

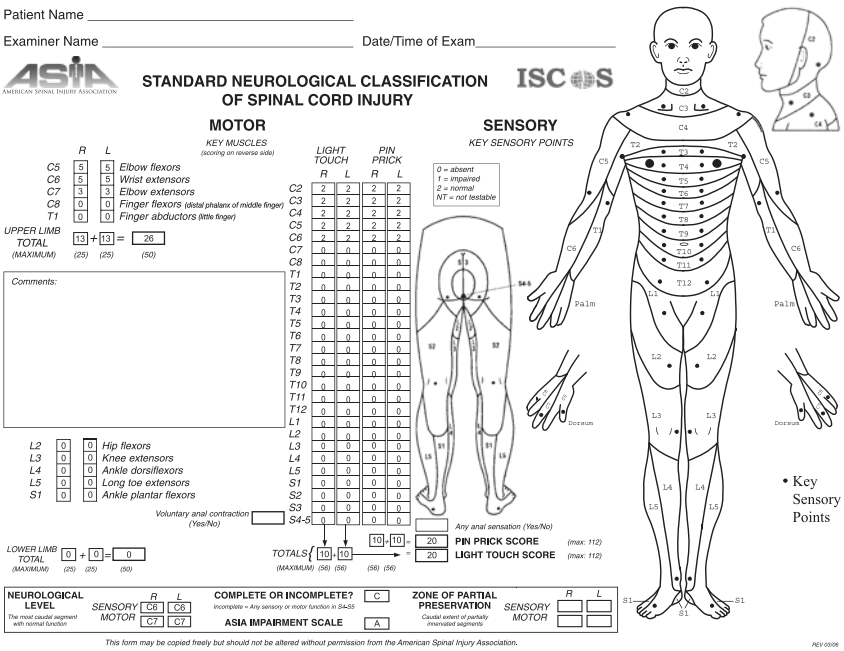

Fig. 9.2 Completed ASIA exam form. Motor level was C7, and sensory level was C6. Neurological level of injury was C6. Patient had a complete injury and was ASIA Impairment Scale Grade A

and/or sensory deficits. A rectal exam must be performed. The exam of the spinal cord injury patient is recorded in accordance with the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), using the guidelines set forth by the American Spinal Injury Association (ASIA). A completed ISNCSCI exam is shown in Fig. 9.2. Proper examination can help localize the level of injury prior to imaging and classify the severity of the injury. When spinal shock (temporary loss of sympathetic tone) is suspected, the bulbocavernous reflex should be tested. The absence of the bulbocavernous reflex supports the presence of a spinal shock [6]. A patient must be out of spinal shock before the final determination of whether a patient has a complete versus incomplete spinal cord injury can be made.

9.2 Differential Diagnosis

A detailed neurological exam will determine if there is a neurologic deficit referable to spinal column trauma and, if so, the level of injury. The neurological level of injury is defined as the lowest level of normal motor and sensory function. In the clinical case presented here, a cervical injury was suspected given that the patient was involved in a high-impact collision and had a neurological level of C6. In

general, if there is suspicion of a cervical injury, spinal immobilization should be maintained along with proper spinal precautions for movement and positioning of the patient.

The differential diagnosis of the cervical spinal cord injury patient includes craniovertebral junction injuries—between the occiput and C2—and subaxial cervical spine injuries—from C3 to T1. Neurologic deficits occur more commonly with certain injury morphologies, including atlanto-occipital dislocation, unstable Hangman's fracture, unilateral facet fracture dislocation, bilateral facet fracture dislocation, burst fracture, and teardrop fracture. Type II odontoid fractures are far less likely to induce neurologic deficits, given the relative width of the canal at that level, though these fractures can cause spinal cord injuries in rare cases.

9.3 Diagnostic Evaluation

A detailed neurological exam will determine the level of injury. The neurological level is defined as the lowest level of normal motor and sensory function. In the clinical case presented herein, a cervical injury was suspected given that the patient was involved in a high-impact collision and had a neurological level of C6. In general, if there is suspicion of a cervical injury, spinal immobilization should be maintained along with proper spinal precautions for movement and positioning of the patient.

Standard of care in the trauma evaluation is to obtain a high-quality CT scan for imaging assessment as recommended by the *2013 Guidelines for the Management of Acute Cervical and Spinal Cord Injuries* [7]. The injury morphology cannot be determined without proper imaging. Plain radiographs were traditionally used for the assessment of cervical spine trauma; however, CT scans have supplanted X-rays given the substantial superiority of CT for injury evaluation [8]. CT scans provide detailed understanding of injury morphology. In addition to osseous evaluation, CT can reveal distraction in the anterior and posterior column or suggest ligamentous damage. In our clinical scenario, the CT scan showed C6-7 bilateral jumped facets with a C6 laminar fracture and C7 superior end plate fracture (Fig. 9.1a–c).

The injury morphology classification can be determined from CT imaging and will guide appropriate surgical intervention. There have been multiple proposed classification systems. The AO Spine Subaxial Cervical Spine Injury Classification System is a more recent system that also guides clinical decision-making. In the case presented, the facet fracture dislocation is classified as Type C (translational) injury [9]. The Subaxial Cervical Spine Injury Classification (SLIC) system includes a point-based system assessing morphology, discoligamentous complex, and neurological status to inform surgical intervention [10].

In cases of bilateral jumped facets, the utility of MRI has been widely debated [11]. The patient with an acute neurologic deficit secondary to cervical spine trauma is best served with early decompression. MRI can delay surgical intervention and,

thus, should be obtained judiciously [12]. Postoperative MRI can document spinal cord injury and confirm successful surgical decompression.

The necessity of MRI prior to closed reduction, regardless of level of consciousness, has been proposed by some authors [13], largely based on the theoretical risk of neurological worsening after reduction in the setting of cervical disk herniation and limited case reports of neurological deterioration after reduction [14]. However, Gelb et al., in their 2013 guidelines on cervical dislocation, found only two documented cases of neurological worsening after attempted closed reduction for cervical dislocation [15, 16]. Multiple studies have reported the safety of closed reduction in awake and alert patients without a pre-reduction MRI [17–19]. In one series from Grant et al., 22% of 80 dislocated cervical patients had an associated disk herniation on post-reduction MRI, but there were no cases of neurological worsening following closed reduction [20]. An additional series from Koivikko et al. reported no neurological deterioration in 65 dislocated patients with no pre-reduction MRI [21]. In 2006, Darsaut et al. showed that soft disk herniations seen on pre-reduction MRI were reabsorbed as seen on post-reduction MRI [22]. In the case of unsuccessful closed retraction or an uncooperative/obtunded patient, a cervical MRI can be obtained prior to open reduction.

In addition, patients with cervical spine injury should undergo evaluation for blunt cerebrovascular injury (BCVI) as recommended by the Denver Criteria [23]. This patient's vascular studies were negative for BCVI. Studies have shown that up to 24% of patients with cervical spine injuries also have a vertebral artery injury [24]. Patients with jumped facets and translocation are at the highest risk for BCVI of the vertebral artery, and delayed therapy places patients at increased risk of stroke. Antiplatelet/anticoagulation medication should be started as soon as deemed safe.

9.4 Clinical Decision-Making and Next Steps

After initial stabilization based on ATLS protocols, the cervical spinal cord injury patient should have an arterial line and indwelling urinary catheter placed. The mean arterial blood pressure (MAP) goal is set at >85 mmHg [25]. More recent evidence supports the placement of a lumbar drain, measurement of intrathecal pressure, and management of SCI in accordance with spinal cord perfusion pressure goals (SCPP >15 mmHg).

In our clinical scenario, CT imaging demonstrated bilateral jumped facets (Fig. 9.1a–c), which requires immediate reduction. Traction has been recognized as a quick and safe technique for closed reduction. In addition, timely reduction has been shown to decompress the spinal cord and improve neurological outcomes and is a recommended option in the AANS/CNS *Guidelines for Management of Acute Cervical Spine and Spinal Cord Injuries* [26–31]. This technique can be applied to the awake and alert patient.

Closed reduction is accomplished using traction in the flexion-distraction vectors. Closed reduction has been shown to be successful up to 70–90% of the time

[13, 32]. Closed reduction is more successful in the setting of bilateral jumped facets than with unilateral fracture dislocations. Traction can be applied with a halo device or, more commonly, Gardner-Wells tongs. It is critical to ensure the forces applied are in the proper vector or risk of further distraction and injury can occur. Fluoroscopy should be utilized frequently as weight is added during traction. It is important to assess for over distraction on imaging. Neurological assessment should be performed frequently, and closed traction should be aborted with any exam changes. Traction should begin with low weights, with the sequential addition of 5–10 lb. Once alignment is attained, the weight can be reduced, and the patient can be placed in light extension to prevent loss of reduction.

If closed reduction is not attempted or is unsuccessful, an open reduction is performed either through a posterior or anterior approach. As mentioned above, MRI can help dictate the approach if there is concern for extruded disk fragment which could favor an anterior approach. However, there is a lack of expert consensus for the appropriate open reduction approach. This was highlighted by Spine Trauma Study Group which surveyed its members and found a poor surgical agreement (kappa <0.1) for management of cervical dislocation [33].

At our institution, closed reduction is not typically attempted for bilateral facet fracture dislocation. Patients are immediately taken to the operating room from the trauma bay for posterior reduction and fixation. We believe this allows the fastest time to cervical reduction within our hospital. Posterior reduction and fixation have been shown to be a successful procedure for realignment and fusion [30]. Furthermore, multiple biomechanical studies have shown the superiority of posterior stabilization over anterior plating [34, 35]. Posterior, open reduction can be achieved by drilling an adequate amount of the superior articulating process to allow for leveraging of the inferior articulating process over the superior articulating process. Due to high biomechanical instability of bilateral facet dislocations, we support multiple level fixation above and below the level of dislocation. In addition, laminectomies should be performed at the site of injury to ensure adequate decompression of the injured spinal cord and prevent compression from anterior pathology. In most cases, we also perform a second, anterior approach, typically in a delayed fashion a few days later, to achieve a 360° fusion and maximize biomechanical stability of the construct.

An anterior approach may also be considered as a standalone intervention for bilateral cervical facet fracture dislocations. The anterior approach has been shown as viable option for both reduction and fixation [36–38]. This approach requires distraction and posterior maneuvering of the cephalad vertebral body which can be accomplished with the use of laminar spreaders or Caspar pins.

A prospective, randomized trial of unstable cervical injuries found no significant difference in fusion rates, alignment, and neurological recovery between posterior and anterior approaches [39]. However, additional work has shown that in the setting of cervical dislocation, 13% of anterior-only cases had postoperative loss of alignment [40]. This concern for loss of alignment in highly unstable dislocations injuries has led to expert support for additional posterior fixation after anterior

approach [41, 42]. Technical difficulty of anterior reduction has also been reported with failure of reduction as high as 25% reported [43].

In this clinical scenario, the patient has bilateral C6–7 facet dislocation with >50% anterolisthesis. This is a three-column injury, with significant disruption of the anterior and posterior tension band. We recommend a circumferential fusion and decompression in patients with bilateral jumped facets. Biomechanical studies have shown the superiority of circumferential fusion in three-column injuries [42, 44]. Unilateral facet dislocations and perched facets do not represent the same severity of injury as a bilateral dislocation and may be managed with a single approach (either anterior or posterior). In addition, patients may have underlying medical conditions, such as diffuse idiopathic skeletal hyperostosis (DISH), ankylosing spondylitis, and osteoporosis, which may warrant long posterior or circumferential fixation for additional stabilization.

The patient in this vignette underwent posterior open reduction with fixation from C5 to T1 and a multiple level cervical laminectomy. The patient subsequently had an anterior discectomy and fusion from C5 to C7 (Fig. 9.3). A postoperative MRI was obtained to show the extent of decompression and spinal cord injury (Fig. 9.4).

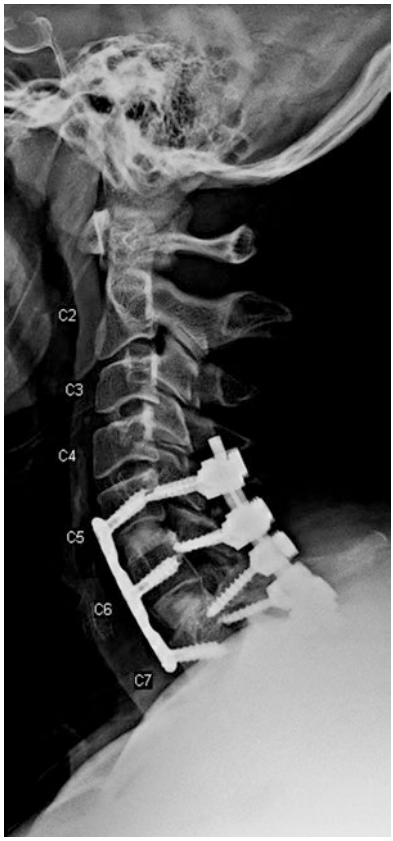

Fig. 9.3 Lateral cervical X-ray demonstrating cervical realignment with anterior and posterior fixation for treatment of bilateral jumped facets

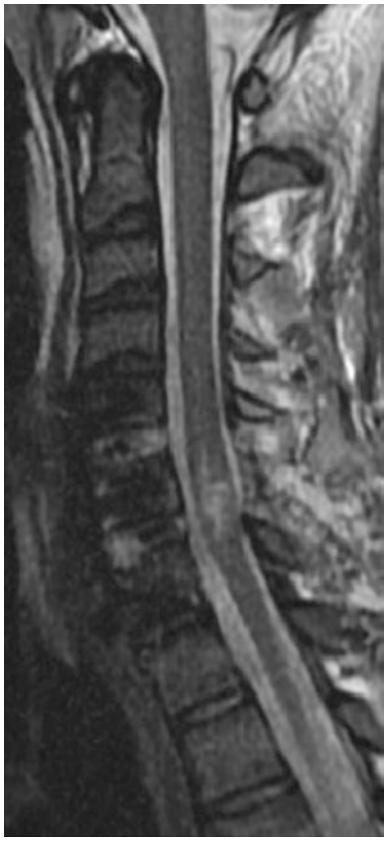

Fig. 9.4 Postoperative T2-weighted sagittal MRI showing circumferential decompression and myelomalacia at the level of injury

9.5 Clinical Pearls

- Cervical facet dislocation injuries should be reduced as quickly as possible (whether open or closed reduction) to achieve decompression of the spinal cord.
- There is a lack of consensus for open reduction approach (posterior vs anterior surgery).
- Circumferential fusion should be strongly considered for bilateral cervical jumped facets.

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Chapter 10
Thoracolumbar Spine Fractures

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Clinical Scenario

A 29-year-old man presents to the Emergency Department (ED) after a fall. He states that he slipped and fell from a ladder from a height of about 5 ft. He landed on his coccyx and experienced immediate onset of pain. He was able to ambulate briefly after the fall but could not continue due to severe low back pain. He denies radiation of pain to the lower extremities. He has not experienced paresthesia, anesthesia, weakness, or incontinence.

10.1 History and Neurologic Exam

On physical examination, he is noted to be hemodynamically stable, alert, awake, and oriented. His motor function and reflexes are normal. His sensation is intact, and he has normal rectal tone without saddle anesthesia. On examination of his back, he has tenderness to palpation over the upper lumbar spine. There are no step-offs. Examination of his cervical spine demonstrates no tenderness, with full range of motion. In patients presenting with trauma to the thoracolumbar spine, care must be taken when considering initial history and physical exam in order to identify other injuries which may be immediately life threatening. A thorough trauma evaluation and systematic primary and secondary survey will aid in identification of

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_10

associated injuries. With respect to neurosurgical considerations, a thorough history can provide vital information regarding the nature of the thoracolumbar injury:

- *Mechanism of injury.* Establish the cause of the injury and the events leading to it. Identifying the forces applied to the injured area (compression, distraction, flexion, extension, and rotation) will aid in determining the type of injury. If the patient is injured in a vehicular accident, determine if the patient utilized safety equipment such as seat belts or helmets and determine the approximate speed and configuration of vehicles involved. For falls, determine the approximate distance of the fall and in what position the patient landed. Mechanism of injury not only helps determine the location and type of thoracolumbar spine injury, but also helps predict the presence and severity of additional injuries.
- *Location of pain.* Identify pain in the neck, back, sacrum, and extremities. Identify any pain wrapping in a band from the back to the chest or abdomen. Determine if back pain is midline or paraspinal. Determine the laterality and distribution of any pain suspected to be radicular in nature.
- *Neurologic symptoms and disability.* Identify sites of weakness. Determine if the patient was able to tolerate ambulation after the injury. If the patient was unable to ambulate, determine why. Determine sites of numbness and paresthesia. Identify any normal actions the patient has been unable to perform since the injury. Specifically document the presence or absence of saddle anesthesia and bowel or bladder dysfunction. Determine if the patient experienced loss of consciousness. Clinicians should have a high index of suspicion for concomitant cranial and cervical injuries in patients with thoracolumbar spine injuries.
- *Previous spinal history.* Determine if the patient has any prior history of thoracolumbar spine surgery or procedures. Determine if they have a history of preexisting back or neck pain, radiculopathy, paresthesia, or weakness. In patients with previous spinal or radicular complaints, determine if the patient's present complaints represent an exacerbation of previous complaints or are distinct in nature.
- *Medical history.* Identify risk factors for fracture and pseudoarthrosis, including osteoporosis and osteopenia, chronic steroid use, diabetes, and tobacco use. Identify patients with congenital abnormalities of bone and cartilage formation.
- *Work and social history.* Determine employment status and type of labor performed. Screen for alcohol and substance abuse. Determine if the patient has assistance from family or friends at home. Screen for abuse as appropriate. An understanding of the patient's employment status and social support systems will aid with disposition planning and recovery after treatment.

In patients with a suspected thoracolumbar spinal injury, care must be taken during physical examination to minimize the risk of exacerbating an existing injury. Cervical spine and cranial injuries commonly accompany thoracolumbar spine fractures and as such in-line stabilization of the cervical spine should be maintained when examining the patient until such injuries can be excluded. The patient should be maintained in thoracolumbar spine precautions, positioned supine on a flat bed, and moved by coordinated log-roll only during the primary and secondary surveys.

A comprehensive, yet focused neurologic examination is necessary to help localize the level of injury in patients with neurologic compromise. A full motor examination, in conjunction with a digital rectal exam and thorough sensory exam, should be performed on all patients with suspected spinal injury. Loss of the bulbocavernosus reflex in a patient with acute paralysis is indicative of spinal shock and is the first reflex to recover after spinal cord injury. A preserved bulbocavernosus reflex is seen with spinal cord severance. Post void residual can be measured by ultrasound to identify urinary retention. Location of neural injury should be differentiated among spinal cord, cauda equina, nerve root, plexus, and peripheral nerve. In the presence of spinal cord and nerve root injuries, the spinal level of injury should be identified to help guide imaging evaluation. For injuries to the spinal cord, the American Spinal Injury Association (ASIA) Impairment Scale is utilized to determine localization and severity of injury [1]. A full neurologic examination should be performed to identify additional sites of neurologic injury including but not limited to intracranial hemorrhage, cervical spine fractures, and craniocervical junction injuries. Of course, it is important to consider the neurologic assessment in the context of the overall trauma evaluation; airway, breathing, circulation, and hemodynamic status must be stabilized first.

Multiple neurologic assessment scales, including the Functional Independence Measure, Sunnybrook Cord Injury Scale, and Frankel scale for Spinal Cord Injury, have been validated and demonstrated to be internally reliable and can be utilized to provide consistency to repeated neurologic assessments [2, 3]. This may also aid in communication between healthcare providers and improve ease of comparison of neurologic assessments at different points in the treatment process. A number of neurologic findings have also been shown to be predictors of neurologic outcome. Intuitively, worse ASIA scores are associated with poor neurologic outcomes, and the absence of sacral sensation and pinprick response are associated with worse recovery of function and poor prognosis for bladder function. Reappearance of urethral or rectal sphincter pressure is associated with bladder recovery, and electromyographic evidence of abductor hallucis motor function has been shown to be the earliest and most accurate predictor of neurologic recovery after thoracolumbar spinal cord injury [4].

As in the present case example, many patients with thoracolumbar spine injuries present without neurologic compromise or with insufficient neurologic signs and symptoms to localize the injury. Evaluation for additional physical localization signs is vital. The length of the spine should be inspected for ecchymosis, abrasions, and deformities. The spine is palpated along its length to identify sites of tenderness and evidence of step-offs that could indicate potential fractured sites.

10.2 Differential Diagnosis

This particular patient's presentation could represent a broad range of injuries. The patient presents with significant axial back pain, exacerbated by weight bearing, after a fall from a ladder. The mechanism of injury and presenting symptomatology are

suggestive of a spinal fracture, and his normal neurologic examination implies that the neural elements have not been compromised during injury or transportation to the hospital. Given the significant mechanism of injury and the patient's substantial back pain, an unstable spinal injury must be considered in the differential diagnosis.

While the patient may simply be experiencing spinal strain and muscle spasm, this should be considered a diagnosis of exclusion. Appropriate diagnostic evaluation must be carried out. The AO Spine thoracolumbar classification delineates spine fractures based on morphology, neurologic status of the patient, and additional associated radiographic features [5]. Fracture morphologies are categorized as compression (A), distraction (B), and displaced (C). Compression morphologies include wedge compression fractures (A1), split or pincer fractures (A2), incomplete burst (A3), and complete burst (A4). Distraction injuries involve the anterior or posterior ligaments and include Chance fractures (B1); osseoligamentous posterior tension band fractures (B2), which often occur in conjunction with a type A fracture; and hyperextension injuries (B3). Neurologic status is assessed as no neurologic signs (N0), transient neurologic deficit (N1), radiculopathy (N2), incomplete spinal cord injury or cauda equina injury (N3), and complete spinal cord injury (N4). Additional modifiers include indeterminate posterior tension band injury (M1) and the presence of comorbid spinal or bony pathologies (M2) [5–9]. The 2019 Congress of Neurologic Surgeons (CNS) Guidelines on the Evaluation and Treatment of Patients with Thoracolumbar Spine Trauma recommends utilizing a classification system or severity score, such as the AO classification or Thoracolumbar Injury Classification and Severity Score (TLICS) to aid characterization of injuries and to improve communication among physicians, but there is insufficient evidence to recommend a universal classification system [10].

10.2.1 Compression Fracture

The typical compression fracture occurs as a result of an axial loading force, with or without a component of flexion. The typical morphology is a wedge-shaped compression of the anterior two-thirds of the vertebral body, without involvement of the posterior vertebral wall or posterior bony or ligamentous elements. CT and plain radiographs demonstrate loss of height of the anterior column of the affected vertebra without retropulsion of bone into the spinal canal or fracture of the posterior elements. MRI may demonstrate increased T2 signal or contrast uptake in acute compression fractures. These fractures are the most common complication of osteoporosis and frequently occur in patients aged over 65 years [11, 12]. An elderly or osteoporotic patient might present with back pain after a seemingly minor injury, whereas a young and healthy patient might present with a similar fracture pattern following a more significant mechanism of trauma. Treatment is typically nonoperative, as these fractures are typically stable and do not require decompression, but this can be controversial. Pain control, kyphoplasty, bracing, and serial imaging without orthotics have been described in the literature with varying reports of efficacy [12–14].

10.2.2 Burst Fracture

Burst fractures are injuries to the anterior and middle column of the vertebra caused by high-energy axial loads [15]. These represent one of the most common fracture morphologies of the thoracolumbar spine and can be associated with radiculopathy, spinal cord injury, and cauda equina compression due to retropulsion of posterior vertebral body fragments into the spinal canal [16]. Burst fractures may be stable or unstable. Radiographic evidence of instability includes increased interpedicular distance, widening of the interspinous or interlaminar distance, sagittal translation of at least 2 mm, 20° or more of kyphosis, more than 50% loss of height, and articular process fractures [17]. Additional signs of instability include posterior ligamentous disruption as seen on advanced imaging, intractable pain, and new or progressive neurologic deficit. Appropriate management of burst fracture is dependent on identifying or ruling out signs or symptoms of instability. Non-operative management for appropriately selected patients may include external orthoses, pain control, and management of osteoporosis. Operative fixation can be utilized in patients with new or progressive neurologic dysfunction, refractory radiculopathy, intractable pain, or risk to orthosis and immobilization that outweighs the risk of surgery [13, 18].

10.2.3 Chance Fracture

Chance fractures, sometimes referred to as seatbelt fractures, are axial plane fractures through the vertebral body or intervertebral disc and the posterior ligaments or bony elements. The mechanism of injury is flexion with distraction due to flexion around an instantaneous axis of rotation anterior to the spine (i.e., the spine is flexed around a point anterior to the spine itself). This was commonly described in motor vehicle accidents involving seat belt lap bands without shoulder restraints [19–21]. Despite the highly unstable nature of this injury pattern, most patients with Chance fractures present without neurologic deficit. These fractures, however, have a substantial association with comorbid intraabdominal injury, occurring in up to 50% of cases [19]. Treatment is typically with open fixation and fusion, with fracture reduction in cases of dislocation.

10.2.4 Fracture-Dislocation

Fracture-dislocation is a relatively uncommon thoracolumbar fracture morphology that typically occurs due to very high-energy trauma involving multiple simultaneous vectors of force, including translation, rotation, and distraction [22]. These injuries are, by definition, highly unstable and frequently present with severe, if not complete, neurologic injury. Due to the substantial energy required to produce such

an injury, there is a strong association with additional injuries, including intraabdominal and vascular injuries that may result in hemodynamic instability. It is vital to identify extraspinal injuries in these patients and to ensure hemodynamic stability prior to consideration of operative thoracolumbar stabilization. Treatment for thoracolumbar fracture-dislocation typically involves fracture reduction and pedicle screw-rod fixation. Cerebrospinal fluid leak is commonly encountered intraoperatively and must be addressed appropriately. Traction is frequently required to obtain fracture reduction [23]. In a series of 50 patients with thoracolumbar fracture-dislocation treated with open reduction and fixation described by Chokshi et al., 35 patients presented with complete spinal cord injury. No patients presented with normal neurologic function, and no patients recovered to normal neurologic function [24].

10.2.5 Minor Fractures

Minor thoracolumbar spine fractures include spinous process, transverse process, and isolated laminar fractures. These types of fractures are typically not associated with neurologic dysfunction or spinal instability and are easily identified on CT imaging. Fractures of this variety may be pain generators but can generally be treated non-operatively with pain management, with or without external orthosis for immobilization [25–27].

10.3 Diagnostic Evaluation

Although initial radiographic assessment often involves CT scans in conjunction with the initial radiographic trauma survey, an initial evaluation with **plain radiographs** can be undertaken to screen for fractures and dislocations of the thoracic and lumbar spine. Plain radiographs also can be utilized for surveillance to check alignment of unstable injuries. While X-rays may work well as an initial screening tool, many small fractures or purely ligamentous injuries may be missed. **CT of the thoracic or lumbar spine**, therefore, can be used to better define the nature and anatomy of spinal fractures and can identify subtle or well-approximated fractures that may be missed on plain radiographs.

Magnetic resonance imaging (MRI) without contrast can also play an important role in the evaluation of suspected fractures of the thoracolumbar spine. MRI provides clear depiction of the neural elements, allowing clinicians to identify compressive pathology in patients with neurologic dysfunction on physical exam. In addition, the anterior and posterior longitudinal ligaments, intervertebral discs, and posterior ligamentous complex can be evaluated for injury or disruption on MRI. Increased Short-T1 Inversion Recovery (STIR) or gradient echo signal within the ligamentous structures or discontinuity of the ligaments are indicative of

ligamentous injury. In up to 25% of patients with thoracolumbar fractures, MRI assessment of posterior ligamentous complex integrity meaningfully influences surgical management [28].

10.4 Clinical Decision-Making and Next Steps

Appropriate management of thoracolumbar spine fractures is dependent on thorough history, physical, and radiographic assessment to identify fracture mechanism and morphology, as well as to determine the degree of instability. Vaccaro et al. established TLICS, which facilitates description of fracture morphology and stability and aids with decision-making with respect to surgical versus non-surgical management [29]. Fractures are graded based on morphology, posterior ligamentous complex integrity, and neurologic status of the patient on a scale of 1–10. Fracture morphology is graded as 1 for compression, 2 for burst, 3 for translation and rotation, and 4 for distraction. Suspected ligamentous injury adds two points, and confirmed ligamentous injury adds three. Nerve root and complete cord injuries add two points, while incomplete cord injuries and cauda equina syndrome add three. Fractures scoring greater than four should be treated surgically, while fractures scoring less than 4 should be treated non-surgically. A fracture with a TLICS score of 4 can be treated surgically or non-surgically at the physician's discretion. TLICS has been reviewed by many authors for validity and accuracy and has been found to be highly accurate for detecting stable injuries. With the use of MRI to assess the posterior ligamentous complex, it is highly accurate in identifying unstable thoracolumbar spine fractures [30, 31].

Medical management of patients with thoracolumbar spine fractures involves addressing multiple organ systems, as well as a proactive approach to prevent further complications. Methylprednisolone administration in spinal cord injury has been studied in an attempt to improve neurologic outcomes; however, there is insufficient evidence to recommend its routine use. In select cases, the complication profile should be carefully considered before the decision to administer methylprednisolone is made [32]. Patients with significant thoracolumbar trauma are also at increased risk of venous thromboembolism. While there is insufficient evidence to recommend for or against a specific screening, prophylaxis, or treatment protocol, thromboprophylaxis is recommended in this patient population [33]. Pooled data from cervical and thoracolumbar spinal cord injury suggests that clinicians may maintain mean arterial pressures above 85 mmHg in an attempt to improve or preserve neurologic function, but that data in thoracolumbar spinal cord injury alone is inconclusive [34]. Additionally, the AANS/CNS joint guidelines recommend maintaining mean arterial pressures at 85–90 mmHg for the first week after injury although there is no robust evidence of benefit [35]. Finally, a number of pressure monitors, originally designed for intracranial pressure monitoring have been used in experimental studies of spinal cord injury, but these devices are not widely used in practice at this time [35].

Patients with thoracolumbar burst fractures and preserved neurologic function may be treated non-operatively. Clinical outcomes have been shown to be equivalent with and without the use of bracing [36]. Additionally, the 2019 CNS guidelines found insufficient evidence to advocate for or against the surgical treatment of thoracolumbar bust fracture when compared to non-operative management, ultimately leaving the management strategy to the discretion of the treating physician [37]. Similarly, open and percutaneous fixation of unstable burst fractures, with or without arthrodesis, has been shown to have similar clinical outcomes [38]. In patients undergoing surgical intervention for thoracolumbar fractures, anterior, posterior, and combined approaches can be considered. While the evidence in the literature is conflicting regarding clinical and radiographic outcomes by approach, the surgeon should plan their operative approach in order to effectively treat the presenting pathology while minimizing complications [39].

Timing of surgical intervention remains controversial. Early surgery is defined variably in the literature, with definitions ranging from less than 8 h after injury to as long as 72 h after injury. Understandably, therefore, the evidence on early versus late surgery is conflicting and inconsistent. Despite this, surgeons can consider early intervention as an option to reduce hospital length of stay and complications [40].

In the present case, a young man presented after a fall from a ladder with intractable back pain and no neurologic dysfunction. A noncontrast CT of the lumbar spine (Fig. 10.1a–c) demonstrated a burst fracture of L1 with significant

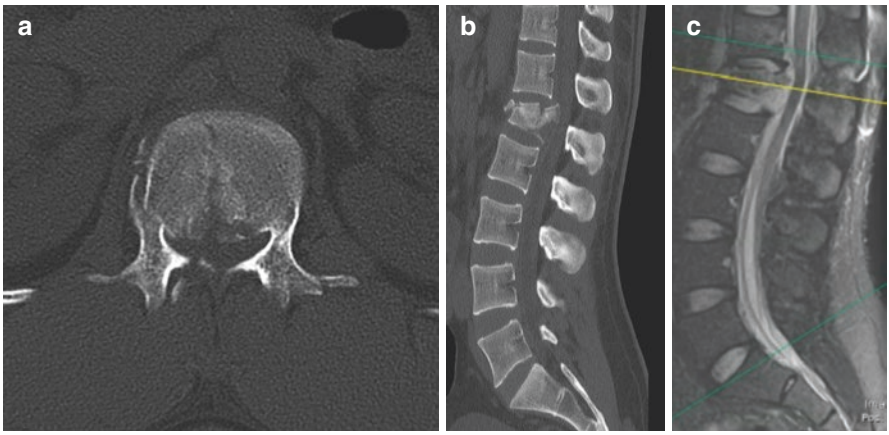

Fig. 10.1 (**a**–**c**) Non-contrast CT scan of the lumbar spine for a patient following a fall from a ladder. (**a**) Axial image demonstrating a burst pattern of injury to the L1 vertebral body, involving the anterior and middle columns, with retropulsion of bony fragments into the spinal canal with resulting significant canal compromise and stenosis. A small laminar fracture on the right suggests injury to the posterior column and raises concern for potential posterior tension band injury. (**b**) Sagittal reconstructed imaging again demonstrating a burst-type fracture of L1 with canal compromise. Despite the recumbent technique of this imaging modality, slight kyphosis across T12 to L2 is noted, which is concerning for posterior tension band injury. (**c**) Mid-sagittal MRI T2-weighted image demonstrating the L1 burst pattern with retropulsed material in the spinal canal. Increased signal is seen within the posterior ligamentous structures, suggesting ligamentous tension band injury

compromise of the spinal canal from retropulsed bone fragments. There was evidence of relative kyphosis at the fractured level, even on recumbent imaging. His intolerance to axial loading and fracture pattern was highly suggestive of instability. An MRI of the lumbar spine demonstrated STIR signal abnormality within the posterior ligamentous complex, confirming posterior tension band injury. Based solely on the CT scan, the fracture morphology was that of a complete burst (A4) with modifier M1 for indeterminate, but suspected posterior tension band injury in the AO classification. The addition of the MRI evidence of posterior tension band injury makes this a B2 morphology due to osseoligamentous posterior tension band disruption. This injury was scored as TLICS 5 given the burst morphology, injured posterior ligamentous complex, and normal neurologic exam. As such, the patient was determined to have an unstable fracture and underwent open treatment with T11 to L3 segmental instrumentation, fracture reduction, and posterolateral arthrodesis. The patient tolerated surgery well and recovered with preserved neurologic function and improved pain.

10.5 Clinical Pearls

- Detailed history and physical exam to identify location of pain and neurologic dysfunction is paramount in patients experiencing thoracolumbar trauma.
- Multiple imaging modalities are utilized for the diagnosis and classification of thoracolumbar fractures: plain radiographs may help screen for obvious fractures and dislocations, CT demonstrates detailed fracture morphology, and MRI helps identify ligamentous and neurologic injuries.
- The AO Spine thoracolumbar fracture classification can aid description of fracture morphology and mechanism.
- TLICS provides a straightforward algorithm for determining need for surgical intervention based on fracture morphology, posterior ligamentous complex integrity, and neurologic injury.
- Treatment strategies for unstable thoracolumbar fractures are varied but aim to achieve fracture reduction and fixation, as well as appropriate decompression of the neural elements.

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Chapter 11
Central Cord Syndrome

John K. Ratliff, Jay Nathan, and Parastou Fatemi

Clinical Scenario

An 81-year-old, right-hand dominant gentleman in previously excellent health presents after a ground-level fall that he sustained while out on his daily walk. He reports new weakness in the right upper extremity, interfering with his ability to use dining utensils. He also finds that his balance and walking distance are impaired. He denies neck pain, but has a new aching dysesthesia of the right arm down to the hand.

11.1 History and Neurologic Exam

Central cord syndrome is a clinical diagnosis, making the history and neurological exam paramount.

Relevant historical details include:

- *Neurologic symptoms*. An abrupt decline in strength in the bilateral upper extremities is mandatory in the diagnosis of central cord syndrome. Determine the degree of impairment and onset. Has the patient been able to ambulate? Has he or she noted any weakness in the lower extremities? Have there been any changes to sensation or bowel or bladder function?
- *Mechanism of injury*. Motor vehicle accidents, falls, and diving injuries are the most common traumatic etiologies of central cord syndrome [1]. High-impact injuries are not always necessary; often, a ground-level fall creates sufficient

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_11

hyperextension in the cervical spine to produce an injury that leads to central cord syndrome. What is the patient's catalog of injuries? Did he or she have a loss of consciousness? Was any cardiopulmonary resuscitation performed?

- *Time course*. Patients with central cord syndrome most commonly had pre-existing cervical spinal stenosis prior to their traumatic injury, but this may not have been diagnosed. It is important to determine if the patient was previously symptomatic, with features of either cervical myelopathy (classically gait imbalance/instability, loss of dexterity, numbness in the hands) or radiculopathy (pain, dysesthesias, weakness in either arm). If the patient presents in delayed fashion after trauma, has he or she experienced any progression or improvement in symptoms? Have any episodes of similar symptoms occurred before?
- *Occupation and activities*. Physical activities in and out of the workplace must be considered when determining mechanism of injury, risk of re-injury, and impact to the patient's desired level of function.
- *Surgical/procedural history*. Has the patient had any operations on the cervical spine, including interventions such as epidural steroid injections? Is there a history of radiation treatment to the head or neck area? These may decrease the structural integrity of the cervical spine or influence the risk of infection.
- *Bone health history*. Diagnoses of osteopenia, osteoporosis, rheumatoid arthritis, ossification of the posterior longitudinal ligament (OPLL), other arthropathy, or renal impairment are associated with greater risk of fracture, traumatic malalignment, and instability in the cervical spine.

Neurological exam should include motor, sensory, and reflex testing. For our patient, physical examination is notable for weakness in bilateral triceps and right biceps, graded 4/5, with normal strength in the lower extremities. A Hoffman sign is present bilaterally. The hallmark finding of central cord syndrome is a marked loss of upper extremity motor function, particularly hand function, in the setting of relatively preserved lower extremity function. Upper extremity impairment need not be symmetric, and spontaneous improvement in function can also occur with a unilateral predominance. Comatose polytrauma patients must have frequent, serial neurological examinations with close attention paid to the motor exam as it emerges. Response to pain in the lower but not upper extremities, particularly in the absence of an intracranial space-occupying lesion, should raise suspicion for central cord syndrome.

Pending imaging workup, all patients with suspected cervical spine injury must have strict precautions ordered to immobilize the cervical spine, including the use of a rigid cervical collar with care to have the neck in a neutral alignment. Once deemed safe to do so, cervical range of motion testing should be performed to evaluate for clinical cervical spinal instability, in accordance with relevant institutional protocols.

11.2 Differential Diagnosis

The differential diagnosis for a clinical process affecting motor and/or sensory function in the extremities may include (but is not limited to) classic acute spinal cord injury, spinal epidural abscess, metastatic epidural spinal cord compression, and

peripheral nerve injury. Factors such as acuity of onset, symmetry or asymmetry of deficit, the presence of a sensory level, and involvement or sparing of particular limbs may help localize the process, as well as suggest the likely pathology.

11.2.1 Acute Cervical Spinal Cord Injury

Central cord syndrome can be considered a specific type of incomplete acute cervical spinal cord injury [2]. However, the nomenclature is distinguished by the pattern of upper versus lower extremity impairment. In classical cervical spinal cord injury, neurologic impairment is observed distal to the lesion, and would be expected to involve *both* the upper and lower extremities. In central cord syndrome, injury primarily occurs to the lateral corticospinal tracts, resulting in upper more than lower extremity weakness [1]. Spinal cord injury is classified in detail using the American Spinal Injury Association, or ASIA, scale [3].

11.2.2 Spinal Epidural Abscess

Infection in the cervical spinal epidural space can cause cervical myelopathy, and a superimposed injury could exacerbate this. Relevant historical considerations include symptoms predating trauma, such as fever, chills, neck pain, neurological dysfunction, and infection risk factors (intravenous drug use, immunosuppressed states, prior infections, cardiac valvular disease, poor dentition, among others).

11.2.3 Metastatic Epidural Spinal Cord Compression

Metastatic deposit(s) from primary malignancy may produce spinal cord compression that is initially clinically occult but becomes apparent or worsens after trauma.

11.2.4 Peripheral Nerve Injury

Injuries to the brachial plexus or upper extremity peripheral nerves can produce weakness in patterns that may mimic radiculopathic or spinal etiologies. However, these rarely occur in a bilaterally symmetric pattern, which should direct localization of the injury to the cervical spine.

Our patient had no prodromal or systemic symptoms prior to this acute trauma and neurological deficit, making infection or malignancy less likely. Peripheral nerve injury is possible, but less likely than a central nervous etiology given the bilateral, symmetric nature of the patient's arm weakness and lack of upper

extremity fractures which might lead to acute nerve compression or avulsion. The sparing of his lower extremity function makes a classic cervical spinal cord injury less likely than the diagnosis of central cord syndrome.

11.3 Diagnostic Evaluation

Magnetic resonance imaging (MRI) of the cervical spine is essential. If the patient has a history of cervical spinal procedures, or if infection or metastatic disease are suspected, MRI should be obtained with and without contrast. Computed tomographic (CT) myelography can be used if MRI is contraindicated, but plain CT imaging is insufficient to evaluate for spinal cord compression. MRI of a patient with central cord syndrome can be expected to demonstrate moderate to severe cervical spinal cord compression and may show hyperintensity on T2-weighted imaging within the injured region of the spinal cord, representing cord edema. Hemorrhage is not usually found with central cord syndrome, but if present, correlates with a greater degree of injury and worse prognosis [4].

Our patient had a cervical spine MRI demonstrating severe spinal stenosis and cord compression at the cervical 4–6 levels, caused by disc herniations, ligamentum flavum hypertrophy, and facet arthropathy with loss of cervical lordosis (Figs. 11.1 and 11.2a). There is hyperintensity of the spinal cord at the cervical 5–6 interspace on T2-weighted imaging, consistent with cord edema (Fig. 11.2b).

If mass lesions are identified that raise suspicion for metastatic disease, additional imaging including MRI of the brain and thoracic and lumbar spine, with and without contrast, should be obtained to rule out additional metastatic deposits

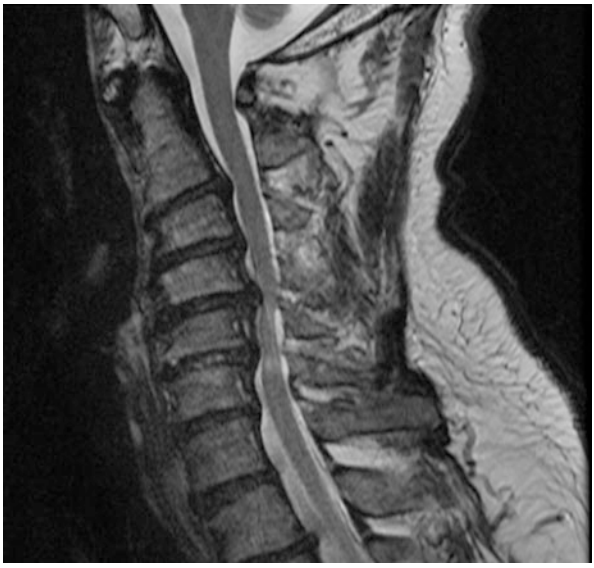

Fig. 11.1 Magnetic resonance imaging (MRI) of our patient's cervical spine, T2-weighted, in a sagittal projection. This demonstrates severe spinal stenosis and cord compression at cervical 4–6 levels, with multilevel disc disease resulting in loss of both disc height and cervical lordosis

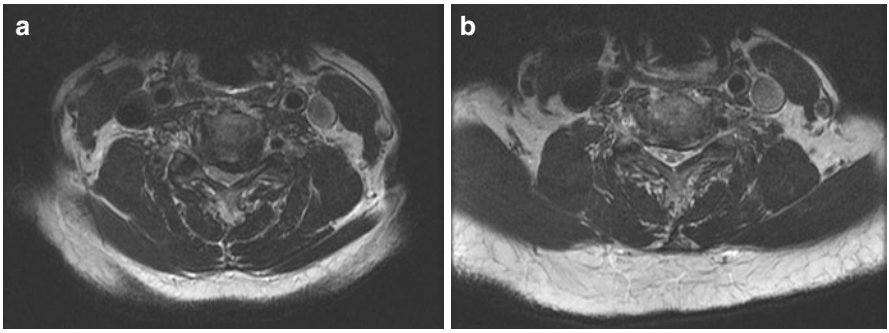

Fig. 11.2 (**a**, **b**) T2-weighted axial projections of our patient's cervical spine MRI, through the cervical 4–5 disc space (**a**) and cervical 5–6 disc space (**b**). These demonstrate the circumferential nature of the degenerative changes resulting in severe spinal canal stenosis, namely disc herniations ventrally and facet joint and ligamentum flavum hypertrophy dorsally. Hyperintense T2 signal within the spinal cord at the cervical 5–6 interspace (**b**) is consistent with cord edema

causing intracerebral dysfunction and/or tandem stenosis. If the patient does not currently have an identified primary malignancy, medical oncologic consultation should be sought for additional testing. Evaluation typically includes CT of the chest, abdomen, and pelvis with and without contrast. Since prostate cancer is a leading cause of metastatic spine disease in men, prostate specific antigen (PSA) testing should be considered. Hematologic malignancies should be evaluated with blood counts and additional testing as needed.

If infection is suspected, blood and urine cultures, and inflammatory markers such as white blood cell count with differential, erythrocyte sedimentation rate, and C-reactive protein should be obtained, and infectious diseases specialist consultation requested.

11.4 Clinical Decision-Making and Next Steps

The natural history of central cord syndrome is generally one of improvement, but the degree and time course of improvement is unknown at initial presentation. It is also possible for patients to plateau in their recovery and subsequently decline, given persistent spinal cord compression and canal stenosis. Over the decades, the surgical treatment paradigm has evolved from early recommendations for non-operative or delayed operative management, to current recommendations for urgent decompression of the stenotic region [1, 2, 5]. Indications for surgical intervention are especially strong in the face of a profound initial deficit or progression rather than improvement. If workup reveals a cervical spinal epidural abscess, this represents a neurosurgical emergency and mandates immediate evacuation and decompression, barring comorbid conditions that prevent anesthesia/surgery. It is important to counsel patients and/or family members that the primary goal of surgery in

central cord syndrome, as in cervical myelopathy, is to decompress the spinal cord to avoid secondary injury. Patients may experience improvement in function after surgery, possibly to the point of no impairment, but currently available diagnostic modalities do not permit predicting the extent and timeline of improvement. Hand function, in particular, is often the last and least likely to improve [1].

Surgery for central cord syndrome can entail anterior, posterior, or combined decompression strategies. The specific approach should be tailored to the location of stenosis (levels and anterior versus posterior), degree of cervical lordosis or kyphosis, body morphology that may impede an approach corridor, and the patient's ability to tolerate prone positioning. Spinal fusion is almost always performed concurrently, given the high rate of cervical spinal instability and kyphosis in the absence of fusion. Patients should be counseled that a risk of spinal fusion, particularly in the setting of degenerative disease, is adjacent segment disease which may require subsequent surgery and extension of fused levels.

Non-operative treatment may be considered in cases of minimal or self-limited symptoms and in patients with significant medical comorbidities. However, close clinical follow-up remains essential, and deterioration should prompt a recommendation to intervene. If the patient had cervical myelopathy or radiculopathy prior to developing central cord syndrome, they should be counseled that they would be unlikely to improve beyond this baseline, and if pre-injury symptoms were already causing a reduction in quality of life or functional status, surgery should be strongly considered.

Given that several months had passed since symptom onset and our patient continued to have a significant impairment with activities of daily living, we advised operative decompression and stabilization. With focal compression at the cervical 4–5 and 5–6 levels, we recommended an anterior cervical diskectomy and fusion at these levels, with post-operative occupational therapy to maintain and hopefully improve upper extremity function.

11.5 Clinical Pearls

- Central cord syndrome is characterized by profound upper extremity dysfunction with relatively preserved lower extremity function, paradoxical to typical presentation of symptoms distal to the level of a spinal cord injury.
- Central cord syndrome often occurs in the absence of bony fracture of the cervical spine and is related to a hyperextension injury in a cervical spinal canal with pre-existing stenosis, typically due to chronic degenerative disease.
- Whereas non-operative or delayed operative treatment was advocated previously, the most common current surgical strategy is one of early operative decompression and stabilization for patients with more than mild or transient deficits.

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Chapter 12
Peripheral Nerve Injury

Yong Shen and Christopher J. Winfree

Clinical Scenario

A 49-year-old male with no significant past medical history presents to the Emergency Department (ED) following an assault with a kitchen knife. He reports being stabbed in the back of the left thigh during the altercation. Immediately afterward, he developed numbness and weakness below the left knee. Neurological examination in the ED shows loss of ankle and toe dorsiflexion, as well as plantarflexion, ankle inversion and eversion, and numbness below the knee sparing the saphenous territory.

12.1 History and Neurologic Exam

This patient likely sustained a lacerating injury to one of his lower extremity nerves. When possible, the nerve surgeon should inquire about the nature of the instrument that caused the nerve injury to allow classification of the nerve injury (sharp v. blunt) and determine the best course of treatment (direct v. graft repair). In this case, the patient reported that the assailant used a sharp kitchen knife. Kitchen knives tend to be slender and relatively sharp, which will cleanly divide the affected nerve. Scalpel blades and glass fragments also tend to cleanly divide nerves. This distinction is important because cleanly divided nerves should be surgically repaired within 72 h of injury, if possible, to limit the amount of nerve retraction that occurs

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_12

after injury. If the nerve ends are allowed to retract too much prior to repair, an interposition graft may become necessary to allow for a tension-free repair. Thus, the timing of the injury is important to note, as it has implications in the management of this patient. Had the patient presented to the ED 2 weeks after being stabbed rather than immediately thereafter, the surgical management would likely be somewhat different.

In contrast to sharp lacerating injuries, blunt lacerating injuries occur when the nerve is divided by a relatively jagged and/or dull instrument. Examples include lawnmower blades, chain saws, and jagged metal in car accidents. The rough edges of these instruments tend to traumatize the cut ends of the severed nerve, resulting in the dying back of the cut ends. It is best to wait a few weeks for this dying back process to occur prior to performing definitive nerve repair; otherwise, the nerve repair might disintegrate and fail. As for the delayed repair noted above, the surgeon should be prepared to perform an interposition graft repair of a blunt lacerating injury.

The timing of symptom onset is also important to note. An immediate loss of neurological function that occurs after the penetrating injury would suggest a direct laceration to the nerve. If the development of neurological deficits occurs in the minutes or hours after the penetrating injury, then that might indicate nerve compression from an expanding mass lesion such as a hematoma or pseudoaneurysm rather than a lacerating nerve injury. These conditions would be managed somewhat differently than a simple nerve repair.

As one would do for any new patient, one should inquire about past medical history to determine perioperative risks. The presence of a coagulopathy or mechanical heart valve, for example, could complicate surgical management of this patient. The presence of diabetes might have implications for wound healing and the likelihood of ultimate nerve recovery.

The physical examination is important for several reasons. The pattern of neurological deficits and location of the penetrating injury will help determine which nerve was injured and at which level. This will be obvious in cases where there is only a single entrance wound but will become more challenging in the context of multiple wounds. A careful sensory and motor examination can help clarify which wound(s) caused the nerve injury, and thus, which wound(s) should be surgically explored. A careful examination may also reveal other injuries such as vascular wounds and muscle tears, which may necessitate the involvement of other subspecialists during surgical exploration.

This patient has a single entrance wound along the back of the distal left thigh, in close proximity to the sciatic nerve, and presents with an examination consistent with a sciatic nerve injury at a distal thigh level (Fig. 12.1). There is no indication that any other nerves were involved or that there is any more proximal level of injury. Thus, surgical exploration would likely be limited to the sciatic nerve at the injured level and not be required elsewhere.

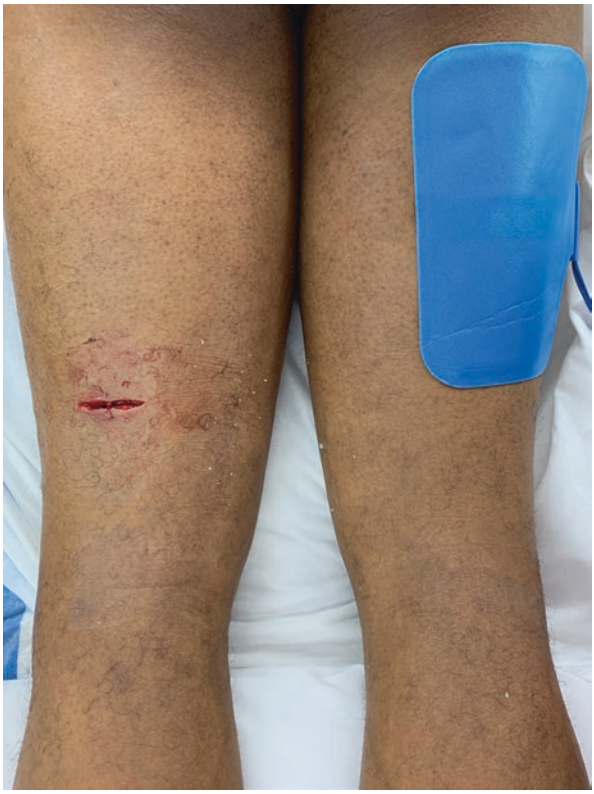

Fig. 12.1 Intraoperative photograph demonstrating the penetrating knife injury along the posterior aspect of the distal left thigh

12.2 Differential Diagnosis

Because this patient presented with a single penetrating injury and reported the immediate onset of neurological deficits, the differential diagnosis is fairly limited. Had the patient been in a rollover motor vehicle accident with multiple crush and penetrating injuries to the lower extremities, the differential would be more extensive. A stretch injury to the lumbosacral plexus could yield a nerve root avulsion injury at a spinal level or simply a nerve stretch injury at a plexus level within the pelvis. A traumatic hip dislocation could stretch or compress the sciatic nerve at the hip level. Alternatively, a thigh hematoma could compress the nerve at that level. A hyperextension knee injury or ankle inversion injury could stretch the nerves in the leg as well, resulting in focal nerve injuries at a variety of levels. Note also that compartment syndromes can result in neuromuscular dysfunction that may mimic focal nerve injuries. Below, we discuss some additional types of peripheral nerve injuries, such as missile injury, compressive injury, and iatrogenic injury, that are helpful to consider during the development of a differential diagnosis, as well as some disease processes that can mimic acute peripheral nerve injury.

12.2.1 Missile Injury

Missile injury is a cause of acute peripheral nerve injury in areas of the world where firearms or other weapons can be accessed. Usually, a missile injury can be diagnosed fairly and easily based on information from the patient's history, the visible missile wound on physical exam, and findings on imaging studies. Missile injury can be caused by low-velocity missiles (from handguns, shell fragments, etc.) or high-velocity missiles (from military and/or hunting rifles, machine guns, etc.). Low-velocity missiles damage peripheral nerves by direct impact, small shock waves, and/or temporary cavitation. High-velocity missiles damage peripheral nerves to a greater extent, due to the high kinetic energy missile creating a shock wave and cavitation that can compress and stretch the nerves. In addition, high-velocity missiles confer greater damage to surrounding soft tissues such as blood vessels, bones, and muscles. Spontaneous recovery occurs in some missile injury cases, unless the missile damage transects fully the peripheral nerve [1]. If the nerve has been transected, then the nerve injury should be treated as for a blunt lacerating injury several weeks after the injury, as described above. If the injured nerve remains in continuity, then the nerve should be allowed to undergo spontaneous recovery for 3–6 months. If no recovery occurs in that time frame, then the nerve should undergo surgical exploration and possible graft repair [2].

12.2.2 Compression Injury

Compression injury is a common type of peripheral nerve injury that occurs due to a compressive force impinging on the nerves and resultant ischemia. In severe cases, the compressive force can disrupt the structure of the nerve as well. In compressive injuries, the nerve is not transected, and nerve continuity is maintained. Compression could result from several circumstances, such as retained foreign bodies and fracture fragments at the time of injury. Compression can also result from iatrogenic mechanisms, such as intraoperative suture ligation, bony instrumentation, or mechanical compression from muscle mispositioning [3]. In addition, hematomas or pseudoaneurysms could result in compression injury to nerves as well.

If an acute compression nerve injury is suspected, a thorough physical exam appropriate to the area in which the injury is likely to be found should be conducted. Imaging techniques such as X-ray, CT, and MRI could be used to investigate the site of injury. Given the acute nature of these lesions, electrodiagnostic studies are not typically part of the diagnostic evaluation.

When a patient presents with neurological deficits in the setting of an acute compressive lesion, a decision needs to be made whether to proceed with surgical decompression of the nerve. Outcomes for acute compression nerve injury surgery are related to timing. If appropriate surgical treatment is delayed, nerve damage can

become irreversible, leading to permanent nerve injury [4]. In theory, it would seem to be a straightforward decision to decompress any compressed nerve in a patient with significant neurological deficits. In reality, the risks of the procedure need to be balanced with the possible benefits. For example, it is a straightforward endeavor to drain a hematoma from the forearm of a young and healthy trauma patient with a compressive hematoma, median nerve compression, and hand weakness. It is not so straightforward to surgically decompress a retroperitoneal hematoma in an elderly, frail, and coagulopathic cardiac patient with a compressive femoral neuropathy after a cardiac stent procedure.

In addition to hematomas causing compression injury to peripheral nerves, traumatic pseudoaneurysm represents a relatively rare cause of acute peripheral nerve compression. A lesion to the arterial wall could lead to intramural blood accumulation, resulting in a thrombosed pseudoaneurysm. Compression of an adjacent peripheral nerve by the thrombosed pseudoaneurysm can result in nerve dysfunction. Typically, these lesions occur in patients after vascular access procedures [5, 6], after blunt trauma, or penetrating injuries [7, 8]. Imaging techniques such as ultrasonography, MRI, and/or CT may be helpful in delineating the anatomy of the vascular lesion. Depending on the severity of the pseudoaneurysm and/or hematoma, less invasive approaches such as ultrasound-guided decompression, ultrasound-guided thrombin injection, endovascular techniques such as embolization and stent-graft placement could be used to treat the thrombosed pseudoaneurysm and release nerve from compressive force. In severe cases, the aneurysm should be resected surgically to release the nerve from compression. At our center, these cases are typically done as collaborative procedures between vascular surgery and peripheral nerve surgery. In most cases, treating the pseudoaneurysm leads to substantial recovery of peripheral nerve function.

12.2.3 Iatrogenic Injury

Iatrogenic peripheral nerve injury may be important to consider under the appropriate clinical circumstances. Mechanisms of injury include stretch, compression, laceration, or disruption by bone fragments or instrumentation [9]. In addition to operative nerve injuries, perioperative nerve injury could result from nerve compression or retraction due to the positioning of patients [10].

The treatment of iatrogenic peripheral nerve injuries should follow the principles outlined above for non-iatrogenic causes. One advantage of the iatrogenic situation occurs when a witnessed, intraoperative acute sharp lacerating nerve transection occurs. In these cases, intraoperative consultation by a nerve specialist should be requested and the nerve repaired shortly after it is discovered while the nerve ends are still surgically exposed [9].

Although a number of medicolegal issues can be present in the setting of iatrogenic nerve injuries, the basic underlying principles of diagnosis and repair do not

change. It is important to note that experimental evidence supports the use of immediate direct repair when possible [11], and clinical evidence suggests that patients are more satisfied when significant treatment delays are avoided [12].

12.2.4 Non-traumatic Mimics of Injury

Finally, it is important to note that other neurological conditions may mimic the presentation of peripheral nerve injuries. For example, an immune-mediated plexopathy such as Parsonage-Turner syndrome can cause acute pain, followed by weakness and sensory loss that resemble the manifestations of an acute peripheral nerve injury. Guillain-Barré syndrome, an acute heterogeneous syndrome, can also cause progressive muscle weakness and absent or reduced deep tendon reflexes that may resemble peripheral nerve injury. In order to distinguish these mimics from true peripheral nerve injuries, the clinician should focus on the patient's history to assess whether the manifestations are consistent with the proposed mechanism of nerve injury. The clinician should also pay attention to the physical exam and, in particular, to the pattern of deficits—whether localized or diffuse in distribution. A pattern of patchy, widespread neurological deficits that are inconsistent with the proposed mechanism of injury, or patterns of neurological deficits and symptoms common to a known disorder such as Guillain-Barré syndrome, should raise the suspicion of an immune-mediated plexopathy or immune-mediated neuropathy mimicking an acute peripheral nerve injury.

12.3 Diagnostic Evaluation

There are a number of diagnostic tools available to optimize the care of this patient. For a straightforward case as this, the history and physical examination may be sufficient to plan an effective surgical treatment. There are circumstances, however, where some additional information might be useful.

Plain X-rays, ultrasound, or CT scanning of the injury site can reveal the presence of foreign bodies within the tissues. Retained metal or glass fragments can not only contribute to further tissue injury, but they might also injure the surgical team during exploration. Retained foreign bodies can be a source of postoperative infection if not removed. Also, retained foreign bodies within the injured nerve can contribute to postoperative neuropathic pain if not removed.

A high-resolution diagnostic ultrasound examination of the nerve can delineate the exact location of the nerve injury. Ultrasound has been shown in studies to provide reliable visualization of nerve injury in most patients, as well as findings such as neuroma formation, axonal swelling or damage, and partial laceration of the nerve [13]. In the case presented here, given the knowledge that some kitchen knives can be quite long and that the sciatic nerve is located fairly deep within the thigh, it is quite possible that the nerve injury did not occur immediately subjacent to the

skin laceration. Knowledge of this would help ensure adequate exposure of the sciatic nerve during surgical exploration.

It would also be useful to know if there are associated vascular injuries prior to embarking on a surgical exploration. Yes, blundering into a vascular injury in the middle of the night can be exciting, but it is quite inconvenient, especially if your vascular surgery colleague is sound asleep at home during your surgical adventure. Vascular imaging, with some combination of ultrasound and/or CT angiography, would be helpful in cases where the injury mechanism might conceivably involve a vascular structure. MR neurography is also increasingly used due to its high-resolution views of nerves and their associated structures, such as vessels, and the ability to distinguish compressive lesions from other forms of lesion [14].

Vascular imaging is also helpful to assess the anatomy when the neurological deficits occur gradually after the penetrating injury occurs. Expansile hematomas and pseudoaneurysms can compress nerves and mimic penetrating nerve injuries. As described above, the treatment of these conditions involves different treatment steps compared to direct nerve suture repair (discussed in Sect. 12.3).

The use of electrodiagnostic studies is not warranted for the majority of acute nerve injuries. It usually takes about 2–3 weeks for denervation changes to occur in the affected muscles following a nerve injury. Thus, while these studies can be helpful in clarifying the extent of injury weeks or months following the nerve injury, they do not alter surgical decision-making in the hours to days following nerve injury.

12.4 Clinical Decision-Making and Next Steps

Our patient underwent CT angiography, which did not reveal the presence of foreign bodies, compressive hematoma, or vascular injury. Thus, the patient was taken for immediate surgical exploration for definitive nerve repair of his sciatic nerve transection. At surgery, the skin laceration was extended for several centimeters along the course of the sciatic nerve above and below the expected nerve injury site. The sciatic nerve was identified and was noted to be cleanly severed at the predicted site (Fig. 12.2). The ends were mobilized and sutured together—with the use of the operating microscope—using fourteen 7-0 Prolene sutures (Fig. 12.3). Given that only a few hours had elapsed since injury, the nerve ends had not appreciably retracted and were easily brought together in a tension-free fashion. During the repair, the nerve ends were lined up to match each proximal and distal fascicle to minimize the risk of mismatch, where sensory fibers are routed down motor bundles (and vice versa). An incidental hamstring muscle laceration was incidentally discovered and repaired as well. The patient was kept in a knee splint for 3 weeks postoperatively to minimize the risk of the patient ripping the anastomosis apart during the healing process.

As the patient case demonstrates, clinical management of lacerations depends on a variety of factors. Lacerations that produce sharp nerve division with minimal gap between nerve segment ends should be treated by direct nerve repair, also known as neurorrhaphy [13]. Neurorrhaphy should be attempted if the gap between nerve

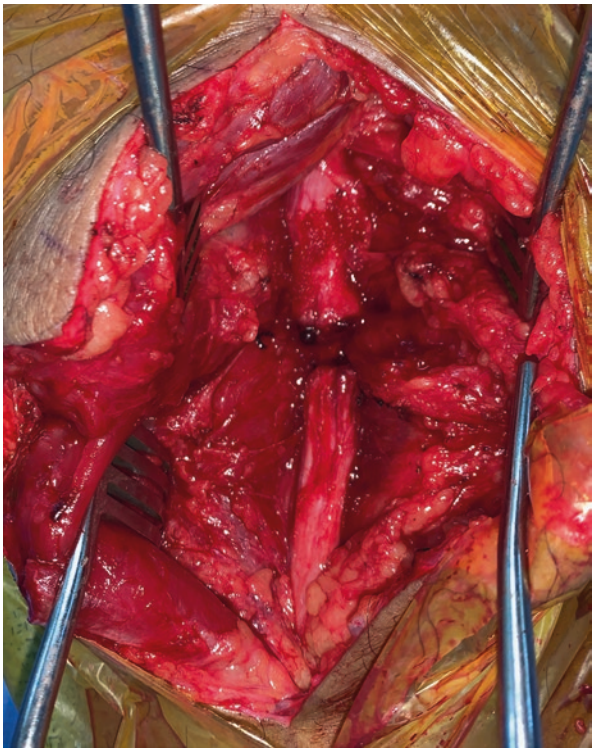

Fig. 12.2 Intraoperative photograph taken after initial surgical exposure of the sciatic nerve at the injured level. Several centimeters of normal nerve above and below the injury are also demonstrated. The nerve has been sharply divided at the injured level. Note the minimal retraction of the nerve ends. The top of the figure is rostral; left is lateral

ends is less than 2–2.5 cm. Tension-free suture repair is the preferred method for nerve injury direct repair, as it has been found to be a major factor in sensorimotor recovery following nerve repair. Direct end-to-end repair generally offers the best outcome, with about 90% of repaired nerves achieving functional recovery.

If the gap exceeds what is possible for a tension-free neurorrhaphy, there are a number of different options available. One option is to place the affected extremity in a position of flexion to permit direct end-to-end repair [15]. The extremity is splinted in the flexed position and then gradually extended over several weeks post-operatively. Another option is to perform a nerve transposition to free up extra length to allow the nerve ends to come together. This strategy is often done for ulnar nerve injuries at or near the elbow [15], with about 2–5 cm gains from transposition combined with feasible elbow and wrist flexion [16].

In cases where there is no possibility of achieving direct end-to-end repair, then a graft may be necessary [13]. For larger gaps, autologous nerve graft remains the current standard of care. However, due to donor-site morbidity associated with autologous nerve grafting, many neurosurgeons have become interested in the use of conduits for laceration repair. Historically, veins were one option for a nerve repair conduit while more recently, synthetic tubular conduits have been used [13]. Currently, processed nerve allograft can be used with good results for short segment nerve gaps up to 50 mm in length, with recent evidence supporting up to 70 mm in length [17].

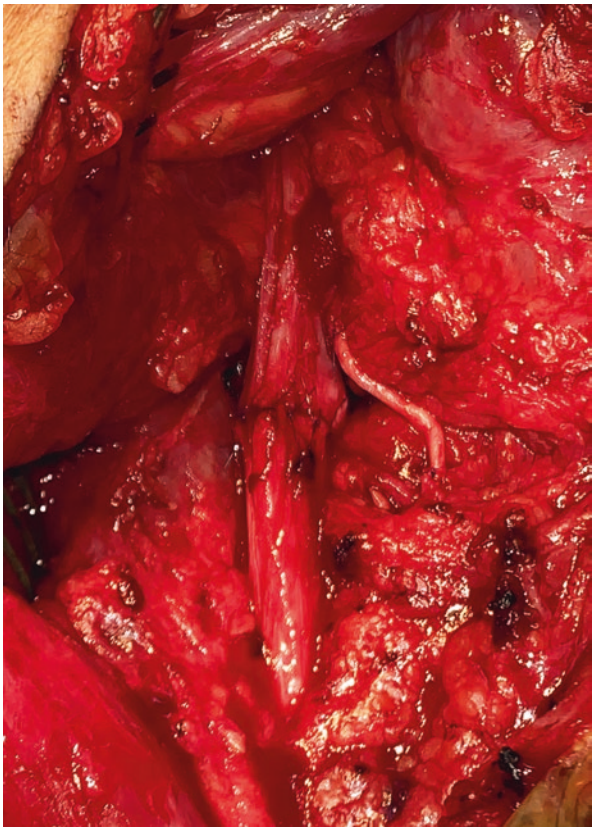

Fig. 12.3 Intraoperative photograph taken after surgical repair of the sciatic nerve at the injured level. The nerve ends have been approximated in a tension-free, end-to-end fashion using multiple 7-0 Prolene sutures. Care has been taken to align the proximal and distal fascicles to avoid mismatch. The top of the figure is rostral; left is lateral

Finally, minor peripheral nerve injuries, especially those at the common sites of nerve entrapment such as the carpal tunnel and cubital tunnel, can result in delayed complications (i.e., nerve entrapment). These nerve entrapment complications can develop weeks after the original nerve injury event, as fibrotic scarring processes begin in and around the nerve to cause compression of the nerve. Should the patient develop these delayed complications, the clinician can gauge the severity of the nerve entrapment and offer the appropriate treatments, whether nonsurgical or surgical.

12.5 Clinical Pearls

- Immediate onset neurological deficit following a penetrating injury mechanism suggests a lacerating nerve injury.
- Sharp lacerating nerve injuries should be repaired within 3 days of injury to limit the risk of nerve retraction and allow for tension-free end-to-end nerve repair.
- Immediate onset neurological deficit following a nonpenetrating injury mechanism suggests a stretch injury to the nerve.

- Delayed onset neurological deficit in the hours following a penetrating injury mechanism suggests the presence of a compressive expansile hematoma or pseudoaneurysm.
- The possibility of an autoimmune plexopathy should be considered in the setting of a delayed onset neurological deficit in the days (or weeks) following an injury, especially if the pattern of deficit is patchy, widespread, and/or is inconsistent with the proposed mechanism of injury.
- Minor nerve injuries, especially at sites normally associated with nerve entrapments, may result in nerve entrapments that develop over weeks as scar forms in and around the nerve and contribute to compression.
- Soft tissue imaging can help to clarify the anatomy of the nerve injury, the presence of foreign bodies, and any associated soft tissue injuries.

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Part II
In the Emergency Department

Chapter 13
Ischemic Stroke

Dimitri Laurent, Coulter N. Small, Michael Goutnik, and Brian Hoh

Clinical Scenario

An 86-year-old, right-handed Caucasian woman is brought into the Emergency Department (ED) by ambulance as a stroke alert. Her daughter accompanies her and states that she was last seen to be neurologically normal at 11:00 PM the night before when she went to bed. This morning, at 7:30 AM, her daughter found her unable to get out of bed. EMS reported that she had right gaze preference, slurred speech, left facial droop, and left hemiparesis. Immediately upon arrival, she undergoes neurologic evaluation by the vascular neurologist and is found to have a National Institutes of Health Stroke Scale (NIHSS) score of 10. The past medical history includes hypertension and diabetes. Her only home medications are amlodipine and aspirin. Her vital signs and blood pressure are within normal limits.

13.1 History and Neurologic Examination

For this patient who woke with new neurologic deficits, there is concern that she suffered an ischemic stroke during sleep. Acute ischemic stroke (AIS) is a neurologic emergency. It is important that clinicians are able to immediately recognize the signs of acute ischemic stroke and act expeditiously. Each minute brain tissue is deprived of oxygen, an estimated 1.9 million neurons are lost [1]. The mainstays of treatment of acute ischemic stroke are intravenous alteplase (IV-tPA) and

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_13

mechanical thrombectomy; therefore, much of the initial evaluation centers around establishing whether the patient is appropriate for these interventions.

Current guidelines dictate the administration of IV-tPA for adult patients (over age 18) with an ischemic stroke who present within 3 h of symptom onset [2]. Recent studies suggest that tenecteplase (another fibrinolytic agent) may be superior to alteplase for vessel recanalization and non-inferior at 3 months with respect to disability outcome; however, alteplase is the only FDA-approved agent at this time [3]. IV-tPA is also indicated for selecting patients presenting between 3 and 4.5 h after symptom onset who meet certain criteria (age <80, without a history of diabetes mellitus or prior stroke, with NIHSS score <25, not taking oral anticoagulants, and without evidence of ischemia involving greater than 1/3 the territory of the middle cerebral artery) [2, 4]. A series of recent randomized controlled trials have proven definitively the benefit of mechanical thrombectomy for the treatment of this disease (Table 13.1) [5–12]. As few as three patients are needed to undergo this intervention in order to see benefit [13].

All patients who present with signs of acute ischemic stroke should undergo a quick, yet thorough history and neurologic examination that includes the following information:

- *Timing*: It is important to ascertain when the patient was last observed to be at neurologic baseline. For patients who awaken from sleep with new neurologic deficit, the timing of stroke is unclear. In these scenarios, magnetic resonance imaging (MRI) of the brain helps to identify patients who are likely to have had a stroke within 4.5 h and are candidates for fibrinolytic therapy. Diffusion weighted imaging that demonstrates a region of restriction (bright spot) that is not hyperintense (bright) in the same area on fluid attenuated inversion recovery (FLAIR) sequence suggests stroke within the past 4.5 h [14]. Current guidelines, based on a moderate quality of evidence, indicate that MRI can be useful in guiding treatment with IV-tPA [2]. For patients with symptom onset less than 6 h from presentation, noninvasive computed tomography angiography (CTA) or magnetic resonance angiography (MRA) should be performed to identify large vessel occlusions and characterize vascular anatomy prior to mechanical thrombectomy. Patients who present 6–24 h after symptom onset are recommended to undergo perfusion imaging to help quantify the volume of reversible brain tissue injury [2].
- *Neurologic symptoms*: Patients suffering an acute ischemic stroke present with sudden onset of neurologic deficits. Inquire about unilateral weakness or numbness (face, arm, or leg); confusion, difficulty speaking, or understanding; visual changes; gait instability, dizziness, imbalance, or loss of coordination; severe headache, nausea, or vomiting; and changes in level of consciousness. The presence of severe headache, nausea, and emesis suggests the presence of a space-occupying lesion or hydrocephalus, which can often mimic an ischemic event. Stroke scales accurately quantify the extent of neurologic deficit, facilitate communication, and identify patients who are candidates for mechanical thrombectomy and fibrinolytic therapy [2]. The NIHSS is a validated, reliable clinical

Table 13.1 Summary of the major randomized clinical trials that have demonstrated the superiority of mechanical thrombectomy over medical management for ischemic stroke

Trial	Year	Principal finding	Primary outcome measure(s)	Imaging modality for infarct volume
DAWN	2018	Endovascular thrombectomy and standard medical therapy 6–24 h after acute ischemic stroke resulted in better outcomes than medical therapy alone	Score on utility-weighted mRS at 90 days	DW-MRI, CT perfusion
DEFUSE 3	2017	Endovascular thrombectomy and standard medical therapy 6–16 h after acute ischemic stroke resulted in better outcomes than standard medical therapy alone	Score on mRS at 90 days	DW-MRI, CT perfusion
ESCAPE	2015	Endovascular therapy and medical therapy improved outcomes compared to medical therapy alone	Score on mRS at 90 days	CTA, non-contrast CT
MR CLEAN	2015	Intraarterial treatment and standard medical therapy within 6 h of acute ischemic stroke improved outcomes compared to medical therapy alone	Score on mRS at 90 days	CTA, MRA, non-contrast CT
EXTEND IA	2015	After administration of alteplase, endovascular thrombectomy, less than 4.5 after acute ischemic stroke, improved outcomes compared to continued administration of alteplase alone	Reperfusion at 24 h; early neurological improvement (≥8-point reduction on the NIHSS or a score of 0 or 1 on day 3)	CT perfusion
REVASCAT	2015	Endovascular thrombectomy and standard medical therapy within 8 h after acute ischemic stroke improved outcomes compared to standard medical therapy alone	Score on mRS at 90 days	DW-MRI, non-contrast CT
SWIFT PRIME	2015	Endovascular thrombectomy and standard medical therapy within 6 h after acute ischemic stroke improved outcomes compared to standard medical therapy alone	Score on mRS at 90 days	CTA, MRA

Source: Nogueira et al. [5], Albers et al. [6], Goyal et al. [7], Berkhemer et al. [8], Goyal et al. [9], Jovin et al. [10], Saver et al. [11], Campbell et al. [12]

assessment to evaluate stroke patients that helps to determine appropriate treatment and prognosticates [15–19]. Furthermore, the NIHSS is the best predictor of future independence and mortality in ischemic stroke patients [20–23].

- *Laboratory analysis*: Hypoglycemia (<50 mg/dL) is the only laboratory finding that should delay the administration of IV-tPA [2]. Hypoglycemia may cause altered mental status that can mimic stroke. Fortunately, glucose levels are

readily obtained via point of care testing in the emergency setting. Baseline troponins should be measured, and a coagulopathy workup should be obtained. In the absence of suspected coagulopathy, one should not await the results of these tests to administer treatment. However, thrombocytopenia (platelet count <100,000 mm^3), elevated International Normalized Ratio (INR >1.7), prolonged activated partial thromboplastin time (aPTT >40 s), and prolonged prothrombin (PT >15 s) are contraindications to IV-tPA [2, 4].

- *Vital signs*: Vital signs should be measured as part of any evaluation in the emergency setting. Patients who are candidates for fibrinolytic should have blood pressure lowered to a target of 185/110 mmHg prior to administering IV-tPA [2]. Blood pressure goals are more liberal for patients not receiving fibrinolytic therapy when there are no comorbid conditions requiring urgent treatment of hypertension (such as an intracranial hemorrhage). It may be reasonable to lower blood pressure by 15% in the first 24 h for patients presenting with a blood pressure greater than 220/120 mmHg. For patients who present with a blood pressure less than 220/120, treatment of hypertension within the first 48–72 h does not improve outcomes [2].
- *Medical history*: IV-tPA should not be administered to patients who have had a stroke within the past 3 months, severe traumatic brain injury within the past 3 months, intracranial or intraspinal injury within the past 3 months, prior history of intracranial hemorrhage, or gastrointestinal hemorrhage or malignancy within the past 3 months [2, 4].
- *Medications*: Patients who have received therapeutic doses of low molecular weight heparin (LMWH) within 24 h should not receive IV-tPA. Patients receiving direct thrombin inhibitors (IIa) or factor Xa inhibitors should not receive IV-tPA unless coagulopathy has been excluded or the patient is confirmed not to have received the drug for at least 48 h and has normal renal function [2, 4].

Other parts of the history may further help guide treatment. These are largely unique scenarios but can provide invaluable information if recognized and communicated to the neurologic team. For example, patients with a history of peripheral vascular disease may have known arterial occlusions that may necessitate alternative access sites during endovascular thrombectomy. In addition, stroke is a recognized complication of coronary angiography [24]. Onset of neurologic deficit may be recognized before completion of the cardiac catheterization. The presence of an arterial sheath obviates a step for thrombectomy, and may shorten the time to clot removal by the neurointerventionalist.

13.2 Differential Diagnosis

This particular patient is an elderly woman who presents with acute onset of left-sided neurologic symptoms that would be referrable to the right cerebral hemisphere. Right gaze preference suggests dysfunction of the right frontal eye fields.

The left hemiparesis, facial droop, and dysarthria localize to the right primary motor cortex. The left hemibody numbness localizes to the right primary somatosensory cortex. Based on this constellation of findings, she is suspected to have a right middle cerebral artery stroke.

A patient who presents with an atraumatic, rapid-onset neurologic deficit is presumed to have an AIS until proven otherwise. AIS is increasingly common in older patients—the incidence doubling every decade after age 55 [25, 26]. Elderly patients presenting with new onset seizure should also be suspected to have had a stroke, as cerebrovascular disease represents the most common cause of newly acquired epilepsy in this population [27, 28]. When a patient's initial presentation is accompanied by severe headache, nausea, or emesis, one should suspect a hemorrhagic stroke, a space-occupying lesion, or hydrocephalus. Hemorrhagic stroke includes intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Primary and secondary brain tumors can present with both neurologic deficits and seizure and should remain on the differential [29].

In the pediatric population, sickle cell anemia is the most common etiology of AIS [30]. Rarely, AIS may have a viral association. There are multiple reports of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—the virus responsible for the COVID-19 outbreak—in association with acute ischemic stroke [31–34]. Non-structural causes of acute neurologic deficit that may present similarly in the elderly include psychosis, hypoglycemia, migraine headache, meningitis, encephalitis, pneumonia, and urinary tract infection [35–37].

AIS represents 87% of all strokes, whereas ICH and SAH account for 10% and 3%, respectively [25, 26]. It is important to discriminate among AIS, ICH, and SAH as the management varies drastically for these three stroke types. The diagnosis will become apparent on initial cranial imaging.

13.3 Diagnostic Evaluation

The patient in this case scenario underwent a focused history and neurologic examination with documentation of an NIHSS score. A non-contrast CT head was performed, demonstrating no acute intracranial hemorrhage (Fig. 13.1a). Furthermore, the Alberta Stroke Program Early CT Score (ASPECTS) was calculated and found to be greater than six. CTA of the head and neck was performed with advanced imaging. She was found to have right MCA stroke with ischemic penumbra (Fig. 13.1b, c).

Patients suspected of AIS are immediately evaluated by a multidisciplinary team comprised of vascular neurologists, specialized nursing staff, and other personnel. The physician will perform a focused history and physical examination to establish a baseline NIHSS. Labs will be drawn, and the patient will undergo dedicated cranial imaging with subtle variation depending on hospital capabilities and institutional practice patterns.

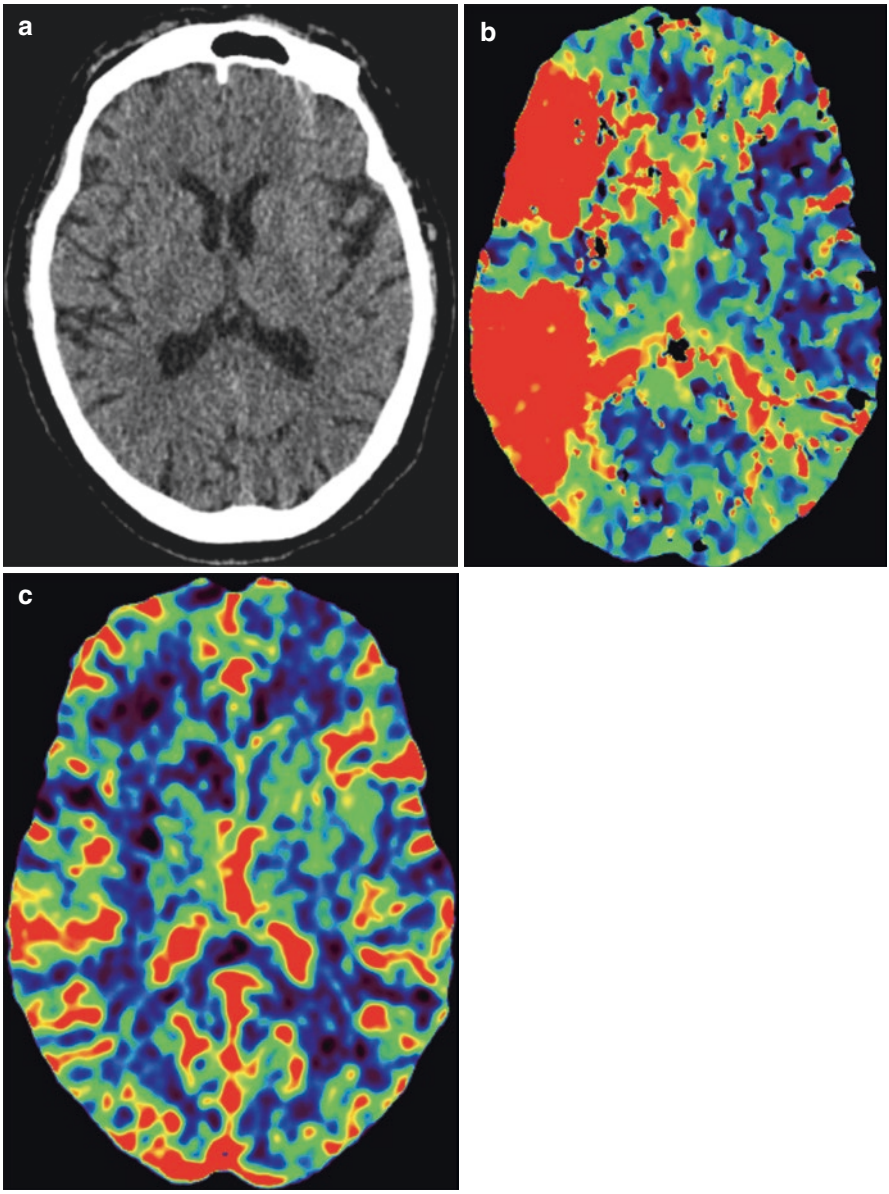

Fig. 13.1 (**a**) Non-contrast CT head demonstrates no evidence of intracranial hemorrhage. (**b**) CT head perfusion sequence demonstrates an increase time to peak in the distribution of the right middle cerebral artery. This is represented as red in the distribution of the right middle cerebral artery. (**c**) CT head perfusion demonstrates preserved blood volume in the right middle cerebral artery. Low blood flow would be represented as dark blue, as is seen in the subcortical white matter under normal physiologic conditions. The finding of increased time to peak in the setting of preserved cerebral blood volume suggests the presence of an ischemic penumbra

A non-contrast CT head is mandatory. This will indicate the presence of an intracranial hemorrhage—which is a direct contraindication for IV-tPA. Furthermore, large volume parenchymal hypodensity is consistent with completed stroke. Fibrinolytic therapy is not indicated in these patients as outcomes are poor, irrespective of treatment. A hyperdense blood vessel noted on CT head often represents the site of vascular occlusion. The non-contrast CT head also allows for calculation of the ASPECTS—a ten-point quantitative score to determine the extent of irreversibly damaged brain in stroke due to middle cerebral artery occlusion (Table 13.2) [38]. The middle cerebral artery territory is divided into ten brain regions, with a point deducted for each region of brain affected by stroke on non-contrast CT head. Current American Heart Association and American Stroke Association guidelines only recommend mechanical thrombectomy for patients with ASPECTS of 6–10 [2]. ASPECTS has high inter-observer reliability, and lower scores predict an increased likelihood of hemorrhagic conversion of infarct, future functional dependence, and mortality [38–41].

Table 13.2 ASPECTS allows for determination of the extent of irreversibly damaged brain tissue in the setting of a middle cerebral artery stroke. The scoring system is based on ten anatomic territories that might be impacted by such a stroke, as documented by the initial non-contrast CT head. Current guidelines recommend mechanical thrombectomy for a score ≥6

Alberta Stroke Program Early CT Score (ASPECTS)		
Structure	Ischemic change (score)	
Caudate	Yes (**−1**)	No (**0**)
Internal capsule	Yes (**−1**)	No (**0**)
Lentiform nucleus	Yes (**−1**)	No (**0**)
Insular ribbon	Yes (**−1**)	No (**0**)
Anterior MCA cortex (M1)	Yes (**−1**)	No (**0**)
MCA cortex lateral to insular ribbon (M2)	Yes (**−1**)	No (**0**)
Posterior MCA cortex (M3)	Yes (**−1**)	No (**0**)
Anterior cortex (M4)	Yes (**−1**)	No (**0**)
Lateral cortex (M5)	Yes (**−1**)	No (**0**)
Posterior cortex (M6)	Yes (**−1**)	No (**0**)

From an initial score of 10, calculate ASPECTS score; scores of ≤7 predict worse functional outcomes at 3 months, based on mRS

Source: Barber et al. [38], https://www.sciencedirect.com/science/article/pii/S0140673600022376?via%3Dihub

Patients should also undergo baseline neurovascular imaging to identify the patency of intracranial and cervical extracranial vessels. CTA can be completed at the time of the initial CT head. If a large vessel occlusion (LVO) is identified, and the patient has salvageable ischemic penumbra, the patient should be expeditiously transported to the angiography suite for mechanical thrombectomy. The decision to proceed to thrombectomy may be based on ASPECTS alone, but advanced perfusion imaging can further delineate the extent of ischemic penumbra. There is significant equipoise among stroke specialists about the utility of advanced imaging, as some physicians feel it may lead to unnecessary delay in vessel recanalization [42]. If a hospital has the capacity to rapidly process imaging to produce a perfusion scan, we feel that this provides excellent information with negligible harm to the patient. However, for patients presenting late—that is, greater than 6 h from last known normal—advanced imaging is recommended; perfusion imaging was obtained per protocol in randomized clinical trials demonstrating the benefit of delayed mechanical thrombectomy [2, 5, 6]. MRA brain, with accompanying DWI sequences, is a reasonable alternative at centers where MRI can be obtained expeditiously.

It is important to image the extracranial circulation as well. Patients may have extracranial cervical or carotid artery occlusions, tandem occlusions, or critical vessel stenosis that would warrant angioplasty or stenting at the time of intervention. Furthermore, imaging of the aortic arch to identify anatomical variants such as bovine arch, arteria lusoria (aberrant origin of the right subclavian artery distal to the left subclavian artery), or an anomalous origin of the vertebral artery can be helpful if identified prior to catheter angiography [43–45]. This allows for the interventionalist to best plan the operative approach to maximize the likelihood of successful, quick recanalization.

13.4 Clinical Decision-Making and Next Steps

In the present case, the patient was noted to have a right gaze preference. Right gaze preference with left hemibody deficits should cue the examiner to a large vessel occlusion. Specifically, such a constellation of neurologic deficits must encompass a sufficiently large vascular territory to affect the frontal eye fields (gaze preference), motor cortex or its fibers (motor deficits and dysarthric speech), and somatosensory cortex or its fibers (hemibody numbness or neglect). She was found to have an MCA stroke with ischemic penumbra on CTA perfusion (Fig. 13.1b, c). Her blood pressure was within normal limits; however, as a “wake up” stroke with uncertain timing of symptom onset, she was not a candidate for intravenous fibrinolytic therapy. The patient was immediately brought to the angiography suite for mechanical thrombectomy. We did not pursue MR imaging to assess candidacy for IV-tPA, as this would result in delay of mechanical thrombectomy. The America Heart Association and American Stroke Association provide guidelines to help with clinical decision-making in this setting (Table 13.3).

Table 13.3 Current guideline recommendations from the 2019 American Heart Association/American Stroke Association for mechanical thrombectomy in ischemic stroke

American Heart Association and American Stroke Association guidelines for mechanical thrombectomy for patients 0–6 h after acute ischemic stroke		
Recommendation	**SOR**	**SOE**
1. Patients should undergo mechanical thrombectomy with a stent retriever if they meet all the following criteria: (A) patient has a prestroke mRS score of ≤1; (B) the causative occlusion is of the ICA or MCA segment 1; (C) the patient is ≥18 years; (D) NIHSS score of ≥6; (E) ASPECTS of ≥6; and (F) treatment can be initiated ≤6 h of symptom onset.	Strong	Meta-analyses of high-quality RCTs
2. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for select patients with acute ischemic stroke caused by occlusion of the MCA segment 2 or MCA segment 3 if treatment can be initiated ≤6 h of symptom onset.	Weak	Randomized
3. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with acute ischemic stroke caused by occlusion of the ICA or MCA segment 1 and have a prestroke mRS score >1, NIHSS score <6, or ASPECTS <6 if treatment can be initiated ≤6 h of symptom onset.	Weak	Randomized
4. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for select patients with acute ischemic stroke caused by occlusion of the vertebral arteries, basilar artery, PCA, or ACA.	Weak	Limited data
American Heart Association and American Stroke Association guidelines for mechanical thrombectomy for patients 6–24 h after acute ischemic stroke		
Recommendation	**COR**	**LOE of QOE**
1. In patients with acute ischemic stroke who are 6–16 h from last known normal and have a large vessel occlusion in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	Strong	Meta-analyses of high-quality RCTs
2. In select patients with acute ischemic stroke who are 16–24 h from last known normal and have a large vessel occlusion in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	Moderate	Randomized

SOR strength of recommendation, *SOE* strength of evidence, *mRS* modified Rankin Scale, *ICA* internal carotid artery, *MCA* middle cerebral artery, *NIHSS* National Institute of Health Stroke Scale, *ASPECTS* Alberta Stroke Program Early Computed Tomography Score, *PCA* posterior cerebral artery, *ACA* anterior cerebral artery, *COR* class of recommendation, *LOE of QOE* levels of evidence vs. quality of evidence
Source: Powers et al. [2]

Once in the angiography suite, the neurointerventionalist must first determine the optimal site for arterial access. The femoral artery is most common, but transradial access for ischemic stroke is becoming increasingly popular [46–48]. For a basilar occlusion with a dominant right vertebral artery, a right transradial approach may be ideal. In addition, a right transradial approach may be preferable for patients with a bovine arch and a left anterior circulation stroke. A basilar

occlusion with a dominant left vertebral artery can be approached through a left transradial or a transfemoral approach. An arteria lusoria represents a contraindication for a right transradial approach. The use of ultrasound for radial artery catheterization has been demonstrated to increase the catheterization success rate in randomized controlled trials and is recommended as an adjunct for all transradial interventions [49]. Ultrasound also allows the surgeon to identify patients in which the ulnar artery provides the dominant perfusion of the distal extremity. In these patients, ulnar access is preferable and is a safe alternative to radial access [50].

Next, it is important to identify the presence of any tandem lesions on preoperative vascular imaging. When confronted with both an intracranial occlusion and an extracranial high-grade stenosis or occlusion, one must decide which lesion to address first. Tandem lesions are estimated to occur in 10–20% of LVOs [51]. No definitive data exist extolling the comparative benefit of treating intracranial or extracranial disease first [52–56]. The first priority is revascularization of the intracranial circulation to save brain tissue at risk. Therefore, we favor addressing the intracranial pathology first whenever possible. Once the patient has confirmed revascularization, we aim to increase cerebral perfusion by addressing flow-limiting extracranial stenosis and reduce the risk of future atheroembolic events by performing balloon angioplasty—with or without stenting. Prior to placing an extracranial stent, consideration should be given to administering dual antiplatelet therapy.

For this patient, CTA of the neck demonstrated occlusion of the right subclavian artery. She did not have any tandem lesions. She underwent right transfemoral angiography for her planned thrombectomy. Angiography confirmed occlusion of the right middle cerebral artery (Fig. 13.2a, b). She underwent mechanical thrombectomy with complete revascularization (Fig. 13.2c, d). Postoperatively, she was transferred to the neuromedicine intensive care unit. On postoperative examination, her NIHSS score was 0. She was discharged home on postoperative day 2, neurologically intact.

13.5 Clinical Pearls

- Any patient who presents with sudden onset of atraumatic neurologic deficit should be suspected of having an acute ischemic stroke until proven otherwise.
- Non-contrast CT head should be performed on all patients suspected of acute ischemic stroke to rule out the presence of intracranial hemorrhage.
- Mechanical thrombectomy has revolutionized stroke care with a number needed to treat as low as three patients.
- Time is brain! Stroke triage must be quick and efficient to minimize time to revascularization.

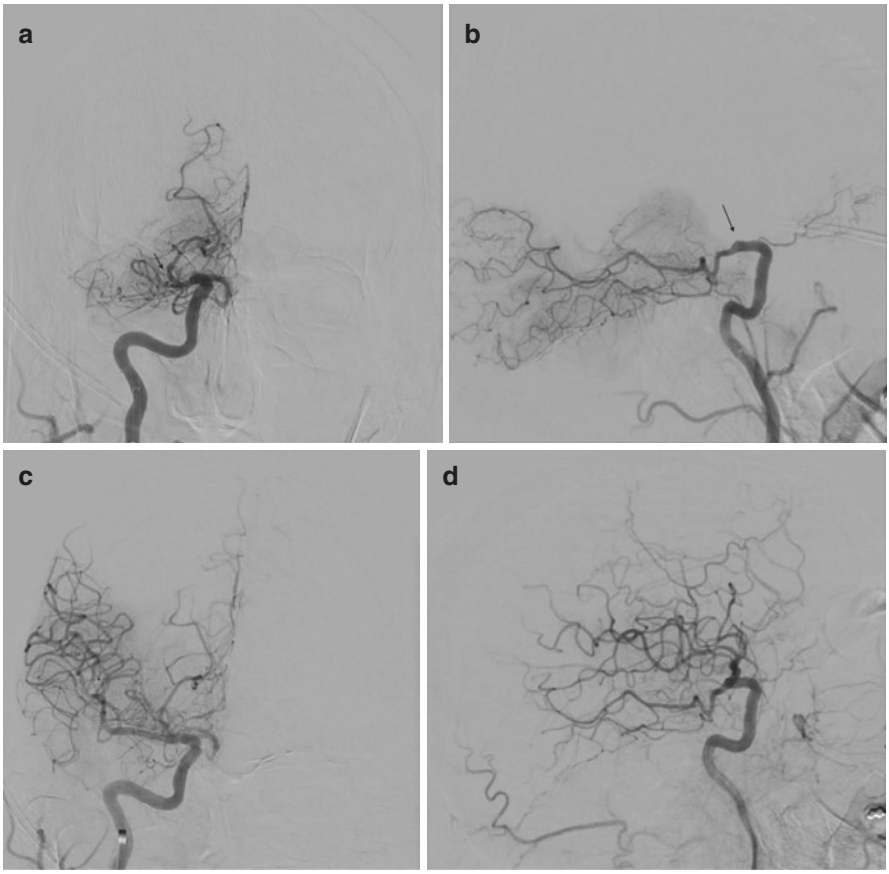

Fig. 13.2 (**a**, **b**) Right internal carotid artery anteroposterior (**a**) and lateral (**b**) injections demonstrate occlusion (arrows) of the right middle cerebral artery. (**c**, **d**) After mechanical thrombectomy is performed, repeat anteroposterior (**c**) and lateral (**d**) right internal carotid artery injections demonstrate revascularization of the occluded middle cerebral artery

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Chapter 14
Spontaneous Intracerebral Hemorrhage (Including Posterior Fossa)

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Clinical Scenario

A 58-year-old male on warfarin for atrial fibrillation was noted to be slurring his speech by a family member, who called Emergency Medical Services (EMS). The patient was found unresponsive by EMS and intubated in the field for airway protection prior to transport to the hospital. Upon arrival, the patient was noted be unresponsive to verbal or painful stimuli, with a Glasgow Coma Scale (GCS) score of 4. Neurological exam was significant for no eye opening, non-reactive 3 mm pupils bilaterally, no corneal reflexes bilaterally, no oculocephalic reflex, no cough reflex, no movements in upper extremities, and triple flexion of lower extremities to painful stimulation. Vital signs showed hypertension with systolic blood pressure in 180s, sinus tachycardia with heart rate in 130s, normal respiratory rate of 18, and oxygen saturation of greater than 90%. Initial lab values showed an elevated INR of 2.6.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_14

14.1 History and Neurologic Exam

Spontaneous primary intracerebral hemorrhage (ICH) is defined as extravasation of blood into the brain parenchyma, not attributable to an underlying lesion. ICH results in significant mortality and morbidity, and timely evaluation, diagnosis, and treatment are critical in both maximizing patient survival and improving functional outcome. The management of ICH should be initiated emergently, to limit hemorrhage expansion and to mitigate the neurological sequelae. This chapter highlights key steps in handling such a medical emergency with particular attention to what may be done while the patient is in the Emergency Department (ED).

Rapid deterioration in the first few hours after spontaneous ICH onset is common [1]; thus, a focused physical exam and history are critical part of patient triage. Patient presentation can vary greatly depending on the location and size of the hemorrhage. ICH most commonly occurs in the basal ganglia (35–75%), lobar locations (15–30%), thalamus (15%), brainstem (5–10%), and cerebellum (5–10%) [2], with varying degrees of mass effect, edema, and midline shift that determine level of consciousness and symptoms. The following information is relevant to obtain with the initial history:

- *Symptoms*. Inquire about the presence of focal neurological symptoms as an initial guide to determining the potential location of ICH.

  Similar to ischemic stroke, ICH symptoms may be focal according to the impacted parenchyma. Frontal lobe ICH can cause frontal headaches with contralateral extremity or facial weakness, while parietal lobe ICH will cause primarily contralateral hemisensory loss. Putaminal ICH can cause both contralateral hemiparesis and sensory loss, in addition to eye deviation and aphasia (in the dominant hemisphere), while thalamic ICH usually results in contralateral hemisensory loss, with hemiparesis if the internal capsule is also affected. Temporal ICH affecting Wernicke's area can lead to receptive aphasia. Occipital ICH can cause visual field deficits, typically contralateral homonymous hemianopsia.

  Infratentorial ICH, involving either the brainstem or cerebellum, is associated with a poorer outcome [3]. Primary or extension of hemorrhage into the brainstem can present with cranial nerve palsies that may cause gaze palsies, eye deviation, ptosis, dysarthria, and tongue deviation. Cerebellar ICH may cause ataxia, vertigo, nystagmus, and dysarthria and is more commonly associated with hydrocephalus due to obstruction of the fourth ventricle.

  Non-focal symptoms such as headache, nausea, emesis, and decreased level of consciousness (ranging from drowsy to comatose) may be an indication of increased intracranial pressure due to mass effect from hematoma, expansion of hematoma, hydrocephalus, or direct compression of the brainstem.
- *Onset and duration of symptoms*. Determine the time and tempo of the onset of symptoms. A sudden onset of focal neurologic symptoms is assumed to be of vascular etiology until proven otherwise [4], which is important as it allows providers to determine which diagnostic imaging modalities and interventions to prioritize. Our case vignette illustrates a typical progression for patients with

severe ICH, with initial focal neurological symptoms followed quickly by further deterioration. Early neurological deterioration may reflect ongoing bleeding and hematoma expansion over hours after symptom onset. Greater than 20% of patients experience a decline in Glasgow Coma Scale (GCS) of more than 2 points between initial EMS contact and ED evaluation [1], and an additional 15–23% of patients show continued deterioration within the first few hours after hospital arrival. This critical state can progress rapidly, and appropriate treatments must be provided in a timely fashion to minimize neurologic injury.

- *Past and recent medical history*. Elicit a focused history of the main risk factors for ICH. A history of chronic hypertension is the most common risk factor for spontaneous ICH. It is essential to be aware of underlying conditions that could be associated with anticoagulation or antiplatelet therapy, including stroke, atrial fibrillation, and coronary or other intravascular stents. Recent surgeries, such as carotid endarterectomy or stenting, should be noted, as these may cause hyperperfusion-related ICH. Recent history of significant accidents or falls should be noted, as this may suggest a traumatic, rather than spontaneous, etiology for ICH. Other risk factors for coagulopathy such as hematologic disorders, cancer, and liver disease should also be considered. Comorbidities such as diabetes, smoking status, and alcohol use provide information on general health and guide long-term stroke management and prevention. Information regarding illicit drugs, particularly sympathomimetic agents such as cocaine which can be implicated in acute hypertension, is relevant. A history of systemic malignancy is relevant as certain brain metastases can present with hemorrhage. Allergies to any medications, contrast, or latex should always be documented. Frequently, as with our case vignette, medical history must be obtained from EMS personnel, family members, or friends due to the moribund condition of the patient.
- *Medications*. Seek a complete list of all prescription and over-the-counter medications or supplements. Of particular interest in ICH patients is the use of anticoagulant and antiplatelet agents, antihypertensive, sympathomimetic drugs, and homeopathic remedies (that might contain "hidden" antiplatelet or anticoagulant activity). If possible, the last dose of these medications should be noted to determine whether reversal agents are appropriate and need to be administered.
- *Family history*. Make note of any family history of strokes, intracranial vascular lesions (such as aneurysms), and coagulopathies.

A focused neurological exam will provide information critical to discern the likely location of and determine the severity of the ICH. Sedation should be held for intubated patients to obtain the best neurologic exam. Pertinent information can be gleaned from a quick assessment that includes the following:

- *Level of consciousness*. Determine the GCS score by assessing eye opening (spontaneously, to voice, to painful stimulus, not at all), verbal response (oriented, confused, inappropriate words, incomprehensible sounds, none) and motor response (to command, localizes to pain, withdraws from pain, abnormal flexion, abnormal extension, none).

- *Cranial nerve/brainstem function*. Assess pupillary reflexes, corneal reflexes, oculocephalic reflex, cough reflex, gag reflex, and tongue protrusion.
- *Motor exam*. Test strength in all extremities. Note asymmetry.
- *Sensory exam*. Test for intact, decreased, or absent sensation in the extremities. Note asymmetry.
- *Language function*. Examine speech fluency, repetition, and ability to name objects, if not intubated, as well as the ability to follow simple and complex commands.

A standardized severity scale should be used not only to systematize management but also to communicate to other providers the extent of injury and prognosis. The National Institutes of Health Stroke Scale (NIHSS) score is commonly used for ischemic stroke and may be incorporated; however, hemorrhagic stroke patients often present with a decreased level of consciousness that affects its utility [1]. A number of other grading scales have been developed specifically for ICH. The most widely used and validated scale is the Intracerebral Hemorrhage (ICH) Score, which grades ICH severity and 30-day mortality based on GCS score, age greater than or less than 80 years, ICH volume greater or less than 30 mL, presence of intraventricular hemorrhage, and supratentorial versus infratentorial origin of hemorrhage [5].

The ICH Score is often used in conjunction with the Functional Outcome in Patients with Primary Intracerebral Hemorrhage (FUNC) score, which evaluates the likelihood of functional independence at 90 days after an ICH event. In addition to the age, ICH volume and GCS score factored into the ICH Score, FUNC more specifically accounts for the impact of ICH location (lobar, deep, infratentorial) and degree of cognitive impairment prior to ICH [6]. Application of these clinical grading scales at the time of presentation enhances communication among providers and with patients' families; a standardized assessment of the severity of hemorrhage may help to guide goals of care discussions when decisions regarding treatment must be made quickly. The ICH and FUNC scores for the patient in this case vignette would predict a high mortality and low probability of functional independence, but such prognostic tools should not be relied upon exclusively in making treatment decisions.

14.2 Differential Diagnosis

ICH can be classified as either primary (i.e., spontaneous) or secondary (i.e., related to underlying lesion) based on its etiology.

Primary ICH is far more common, accounting for 80–85% of ICH cases, and results from the rupture of small cerebral vessels secondary to small vessel disease. More than 50% of primary ICH events are correlated with hypertensive arteriosclerosis; 30% are associated with cerebral amyloid angiopathy (CAA) [7]. Hypertension-related ICH is more commonly seen in younger patients, with hemorrhage volumes of less than 30 mL. Elevated BP causes high pressure and

degenerative changes within small penetrating vessels that result in ICH, most frequently located in the basal ganglia, thalamus, cerebellum, and pons. In contrast, CAA-related ICH is more likely to occur in patients greater than 70 years old, due to the presence of increased amounts of amyloid with advancing age. Beta-amyloid protein preferentially deposits within cortical vessels; disruption of these vessels typically causes large, superficial lobar hemorrhages of greater than 30 mL, most commonly in the parietal and occipital lobes [8]. This patient population has a higher risk of recurrence: 10.5% compared to 2% for hypertensive ICH [9, 10]. Lobar ICH in a younger patient is more likely to be secondary.

Secondary ICH can result from any of the following:

- Underlying vascular lesions, such as arteriovenous malformations, cavernous malformations, aneurysms, and arteriovenous fistulae.
- Sinus/venous thrombosis with venous infarction and hemorrhagic conversion.
- Hemorrhagic conversion of an ischemic stroke.
- Coagulopathy, either congenital or secondary to factor deficiencies, liver disease, renal disease, or medications/homeopathic remedies.
- Intracerebral tumors: primary neoplasms rarely present with significant hemorrhages, although hemorrhages in both low and high-grade gliomas have been observed. Systemic malignancies associated with hemorrhagic metastatic lesions include renal cell carcinoma, choriocarcinoma, melanoma, and thyroid carcinoma [11].

Although less common, these secondary causes must always be ruled out as their management and outcome differ from that of primary ICH, requiring additional diagnostic testing and specialized interventions. Vascular malformations and abnormalities require dedicated vascular imaging to characterize the lesion and to determine definitive treatment to prevent re-hemorrhage. Neoplastic lesions will require additional systemic diagnostic imaging to determine the primary malignancy, if not already known, in collaboration with medical oncologists, radiation oncologists, and neuro-oncologists. Coagulopathy may require medications for reversal or deficiency replacement. If the patient's coagulopathy is congenital or secondary to organ dysfunction or disease, realistic transfusion thresholds and goals must be established.

14.3 Diagnostic Evaluation

14.3.1 Imaging

Elements of the patient's history and physical exam—namely, acute onset and rapid progression of neurologic deficits, as well as decreased level of consciousness—raise strong suspicion for a stroke event. Urgent diagnostic brain imaging is necessary to confirm and characterize the stroke type.

A noncontrast computed tomography (CT) of the head is the best initial diagnostic test that allows rapid differentiation of ischemic from hemorrhagic stroke. Acute hemorrhage will appear hyperdense, while an ischemic stroke will show hypoattenuation in the infarcted territory with associated loss of gray-white matter differentiation and sulcal effacement. Compared to other modalities, CT scans are fast, inexpensive, and readily available. Intraventricular hemorrhage and hydrocephalus can also be identified readily on CT. In this case, noncontrast CT of the head demonstrated an acute 5.3 × 4.5 × 3.5 cm left cerebellar hemorrhage with extension into the fourth ventricle (Fig. 14.1), obstructive hydrocephalus (Fig. 14.2), effacement of basal cisterns, and transtentorial herniation (Fig. 14.3).

To evaluate the cerebral vasculature and assess for underlying vascular lesions, CT angiography (CTA) can be obtained with the noncontrast CT head sequence as part of the acute stroke imaging. These studies are helpful in identifying underlying causes of the hemorrhage, including congenital or developmental vascular anomalies, fistulas, tumors, and Moyamoya disease [12]. Vascular imaging should always be considered in young, normotensive patients who are clinically stable and without obvious cause of ICH. Vascular imaging should also be considered in the presence of abnormal radiological findings suggestive of a vascular abnormality or

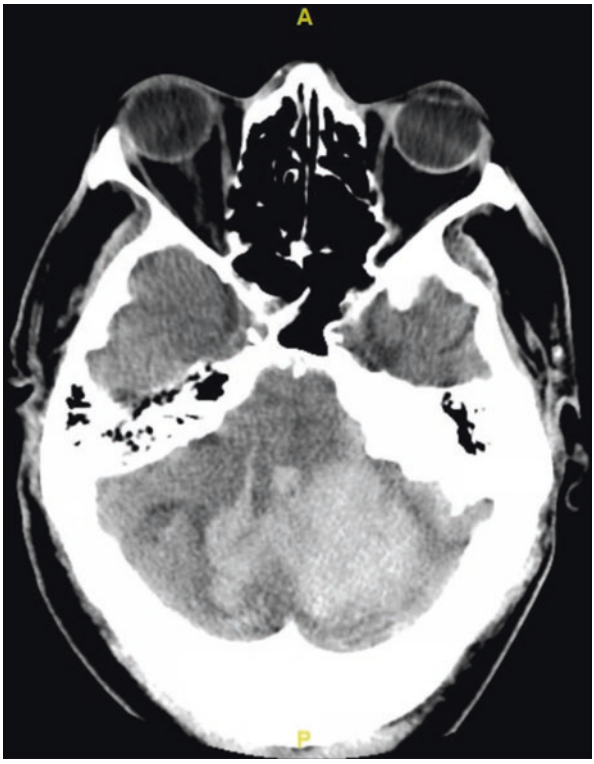

Fig. 14.1 Axial noncontrast CT head demonstrating a large left cerebellar hematoma with intraventricular extension to the fourth ventricle

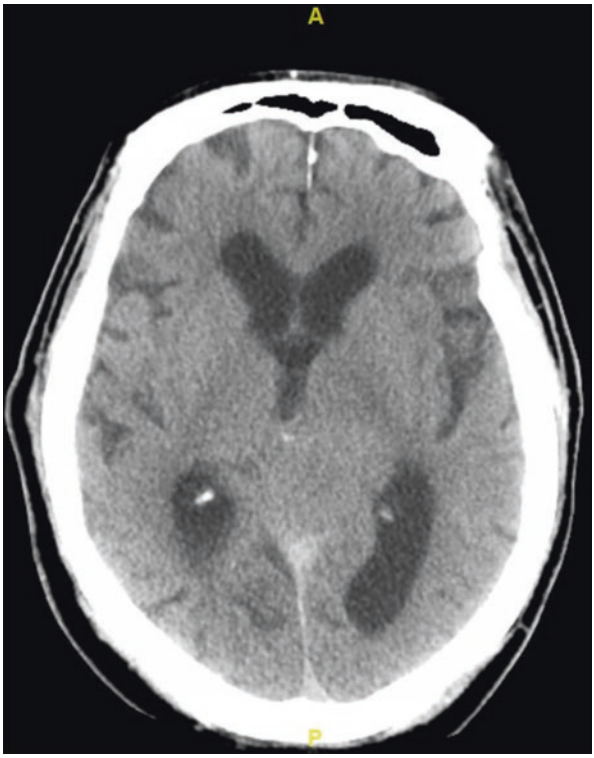

Fig. 14.2 Axial noncontrast CT head demonstrating obstructive hydrocephalus with dilatation of the bilateral lateral and third ventricles

underlying mass, such as subarachnoid hemorrhage, enlarged vessels or calcifications along the hematoma margins, hyperattenuation along the venous drainage path, an atypical hematoma shape or location, and surrounding edema that is out of proportion to the presumed age of the ICH. Additionally, contrast within the hematoma, termed an angiographic "spot sign," can help identify patients at risk for hematoma expansion [13]. CT venography should also be obtained if ICH location, edema, or abnormal signal in sinuses suggest a cerebral vein or sinus thrombosis that may have caused an infarct with hemorrhagic conversion [1]. If non-invasive vascular imaging suggests an underlying lesion, digital subtraction angiography (DSA) can further characterize underlying vascular abnormalities. In patients with negative CT and MR studies, DSA should still be considered, except for those over the age of 45 with pre-existing hypertension and thalamic, putaminal, or brainstem hemorrhage [14].

Magnetic resonance imaging (MRI) can also detect acute hemorrhage of less than 6 h in age with equal efficacy on gradient echo and T2* susceptibility-weighted sequences [15]. However, MRIs are associated with higher cost, are more time-consuming, and are dependent on facility availability, precluding MRI as the first imaging choice in the ED [1]. In a stable patient with a non-expanding hematoma,

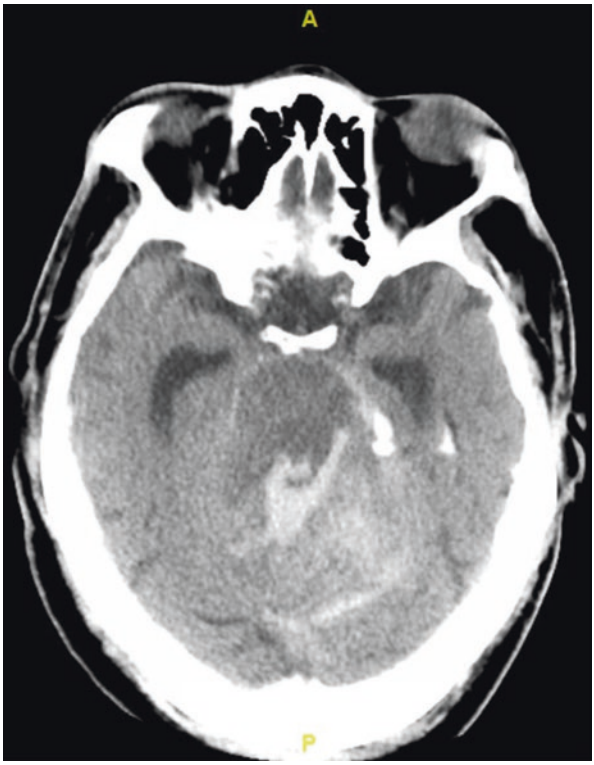

Fig. 14.3 Axial noncontrast CT head demonstrating hemorrhage involving left cerebellum with upward transtentorial herniation

gadolinium-enhanced MRI of the brain can be obtained to determine the age of the ICH and to evaluate for underlying structural lesions as secondary causes. Diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences are also useful in determining if the ICH might represent hemorrhagic conversion of an ischemic infarct.

14.3.2 Laboratory Tests

Upon admission, all patients should have the following serologic testing:

- Comprehensive metabolic panel to evaluate for electrolyte abnormalities that require immediate correction, hyperglycemia which is associated with worse outcomes, and renal function if iodinated contrast agents or gadolinium-based contrast agents will be administered for CT and DSA, or MR, respectively. Iodine-containing contrast media can cause contrast-induced nephropathy (CIN), typically in patients who have underlying poor or deteriorating renal function with estimated glomerular filtration rate (eGFR) of less than 30 mL/min; these

patients have a 5–15% risk of developing CIN. Gadolinium-based contrast medium rarely causes nephrogenic systemic fibrosis, although those with stage four or five chronic kidney disease (defined as eGFR of 30–40 mL/min and less than 30 mL/min respectively), those undergoing dialysis, or those in acute renal failure, are at slightly increased risk [16, 17]. Consulting radiology may be helpful in selecting the least nephrotoxic gadolinium-based agent and the lowest possible dose without compromising diagnostic yield. Patients presenting with poor renal function would benefit from evaluation by a nephrologist to determine dialysis needs after contrast administration and when contrast may be administered again if needed.

- Complete blood count, internalized normalized ratio (INR), prothrombin time, and partial thromboplastin time to evaluate for anemia, thrombocytopenia, or coagulopathy that requires immediate reversal or transfusions.
- Cardiac enzymes, in addition to an ECG, to evaluate for active coronary ischemia or prior cardiac injury.
- Toxicology screen to evaluate for cocaine or other sympathomimetic drugs of abuse that are associated with ICH [18].

14.4 Clinical Decision-Making and Next Steps

14.4.1 Critical Care

Patients with ICH are often neurologically and medically unstable, especially in the days following onset; ideally, these patients should be treated at a facility by a multidisciplinary team of neurosurgeons, neurologists, neurointensivists, and neurocritical care-trained nurses. If these resources and specialists are unavailable, rapid transfer to a facility with these capabilities should be initiated upon arrival. Patients should be admitted to a stroke unit or neuroscience intensive care unit (ICU) where they can receive frequent vital sign checks, neurologic assessments, and continuous cardiopulmonary monitoring to minimize secondary neurologic injury from the initial hemorrhage and to prevent re-hemorrhage; treatment in a dedicated neuroscience ICU is associated with a lower mortality rate [19].

14.4.2 Acute Management

In the ED, initial management includes attention to airway, blood pressure, and circulation. Level of consciousness may change rapidly; thus, airway management and cardiovascular support should be prioritized to ensure adequate cerebral blood flow and oxygenation. Patients should be evaluated immediately for ability to protect their airway; in the setting of a depressed level of consciousness, concern for

aspiration risk and/or signs of impending respiratory failure, the airway should be secured promptly, if not already addressed in the prehospital setting. Vital signs should be continuously monitored for hemodynamic instability. Elevated blood pressure (BP) is very common in acute ICH [20] due to pain, increased intracranial pressure (ICP), stress, and premorbid hypertension. High systolic BP is associated with greater hematoma expansion, neurological decline, dependency, and death after ICH [21]. Acute BP treatment is one of the mainstays in ICH management, as discussed below. Although less common, hypotension can also be present; patient should be evaluated for potential causes, such as hypovolemia, hemorrhage, and cardiopulmonary etiologies, and treated with fluid resuscitation, vasopressors, and etiology-specific interventions if necessary.

14.4.3 Blood Pressure Control

Systolic blood pressure control should be initiated immediately in the ED to prevent hematoma expansion. Studies have shown no significant reduction in cerebral blood flow within the perihematomal area related to early intensive lowering of SBP to <140 mmHg within several hours of ICH onset. However, intensive BP lowering to <140 mmHg versus standard management to a target of <180 mmHg has not shown definitive outcome benefit and may increase rate of adverse renal events [22]. It is, nonetheless, reasonable to lower SBP to a target of <140 mmHg in patients presenting with SBP between 150 and 220 mmHg, with goals to stabilize the hematoma and to improve functional recovery in survivors [4, 23]. Speed and degree of BP reduction vary depending on the agent and mode of delivery; commonly used agents include intravenous hydralazine, labetalol, and nicardipine infusion.

14.4.4 Reversal of Coagulopathy

Immediate cessation of antiplatelet and anticoagulant medication and supplements is necessary. Warfarin is a commonly prescribed oral anticoagulant drug, and rapid correction of INR is recommended as warfarin-related ICH is associated with greater hematoma volume, risk of hematoma expansion, and morbidity and mortality [24]. Fresh frozen plasma (FFP) and intravenous vitamin K have been the first-line treatment for years; however, modern therapies have emerged, including prothrombin complex concentrate (PCC), and activated PCC factor VIII inhibitor bypassing activity (FEIBA); PCCs provide more rapid reversal and reduce adverse events attributable to volume overload associated with FFP [4]. Recombinant activated factor VIIa is not recommended for reversal of warfarin as it does not replace all clotting factors and may not be as effective despite normalization of INR [4].

Patients with an acute ICH while on heparin treatment may be reversed with protamine.

In recent years, use of direct oral anticoagulants, such as dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban**,** has increased tremendously due to less frequent need for laboratory monitoring, more predictable dosing, lower incidence of major bleeding, and shorter half-life [25]; however, the use of reversal agents in clinical practice is not well-defined due to availability, preparation, cost, potential risk of thrombosis, and lack of data on comparing the different reversal strategies. Idarucizumab can be used for reversal of dabigatran; if unavailable, activated PCC may be used. Andexanet alfa can be used for reversal of apixaban and rivaroxaban, and for off-label treatment of edoxaban and betrixaban-associated bleeding; if unavailable, four-factor PCC may be administered [26].

Those with severe coagulation factor deficiency or severe thrombocytopenia should receive replacement therapy and/or platelet transfusions per 2015 AHA/ASA guidelines [4]. Routine platelet transfusion for patients taking antiplatelet therapy is not recommended as this has been associated with worse outcomes, including greater odds of death and dependence at 3 months [27]. It would be reasonable, however, to consider transfusion for those undergoing invasive interventions, such as external ventricular drain (EVD) placement or surgical hematoma evacuation [28].

14.4.5 Intracranial Pressure Monitoring

Rising ICP can present as headache, nausea, emesis, and depressed mental status and is typically caused by hydrocephalus secondary to obstruction from intraventricular hemorrhage (IVH), mass effect, or edema. Means of rapidly lowering ICP until a definitive neurosurgical procedure can be done, if needed, include elevation of the head of the bed to 30° and rapid infusion of 20% mannitol or hypertonic saline. Patients may be temporarily hyperventilated to a goal pCO_2 of 30–35 mmHg. However, this should be done cautiously as the resulting cerebral vasoconstriction may contribute to cerebral hypoperfusion.

Placement of an EVD permits monitoring of ICP to guide therapy and therapeutic drainage of cerebrospinal fluid to address raised ICP and hydrocephalus, when needed. IVH occurs in 45% of patients with ICH and is associated with increased mortality and worse outcomes [29]. Although an EVD aids in the drainage of both CSF and blood, maintaining catheter patency can be difficult due to frequent obstruction by clot. Intraventricular administration of fibrinolytic agents, such as recombinant tissue-type plasminogen activator (rtPA) may be given to accelerate clearance of hemorrhage by lysing clots with fairly low complication rates; length of stay in the ICU was noted to be shorter in patients with IVH with obstructive hydrocephalus who received rtPA, although better outcomes were not observed

[30]. Intraparenchymal ICP monitoring devices are also available, but do not permit therapeutic drainage of CSF. Patients with small hematomas and limited IVH, without impairment in level of consciousness, will not require measures for acute lowering of ICP and may be monitored. Current guidelines recommend placement of an ICP monitoring device and treatment of elevated ICP in patients with a GCS of equal to or less than 8, evidence of transtentorial herniation, or patients with significant hydrocephalus or IVH; ICP should be maintained at a goal of less than 20 mmHg, with a cerebral perfusion pressure target of 50–70 mmHg [4]. Particular caution should be exercised when considering EVD placement in a patient with posterior fossa hemorrhage. In our case vignette, for example, the patient shows evidence of IVH and obstructive hydrocephalus in the setting of a low GCS. However, EVD placement alone may induce upward herniation, and current guidelines favor concomitant surgical evacuation of the hematoma, rather than EVD alone [4].

14.4.6 Antiepileptic Drug (AED) Prophylaxis

Clinical seizures have been noted in up to 16% of patients within 1 week of ICH onset. The greatest risk factor for early seizures is cortical involvement of ICH [31]. Routine seizure prophylaxis is not associated with improved neurological function and is not recommended [32]. For patients presenting specifically with lobar ICH, prophylactic antiepileptic drugs can reduce the number of clinical seizures, although the association with outcome or mortality is not clear [33]. Continuous EEG monitoring is recommended in ICH patients who have depressed mental status that is out of proportion to the degree of injury in order to evaluate for electrographic seizures which can be present in 28–31% of ICH patients [1]. If electrographic or clinical seizures do occur, they should be treated, as the risk of recurrence is 43% for early post-stroke seizure and 50–60% for late post-stroke seizure. Currently, there exists insufficient evidence regarding the comparative effectiveness of various AEDs to provide specific recommendations with regard to agent, dose, or duration of therapy for post-stroke seizures. However, newer agents such as levetiracetam are less likely to cause drug interactions and are reasonable choices for initial AED therapy [34].

14.4.7 Surgical Management

While initial medical management for stabilization in the ED or ICU is important, timely neurosurgical evaluation is essential in select cases. Surgical intervention for evacuation of hematoma may prevent or treat herniation, lower ICP, and decrease mass effect, if present.

For patients—such as the man in this clinical vignette—presenting with posterior fossa ICH, indications for surgery are more definitive, and time to

decompression and evacuation is critical. Due to the anatomical constraints of the posterior fossa, patients with cerebellar and brainstem hemorrhages can deteriorate rapidly due to obstructive hydrocephalus, direct compression of the brainstem, or indirect compression via mass effect or edema. Infratentorial ICH is an independent risk factor for mortality, regardless of hematoma volume [1]. Although no randomized controlled clinical trials investigating the benefit of early surgical evacuation of hematoma compared to conservative management have been completed, current observational studies suggest that evacuation of cerebellar ICH greater than 3 cm in diameter, with associated brainstem compression or acute hydrocephalus, may potentially provide better outcomes [35]. A meta-analysis of these studies showed surgical evacuation of cerebellar hemorrhages greater than 15 mL was not associated with better functional outcome, but was associated with improved survival [36]. Brainstem hemorrhages are not surgical candidates due to the devastating nature of the underlying insult.

Indications for surgery vary based on the location of the hemorrhage; compared to infratentorial ICH, indications for supratentorial ICH patients are more controversial. Although a number of trials on surgery for evacuation of supratentorial ICH have been conducted, the best candidate for and timing of intervention are still not yet well established. The STICH II trial showed a trend toward better outcome in patients with superficial lobar hemorrhage who underwent early surgery (within 12 h) as opposed to initial conservative therapy [37]. When these results were combined with 13 other studies for a meta-analysis, a significant outcome benefit was associated with surgery, although the findings are limited by heterogeneity among included studies. Despite the unclear definitive benefit of early decompression and hematoma evacuation, it may still be considered a life-saving measure in deteriorating patients who are in a coma, have a large or expanding hematoma with significant midline shift, or who have elevated ICP refractory to conservative treatments, to reduce mortality [1, 38].

The MISTIE III trial investigated the utility of minimally invasive hematoma evacuation, coupled with alteplase thrombolysis, for moderate to large ICH. While the procedure was found to be safe and reduced mortality, it has not been adopted widely for routine care in supratentorial ICH patients, as the procedure did not improve functional outcomes at 1 year [39]. In patients with primarily IVH and minimal ICH (<30 mL), a randomized controlled trial of thrombolytic to expedite clearance of hemorrhage, CLEAR-III, found reduced mortality, but not significant improvement in overall functional outcome [31, 40].

Despite uncertain benefit with respect to functional outcomes, surgical intervention has been associated with improved mortality and can be a life-saving measure for select patients with supra- or infratentorial ICH; neurosurgical evaluation remains key in determining whether surgical intervention is appropriate on an individual basis.

14.5 Clinical Pearls

- ICH is a medical emergency that requires prompt evaluation and treatment to reduce mortality and morbidity and maximize functional outcome. Management begins even prior to ED arrival, and frequent assessments are critical.Have a low threshold to secure the airway if level of consciousness is depressed.
- Initiate systolic blood pressure control immediately, in conjunction with continuous cardiovascular monitoring.
- Correct coagulopathy and administer agents for reversal of anticoagulants immediately.
- Rapid treatment of raised ICP and neurosurgical evaluation of the need for CSF drainage and/or surgical decompression is essential.
- Prompt admission to a neurological ICU or stroke unit for specialized care is advisable.

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Chapter 15
Aneurysmal Subarachnoid Hemorrhage

Ryan P. Lee and Judy Huang

Clinical Scenario

A 32-year-old female was brought to the Emergency Department (ED) by an ambulance after she complained to her husband of spontaneous, sudden onset, severe headache while doing yard work. On arrival, she is sleepy and only opens her eyes briefly to gentle stimulation. The light is bothersome to her. She has a medical history of pre-diabetes and asthma. Her husband remarks that she has had headaches and migraines in the past, but nothing this severe. There are no external signs of trauma. She is oriented, but only answers questions in short, one- or two-word responses. All of her extremities move well and symmetrically to command, but she is lethargic. She is little nauseated but has not vomited.

15.1 History and Neurologic Exam

Acute onset, severe headache presents a particular challenge, in so far as the potential differential diagnosis is broad, yet prompt evaluation and triage are essential. While most headache etiologies are benign, many may require swift, directed treatment that can be lifesaving. In general, taking a history in this scenario should cover:

- *Features of the headache*. Headache characteristics may be highly variable. Elucidating specific features may be helpful and even diagnostic. Determine headache onset (i.e., was it abrupt, gradual?), location (e.g., frontal, retro-orbital,

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_15

holocephalic, posterior), duration, character (e.g., throbbing, sharp, dull, achy), aggravating factors (e.g., light, Valsalva, noise, position), alleviating factors (e.g., medication), timing (e.g., is it worsening, improving, or fluctuating?; does it relapse and remit?), and severity (i.e., 1–10 scale). Events leading up to headache onset can also be important (e.g., onset during or after strenuous activity).

- *Associated and constitutional symptoms*. Are there any associated symptoms that may be relevant, like nausea, vomiting, neck pain or stiffness, vision blurriness, double vision, dizziness, instability, neck pain, or weakness? Are there reports of any fever, chills, or infection symptoms? Are there reports of any ear pain or drainage or any sinus issues?
- *Neurologic symptoms*. Is the patient's mental status altered or is his or her level of consciousness depressed? Are there signs of high intracranial pressure? Are there any cranial nerve deficits? Is there focal or global weakness? Is there numbness or paresthesias of any extremity? Is there any erratic or unusual behavior? What is the pattern of speech?
- *History of trauma*? Determine if the headache is related to trauma. Was there any trauma in the recent history, even if it was minor? If there was trauma at time of onset of headache, such as fall, be sure to elicit if the fall happened before or after the headache started. Sometimes, headache may signal a neurologic event that caused a fall. Are there any other injuries?
- *Medical history*. What is the patient's medical history? Is there a history of headaches or migraines? Any cancer history? Are there any neurologic conditions that may predispose to headache, high intracranial pressure, or an intracranial tumor or mass lesion? Is there a history of a procoagulable state that might cause venous sinus thrombosis? Or a bleeding disorder that might have led to intracranial hemorrhage? Is there a history of hypertension or hypertensive emergency? Is there history of immunocompromise that may predispose to intracranial infection? Were there any recent infections? Are there potentially relevant, pre-existing cardiovascular, neoplastic, hematologic, or infectious conditions that might place this patient at risk for intracranial hemorrhage or intracranial aneurysm? Are there any conditions, like polycystic kidney disease, that might predispose to or be associated with intracranial aneurysms?
- *Medications*. Is the patient taking any antiplatelet or anticoagulant medications? Is the patient taking any procoagulant medications? This includes a review of herbal supplements—many of which have antiplatelet, anticoagulant, or procoagulant activity. Have the patient's medications changed recently (e.g., change of antihypertensive regimen)? All medications, both current and recent, should be recorded and reviewed.
- *Surgical history*. Does the patient have a history of any intracranial or neurosurgical procedures? Does the patient have a history of tumor removal, and could he or she potentially now have a brain metastasis? Has the patient undergone any recent sinus, dental, or otologic procedures that could have precipitated intracranial infection?

- *Social history*. Is there a history of substance use or abuse? Cocaine and amphetamine use can precipitate headaches via vasculitis, SAH, or hypertensive crisis. Eliciting work history, hobbies, and living conditions may also be relevant.
- *Family History*. Is there a family history of headache disorder? Are there any neurologic conditions or cancer syndromes that run in the family? Are there any family members with cerebral aneurysms or prior SAH? Many patients will remember these events as "stroke" or "bleeding on the brain."

Try to obtain further history from relatives, friends, or anyone else available if the patient is not communicative, confused, or too lethargic. This extra effort can be critical and can completely change the direction of workup and management.

The initial encounter with every patient should involve assessment of the "ABCs": airway, breathing, and circulation. This is of particular importance in a patient with a depressed level of consciousness, and one should be constantly reevaluating the need for airway protection and mechanical ventilation. If there is concern for trauma, assessment of circulatory blood volume is critical in the event there might have been external or internal hemorrhage. Essential elements of physical and neurologic assessment include:

- *Vital signs*. Vital signs should be reviewed. Headache may be accompanied by tachycardia and hypertension secondary to pain; however, other causes should be considered. Bradycardia, accompanied by depressed level of consciousness, should raise concern for raised intracranial pressure. Bear in mind that bradycardia, alone, may reflect beta-blockade or a normal physiologic state in the appropriate individual. Fever should trigger concern for infection but note that patients can experience fever with non-infectious intracranial pathologies as well. For instance, fever may also occur in the setting of recent clinical or ongoing subclinical seizure.
- *Glasgow Coma Scale (GCS) score*. Quickly calculate the patient's GCS. This involves (a) eye opening, (b) verbal response, and (c) motor response. With a depressed GCS (14 or less), imaging should be obtained urgently, usually starting with non-contrast head CT. If there is reasonable concern for intracranial hemorrhage and secondary neurologic decline or cardiopulmonary complications, the patient should be monitored when going to the CT scanner and should be accompanied by appropriate level of staff.
- *Cranial nerve, motor, and sensory exam*. A cranial nerve exam should be performed, followed by a brief motor and sensory exam. Remember that just because a patient is "nonfocal" does not mean there is no intracranial concern. Global level of consciousness is just as important. A globally depressed level of consciousness—independent of a lateralizing or focal finding—may reflect bilateral cerebral or brainstem level dysfunction.
- *Cutaneous signs of trauma or prior surgery*. During the exam, evaluate for any signs of trauma or potential occult injuries. Evaluate for surgical scars, particularly on the head, that may indicate previous cranial surgery.

- *Meningismus*. With concern for infection, be certain to check for nuchal rigidity and light sensitivity. Note, however, that these may be present in the setting of spontaneous SAH without infection.

15.2 Differential Diagnosis

The differential diagnosis for headache can be broad. A description of severe, spontaneous, sudden onset headache narrows it somewhat. Strong familiarity with the differential diagnosis in this setting is crucial because thorough history is not always available and initial imaging can be negative or equivocal. The term "thunderclap headache" is often used to describe severe, sudden onset headache that reaches maximum intensity within a few minutes. However, in reality, it is often difficult to determine if the headache meets these specific criteria, and the pathologies that supposedly present with thunderclap headache can also present more gradually.

15.2.1 Common Causes of Sudden Onset, Severe Headache

Aneurysmal subarachnoid hemorrhage. With sudden onset, severe headache—such as in the case of our patient—this diagnosis should always be considered. Classically, patients will describe the "worst headache of life." However, the headache may not be particularly severe, mildly symptomatic cases are frequently misdiagnosed on initial encounter, most frequently as migraine or tension-type headaches [1]. Index of suspicion should remain high. Patients may also have nausea, vomiting, neck pain, photophobia, depressed level of consciousness, confusion, seizures, cranial nerve palsies, or other neurologic deficits. Aneurysmal SAH is highly possible in our patient, but certainly other etiologies are conceivable at this point also. It is important to note that aneurysmal SAH patients are often found down and are brought in as trauma patients, whether or not the hemorrhage preceded a true trauma. This is important to consider when reviewing cases of purported traumatic SAH.

Perimesencephalic (pretruncal) subarachnoid hemorrhage. This entity may present similarly to aneurysmal SAH, but is usually less severe. "The patient looks much better than the CT" is a common quip in this setting. By definition, no explanatory lesion is found on angiography, and the SAH fits a specific pattern. The blood is typically centered immediately anterior the midbrain or pons but does not extend to the lateral Sylvian fissures or superficial interhemispheric fissure, and there is no frank intraventricular hemorrhage [2]. Patients may present with nausea, vomiting, meningismus, and photophobia, but neurologic deficits and significantly depressed level of consciousness are uncommon. This is a diagnosis of exclusion and could fit with our patient's presentation as well.

Reversible cerebral vasoconstriction syndrome (RCVS). This is a group of entities with an evolving definition, but, in general, characterized by single or recurrent thunderclap headaches and reversible segmental vasoconstriction on angiographic imaging [3]. There are many associations, including sexual activity, pregnancy, medications, and illicit drugs. SAH may occur in association with RCVS, though the pattern of bleeding more commonly involves the convexities than the basal cisterns.

Without the benefit of imaging, all three of these entities remain possibilities for our patient.

15.2.2 Others Causes of Sudden Onset, Severe Headache

The following are not necessarily less common causes of headache, but are typically characterized either by more gradual onset or lesser severity of symptoms.

Non-perimesencephalic, non-aneurysmal subarachnoid hemorrhage. Spontaneous SAH without aneurysmal source or fitting a perimesencephalic pattern is uncommon, with a wide range of potential underlying etiologies. These include arteriovenous malformations, arteriovenous fistulas, cavernous malformations, cerebral amyloid angiopathy, coagulopathies, qualitative or quantitative platelet dysfunction, and many of the pathologies listed below. The patient may be asymptomatic or manifest with headache, seizure, or neurologic deficit.

Meningitis. The patient may also have a fever, photophobia, meningismus, leukocytosis, focal neurologic deficit, or seizure. The patient may have a history of recent sinonasal procedure, neurosurgical procedure, immunocompromise, bacteremia, or endocarditis. Systemic or intracranial infectious processes may precipitate formation of mycotic aneurysms, which can rupture, causing SAH. These aneurysms and their hemorrhages are often distal in the cerebral vasculature.

Venous sinus thrombosis. This is suggested by signs of elevated intracranial pressure, including papilledema, headache, abducens palsy, or other extraocular movement restriction. The patient may be post-partum or procoagulable. There may be global or focal neurologic deficits.

Pituitary apoplexy. This diagnosis is supported if there is a history of a pituitary adenoma or signs of hypopituitarism. The symptoms on presentation may be quite varied, including severe headache, sudden visual loss and/or ophthalmoplegia, and cardiovascular collapse or diabetes insipidus due to acute hypopituitarism.

Hypertensive crisis. The patient will typically have a history of hypertension, often with recent medication change or compliance issues. However, hypertension can be a consequence of headache, or the hypertension may be caused by another etiology.

Posterior reversible encephalopathy syndrome. This is usually more insidious in onset and may be accompanied by seizure and neurologic deficits. It often occurs in the setting of hypertensive crisis, pre-eclampsia, or immunosuppressive therapies.

Migraine. Patients usually have a history of migraines. They are usually more gradual in onset and may be preceded by an identifiable aura.

Brain tumor. Headaches from brain tumors are usually gradual in onset, but hemorrhage or hydrocephalus may precipitate an acute onset or exacerbation.

Hydrocephalus. Headaches from hydrocephalus are usually more gradual in onset and usually accompanied by progressive altered mental status. Papilledema and abducens palsy may be present. Headaches due to tumor or hydrocephalus may be characteristically worse in the morning upon waking.

Carotid or vertebral artery dissection. Dissection may be related to a traumatic event and can precipitate an ischemic stroke. Cervical dissection may cause a Horner's syndrome.

Other vasculitides/vasculopathies. Presentation will be variable. There may be hemorrhage, and vascular imaging may or may not be diagnostic at initial screening.

Other causes of headache to consider. Sinusitis, spontaneous intracranial hypotension, intraparenchymal hemorrhage, subdural hemorrhage, ischemic stroke, giant cell arteritis, colloid cyst of the third ventricle, acute angle-closure glaucoma.

15.3 Diagnostic Evaluation

The initial diagnostic test for sudden onset, severe headache should be **CT of the head without contrast**. This modality has high sensitivity for acute SAH, other intracranial hemorrhages, mass lesions, and hydrocephalus. However, it may be negative in the case of RCVS, meningitis, venous sinus thrombosis, hypertensive crisis, migraine, or dissection. It is interesting to note that all of these pathologies—save for migraine—can rarely cause small to moderate amounts of SAH.

Sensitivity of non-contrasted head CT is highest in the first few days after SAH, including 98.7% within the first 6 h (if there are no neurologic deficits) [4]. If the patient is presenting in delayed fashion, CT may be negative [5]. In the case of a negative non-contrast head CT but sufficient clinical suspicion for SAH (and without other cause seen on that initial study), a **lumbar puncture** should be performed [6]. CSF should be analyzed microscopically for the presence of red blood cells. Xanthochromia—the result of red blood cell lysis and breakdown—may be apparent grossly upon collection or after centrifuge of the sample. Of note, red blood cells may also be present in the CSF in the setting of meningitis secondary to herpes simplex virus. Beyond cell count, other routine studies such as protein, glucose, and culture should not be neglected. Opening pressure should also be obtained, but is only accurate in the lateral decubitus or prone position.

In virtually all cases of acute SAH, **CT angiography (CTA) of the head** should be performed next to evaluate for aneurysmal origin or other vascular lesions. The exception would be cases that are clearly trauma-induced, mild-moderate SAH where there was no preceding headache or neurologic complaint. CTA of the head should also be performed alongside lumbar puncture in CT-negative cases with sufficient clinical suspicion for aneurysmal SAH. Sensitivity of modern CTA for aneurysms <3 mm is over 87% [7]. CTA may also reveal the segmental vasoconstriction representative of RCVS, but sensitivity is limited. **MR angiography (MRA) of the head** is an alternative but typically takes longer to obtain and requires a longer acquisition time. It is also more expensive and may not be as readily available at CT in many centers, particularly at night. The benefit of MRA is that it can be done in patients with renal failure as it does not require contrast.

Concurrent with initial imaging, **basic lab work** should be sent on these patients. This should include complete blood count, basic chemistry, and coagulation factors. Urine or serum toxicology can also be considered in cases of altered mental status, suspected ingestions, or suspected illicit drug use. In women, a pregnancy test should be sent, even with very low suspicion.

While the sensitivity of modern, high-quality CTA is quite high for vascular lesions in this setting, **digital subtraction catheter angiography** (DSA) remains the gold standard. In cases of spontaneous SAH, or when there is uncertainty on the role of trauma as a cause or result, catheter angiography should be considered after negative CTA if there is still reasonable suspicion for an aneurysm or vascular lesion. Furthermore, many institutions, including ours, will still perform catheter angiography even with an explanatory lesion on the CTA. Catheter angiography helps to characterize the lesion and related anatomy, may reveal occult lesions, and permits real-time therapeutic intervention, if appropriate. This modality is also more sensitive than CTA for the vasoconstrictive changes seen in RCVS and vasculitis.

CT venography of the head would be most beneficial when there is sufficient suspicion of venous sinus thrombosis. This diagnosis might be considered in a patient with a procoagulable condition or taking a procoagulant medication, with notable headache and with or without depressed level of consciousness. Non-contrast CT head may show cerebral edema, parenchymal hemorrhage, small amounts of SAH, or hyperattenuation in the suspected location of a venous sinus, which should prompt further investigation of this diagnosis with CT venography. **MR venography of the head** can be considered as an alternative to CTV.

Brain MRI with and without gadolinium can be useful and diagnostic in many causes of severe headache. Brain MRI can show SAH not seen on CT (particularly in subacute hemorrhages more than several days old) [8], may reveal a mass lesion such as cavernoma or tumor, may reveal edema secondary to venous sinus thrombosis or in the setting of PRES, may reveal a pituitary tumor with signs of apoplexy, or may reveal signs of meningitis or discrete infection. The threshold for obtaining MRI should be low.

15.4 Clinical Decision-Making and Next Steps

Our patient presented with acute, severe, spontaneous headache without trauma. This presentation, in and of itself, should raise suspicion of aneurysmal SAH as a diagnosis to be ruled out quickly, regardless of mental status. She should undergo non-contrast CT of the head as initial imaging in this scenario. Even with headaches that are less acute or less severe, but associated with altered mental status or neurologic deficit, non-contrast head CT should also be strongly considered. In the case of our patient, head CT (Fig. 15.1) showed thick SAH in the basal cisterns bilaterally and the proximal left Sylvian fissure, with small amounts of layered blood in both occipital horns. The presence of subarachnoid hemorrhage and the specific distribution of blood—independent of identification of a discrete aneurysm—is sufficient to set her on the management trajectory for an aneurysmal bleed.

A neurosurgeon should be consulted emergently upon diagnosis of SAH. The non-contrast head CT should also be assessed for signs of developing hydrocephalus, which is common after SAH and frequently requires CSF diversion. There may also be signs of cerebral edema, midline shift, or herniation that may alter management. For communication and prognostication purposes, the initial neurologic status is classified by severity of deficit using the Hunt and Hess scale and World

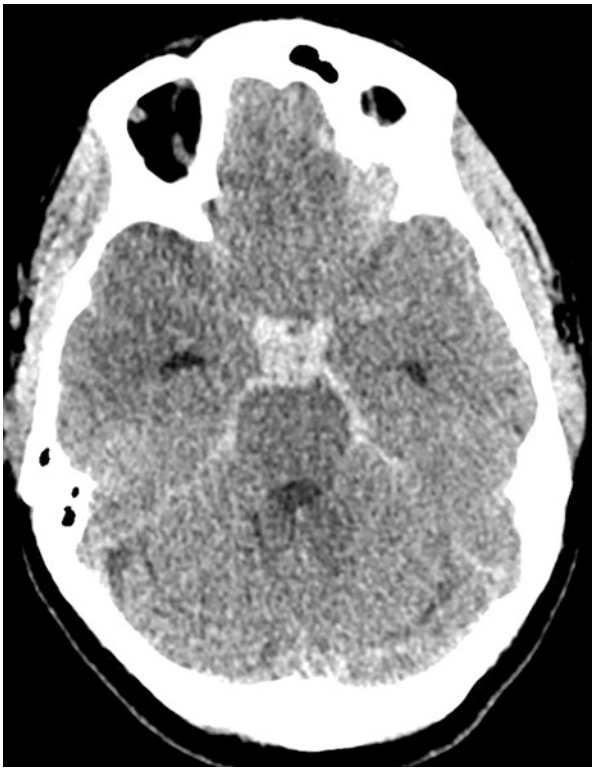

Fig. 15.1 Axial non-contrast head CT showing diffuse subarachnoid hemorrhage in the basal cisterns, concerning for aneurysmal rupture

Federation of Neurological Surgeons (WFNS) grade [9, 10]. This patient would receive a Hunt and Hess score of 3 (lethargic) and WFNS grade of 2 (GCS 13–14 without deficit).

Initial lab work should be obtained, including CBC, basic chemistry panel, INR, and PTT. The labs should be reviewed for thrombocytopenia or coagulopathy. Low sodium should be investigated, as should any other electrolyte derangement. Rarely does renal failure prevent use of iodinated contrast for emergent CT or catheter angiography in this setting. Our patient's sodium was 134, so it was planned to recheck this value after a short interval, to exclude a further drop. Approximately 30–50% of aneurysmal SAH patients develop hyponatremia [11]. Syndrome of inappropriate ADH (SIADH) accounts for approximately two-thirds of cases, but cerebral salt wasting, iatrogenic hypervolemia, dehydration, and cortisol deficiency are also common [11]. Hyponatremia may worsen cerebral edema and mental status and may lower seizure threshold.

If not done already at this point, the patient's medical history and medications should be reviewed to ensure there is no history of coagulopathy, bleeding diathesis, antiplatelet use, or anticoagulant use. If yes to any, it should be addressed emergently to prevent further hemorrhage. This screen was negative in our patient.

The patient's vital signs should be monitored continuously. Blood pressure should be controlled to prevent re-hemorrhage, with the latest guidelines suggesting a ceiling of <160 mmHg [6]. Our patient was hypertensive, possibly from pain, so a vasodilator drip was initiated. The patient's mental status and neurologic exam should be re-evaluated at least every hour to ensure there is no need for intubation for airway protection or measures to control an elevated ICP. With a GCS score of 14, our patient did not require intubation and did not raise concern for elevated ICP. Many providers will administer a prophylactic antiepileptic drug (AED) at this point for seizure prophylaxis, although the effect on functional outcome remains controversial. Early seizures occur in about 15–20% of aneurysmal SAH patients, with increased blood burden and poor clinical grade as risk factors [12, 13]. Our practice is to continue the AED regimen for at least the duration of hospitalization given the favorable side effect profile of newer agents, but many choose to discontinue prophylaxis after securing the aneurysm.

No lumbar puncture was necessary in this patient as the SAH was proven on non-contrast head CT. A lumbar puncture would have been necessary if the non-contrast head CT was negative. Some centers use MRI instead of lumbar puncture to rule out SAH in this setting, depending on pre-test probability.

If non-traumatic SAH is identified by non-contrast CT head or LP, the next step would be to obtain a CTA of the head. The primary goal is to rule out aneurysm, which optimally should be secured within 24–48 h due to the high risk of recurrent hemorrhage, with the potential for neurologic worsening. CTA may also identify another culprit vascular lesion, such as arteriovenous malformation, arteriovenous fistula, arterial dissection, RCVS, or other vasculitis/vasculopathy. Some of these entities will require directed management, making accurate diagnosis important. In this patient, CTA did not show an aneurysm, vascular lesion, or other abnormality. Despite high sensitivity of modern, well-performed, high-quality CTA, catheter

digital subtraction angiography (DSA) is the gold standard and should be performed to more definitively rule out aneurysm or these other pathologies. Blood burden may obscure the etiologic vascular lesion and, again, CTA sensitivity is more limited for aneurysms <3 mm.

At this point, the differential diagnosis for SAH should be revisited. With a classic "aneurysmal" pattern of SAH—that is, diffuse blood in the basal cisterns—the most likely differential includes occult aneurysm, non-aneurysm vascular lesions (e.g., AVM, AVF, cavernoma), and perimesencephalic SAH. Other causes of SAH are more likely to cause focal or convexity/cortical SAH. This list of other causes is long and includes RCVS, mycotic aneurysm, arterial dissection, PRES, venous thrombosis, tumor, ischemic stroke, cerebral amyloid angiopathy, cocaine/amphetamine abuse, thrombocytopenia, anticoagulation use, spinal lesions, and other vasculitides/vasculopathies. Alternate etiologies might be entertained if formal catheter angiogram does not show an aneurysm, or if the clinical scenario suggests. Further investigation in such cases would likely include MRI of the brain ± cervical spine, with and without gadolinium.

Despite a negative CTA in our patient, catheter angiography (Fig. 15.2) did reveal a small saccular aneurysm of the left internal carotid artery at the branchpoint of the left posterior communicating artery. This, therefore, fit with an overall diagnosis of aneurysmal SAH, with a falsely negative initial head CTA. This also reinforces why clinical suspicion is so important in driving the diagnostic evaluation.

All aneurysmal SAH patients should be given enteral nimodipine and admitted to the ICU with close cardiopulmonary and neurologic monitoring [14]. The aneurysm should be secured via microsurgical clipping or by endovascular means within 24–48 h in order to prevent re-hemorrhage and consequent poorer outcomes [15]. Our patient was transported to the neuro-ICU, and a plan was made for aneurysm

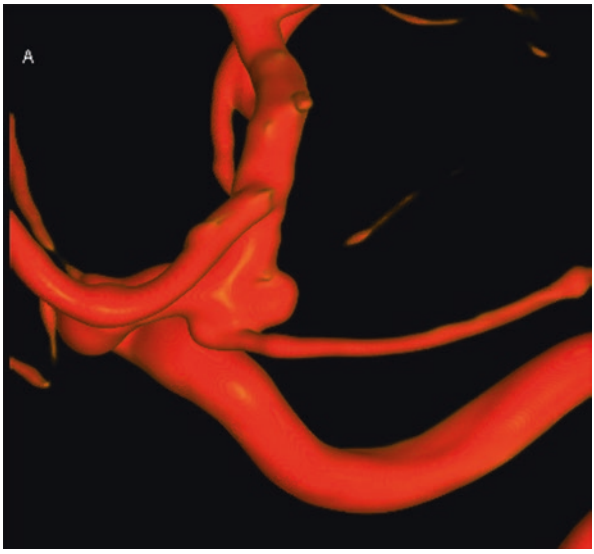

Fig. 15.2 Three-dimensional reconstruction of a digital subtraction catheter angiogram after injection of the left internal carotid artery showing a broad-based saccular aneurysm at the branch point of the left posterior communicating artery

obliteration the next morning given that it was already late evening. Emergent surgical intervention is typically reserved for continued, actively extravasating, large space-occupying hematoma requiring evacuation, or need for bony decompression.

In general, endovascular treatment is favored when the patient is a candidate for both endovascular and surgical obliteration. For the 2143 patients with ruptured intracranial aneurysms randomized in the International Subarachnoid Aneurysm Trial (ISAT), there was a lower rate of death or dependence in the endovascular group (23.5%) compared to the microsurgical clipping group (30.9%, $p = 0.0001$) [16]. Similarly, in the Barrow Ruptured Aneurysm Trial (BRAT) of 472 patients, there was a lower rate of poor outcome (mRS >2) in the endovascular (23.2%) compared to the surgical group (33.7%, $p = 0.02$) [17]. Endovascular management is also often chosen for older patients, patients with worse grade on presentation, and basilar apex aneurysms.

Surgical clipping and endovascular coiling were both considered for this patient, but microsurgical clipping was favored given a broad neck of the aneurysm, young age of the patient, and ability to fenestrate the lamina terminalis concurrently. While the aneurysm probably could—from a purely technical perspective—be coiled with stent-assistance, the use of a stent would have required antiplatelet therapy which is relatively contraindicated and disfavored in the case of acute SAH—particularly when clipping is also a viable option. For the same reason, flow diversion is typically avoided in the setting of acute SAH.

Several hours later, the nurse noted that the patient was only opening her eyes to painful stimulation, was only withdrawing to painful stimuli in her extremities, and was only mumbling when asked questions. Her pupils were 4–5 mm, equal, and reactive. Decline in mental status at any point should prompt re-imaging with non-contrast head CT. However, before traveling to the scanner, the patient's airway should be secured by intubation (given a GCS of 8). Early decline in mental status can be secondary to any number of issues, including seizure, re-hemorrhage, hydrocephalus, increased intracranial pressure, herniation, and even, hyponatremia. Therefore, labs should be rechecked as well. Her sodium came back at 135. Her head CT (Fig. 15.3) showed stable hemorrhage compared to prior imaging, but now with moderate ventriculomegaly and loss of defined cerebral sulci. Her decline in mental status was most likely attributable to hydrocephalus, and she met criteria for urgent, temporary CSF diversion. Rates of acute hydrocephalus in aneurysmal SAH vary greatly depending on the study population, ranging from 25% to 75% [6]. Presence of ventricular blood and amount of total blood are predictive of deterioration in level of consciousness from hydrocephalus [18]. Amount of subarachnoid blood and presence of intraventricular blood is also predictive of cerebral vasospasm, as objectified by the Fisher grade.

In a scenario of declining mental status (usually with a GCS of 8 or below) and imaging evidence of hydrocephalus or elevated intracranial pressure, a bedside external ventricular drain (EVD) is typically placed. An EVD may also be placed in borderline patients who will be under general anesthesia for catheter angiogram or other procedures. This procedure was performed emergently in our patient. Upon

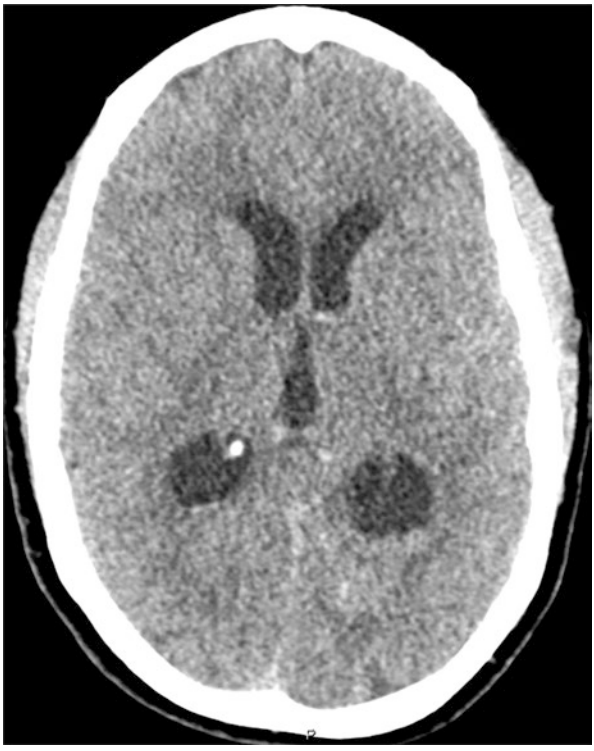

Fig. 15.3 Axial non-contrast head CT showing ventricular enlargement from developing hydrocephalus

placing the ventriculostomy catheter, her opening pressure was noted to be approximately 30 mmHg. A head CT was performed to confirm catheter location, and she was drained continuously, with caution not to over-drain in the setting of a still-unsecured aneurysm. Typically, we start with a height setting of around 20 cmH_2O. Shortly after, she began to open her eyes and follow commands again. Of note, lumbar drainage is also an option in patients without intracranial mass lesions, herniation, or obstructive pathology.

Hours later, in the early morning, the nurse noted another decline in exam. The patient was not opening her eyes and was localizing to pain with the left upper extremity but was just withdrawing to pain in the right upper extremity and bilateral lower extremities. Her pupils were 3–4 mm, equal, and reactive. As before, labs should be rechecked and consideration made for re-hemorrhage, seizure, and increased intracranial pressure. The EVD was confirmed to be patent, and the EVD was recording an ICP of 9 mmHg with a good pressure waveform, excluding hydrocephalus or increased intracranial pressure as a cause of her exam decline. The patient was taken for stat non-contrast head CT, which did not show any new hemorrhage; the ventricles had decreased in size since last imaging. The sodium came back at 126. Seizure should be strongly considered in this setting, given the lack of radiographic explanation and the fact that hyponatremia is known to lower seizure threshold. The patient was loaded with a second AED and placed on continuous

EEG, which showed epileptic activity. Hypertonic saline was also given intravenously to bring her sodium back into the normal range. Her mental status improved over the next few hours as a result. While quick correction of sodium in this setting is appropriate given both the acute drop and that the patient is symptomatic, greater caution is necessary when sodium drop has occurred more slowly (i.e., >24 h).

Later in the day she underwent a successful and uneventful craniotomy for microsurgical clipping of the left posterior communicating artery aneurysm. Her neurologic exam upon return to the ICU was somnolent but eyes open to voice, pupils 3 mm and reactive, following commands with good strength in all four extremities symmetrically.

Even after securing the aneurysm, the course of these patients can be quite tenuous. ICU comorbidities are common, such as pneumonia, cardiac ischemia or arrythmia, and venous thromboembolism. Neurologically, the primary focus is preventing and managing vasospasm and delayed cerebral ischemia (DCI). This phenomenon usually occurs 4–21 days after the ictal event and can be predicted by initial subarachnoid and ventricular blood burden via the Fisher and modified Fisher scores [19, 20]. It is important to recognize the difference between vasospasm, an angiographic finding, and DCI, the ischemic event and territory, which do not always correspond [21].

Current recommendations for prevention of vasospasm/DCI are to maintain euvolemia and normal circulating blood volume [6]. Nimodipine is given for 21 days or until hospital discharge, whichever is sooner. High-risk patients are typically monitored in an ICU setting and kept in the hospital for at least 14 days. Transcranial doppler ultrasound (TCD) may be used as a screening tool but can be inconsistent. TCD and radiographic evidence of vasospasm do not necessarily warrant treatment, and heavier reliance should be placed on the clinical exam.

By day 4, the patient had been doing well neurologically but was still intubated; EVD weaning had not yet been attempted. Around mid-afternoon, the nurse noted that the patient was only opening her eyes to voice, was localizing with the left upper extremity, withdrawing both lower extremities, and not moving the right upper extremity. Otherwise, her cranial nerves were unremarkable. Just as with previous exam declines, one should consider new hemorrhage, hydrocephalus, increased intracranial pressure, herniation, and seizure. However, she was now in the vasospasm/DCI window, so this was a possibility as well. Radiographic vasospasm occurs in about two-thirds of patients, and DCI in about 20% [21]. Our patient's modified Fisher score was 4, making her risk of DCI higher, at about 40% [20].

At bedside, the ICP was confirmed in the mid-normal range with a good waveform on the monitor. The CSF was clear, without new blood. The patient was hemodynamically stable, with a mean arterial pressure (MAP) 83 mmHg and systolic blood pressure 129 mmHg. The next step was emergent imaging with at least head CT and CTA. CT-perfusion (CTP), if available, may provide an estimate of potentially salvageable ischemic penumbras [22].

CTA/CTP revealed diffuse bilateral vasospasm with a large area of hypoperfusion in the left MCA territory without completed infarct, compatible with ongoing

DCI. At this stage, blood pressure augmentation should be employed with close monitoring for improvement in the clinical exam. The augmented goal range is usually decided based on the patient's baseline up until this point, and often requires both fluid and vasopressor infusions. A good starting point is 10–20% higher than baseline without vasopressors. Despite several hours of successful elevation in her MAP and SBP, the patient did not respond. She was taken to the angiography suite to undergo local administration of intra-arterial vasodilators [23]. On return, she was localizing both upper extremities symmetrically. Blood pressure augmentation continued as she was at high risk for further ischemic events.

Fortunately, the rest of her hospital course was uncomplicated. She was weaned from the ventilator and ventricular drain a few days later. Acute hydrocephalus after hemorrhage often resolves, and only about 20–60% of patients with temporary drainage will need permanent shunting [24]. The likelihood of shunt dependence is greater in the setting of intraventricular hemorrhage and/or vasospasm [25]. Before removal, ventricular drains are typically "challenged" by clamping and assessing for radiographic change or clinical decline, neither of which occurred in our patient. She was discharged to inpatient rehabilitation on hospital day 16.

15.5 Clinical Pearls

- Aneurysmal SAH should be on the differential for any acute, severe headache or change in mental status; it is frequently missed.
- There are many causes of spontaneous SAH. Vascular imaging is warranted—at minimum, with CTA—to evaluate for aneurysmal source or vascular lesion in the setting of spontaneous SAH.
- Maintain a low threshold for obtaining a formal cerebral angiogram—even if CTA is negative—when clinical suspicion is high.
- Trauma may be the end result of an aneurysmal rupture, not necessarily the cause.
- Rapid diagnosis is key. The early re-hemorrhage rate is high. Ideally, aim to secure the aneurysm within 24 h.
- Even after securing the aneurysm, patients require extreme vigilance and specialized care given high risk for both neurologic and non-neurologic complications, including vasospasm/DCI, pneumonia, and thromboembolic events.

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Chapter 16
Pituitary Apoplexy

Jack Rock and Karam Paul Asmaro

Clinical Scenario

A 62-year-old man presents to the Emergency Department with sudden-onset severe headache followed by decreased visual acuity. He has a past medical history of hypertension, diabetes mellitus, and asthma. He complains of nausea and emesis, but denies photophobia, diplopia, or weakness/numbness of his face or extremities. The patient also complains of "blurry vision." Ophthalmological evaluation reveals decreased visual acuity that corrects with pinhole testing. Neurological evaluation is otherwise unremarkable. Vital signs are stable and routine laboratory analysis is unremarkable. A non-contrast CT head reveals a heterogeneously hyperdense sellar-suprasellar mass with expansion of the sella turcica and osseous erosion of the dorsum sellae.

16.1 History and Neurologic Exam

The major neurosurgical consideration for a patient presenting with sudden-onset headache and visual symptoms is intracranial pathology. A consistent complaint is the sudden onset of headache in upward of 80% of patients with pituitary apoplexy; it is described as retro-orbital, bifrontal, or diffuse. The remainder of the clinical

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_16

manifestations, however, can develop over minutes to days. Nausea and emesis—due to meningeal irritation—are present in 60% of patients, sometimes combined with other signs of meningeal irritation such as photophobia, nuchal rigidity, and fever. It is important to note that the presenting signs and symptoms of pituitary apoplexy are variable and range from mild to life-threatening, necessitating a thorough history and examination to establish the diagnosis.

- *Hypopituitarism*. It is imperative to establish whether the patient has been experiencing systemic signs and symptoms of pituitary hypopituitarism secondary to endocrine axis dysfunction as the result of a non-functioning pituitary adenoma (NFPA) causing gland dysfunction. The prevalence of pituitary and endocrine dysfunction in patients harboring a pituitary tumor is reported as 35–85%; complete or pan-hypopituitarism occurs less frequently (5–30% of cases) [1].
  - *Growth hormone deficiency*. Growth hormone is the most frequently affected axis, with two-thirds or more of patients with NFPA harboring growth hormone deficiency. Decreased growth hormone production can stunt the growth of a child and cause muscle atrophy with fatty replacement; increased low-density lipoprotein (LDL) cholesterol, increased osteoporosis, decreased memory and energy levels in adults.
  - *Hypogonadism*. Central hypogonadism has a prevalence of 35–95% in patients with a NFPA. The symptoms in a postpubertal adult are usually ambiguous and might include loss of libido, erectile dysfunction, depression, lethargy, cognitive decline, osteoporosis, muscular atrophy, and even reversal of secondary sexual morphology. It can cause infertility in both men and women and be responsible for amenorrhea and hot flashes due to decreased estradiol levels.
  - *Hypothyroidism*. Secondary hypothyroidism produces a state of thyroxine deficiency leading to fatigue, lethargy, cold intolerance, diminished appetite, constipation, myxedema (nonpitting edema), dry skin, brittle hair, anemia, bradycardia, and delayed relaxation of deep tendon reflexes. Upward of 80% of patients with a NFPA have been reported to have central hypothyroidism.
  - *Adrenal insufficiency*. Dysregulation of the hypothalamic–pituitary–adrenal axis can lead to decreased ACTH levels which can have profound consequences on the peripheral vascular system tone, leading to bradycardia and hypotension that can be fatal. However, adrenal insufficiency more commonly manifests as a state of lethargy, lassitude, decreased sexual drive, weight loss secondary to anorexia, hyponatremia, and hypoglycemia. The presence of postural hypotension and tachycardia has also been reported. Acute central adrenal insufficiency after pituitary apoplexy has been reported in up to 70% of patients and may be catastrophic if left unrecognized and untreated (see management below).
  - *Diabetes insipidus*. The loss of free water regulation is a less frequent finding, with less than 10% of patients harboring pituitary tumors exhibiting symptoms associated with posterior gland dysfunction. Affected patients exhibit polydipsia and polyuria, with frequent night-time awakening to urinate due to the loss of vasopressin release from the neurohypophysis. The incidence of

diabetes insipidus after pituitary apoplexy has been reported to be present in up to 20% of patients [2].

- *Pituitary hypersecretion*. Functioning tumors are less likely than their NFPA counterparts to present as pituitary apoplexy, they account for less than 10% of cases.
  - *Acromegaly*. Growth hormone excess in adults causes acral changes such as enlargement of the hands and feet causing increasing glove, ring, and shoe sizes. Facial morphology becomes coarse, with enlargement of the nose and frontal skull bones, as well as widening of the maxilla and interdental spaces. Due to the slow rate of change, it is recommended to ask for old photographs such as a driver's license to compare characteristics. Other manifestations of raised growth hormone and IGF-1 levels are sleep apnea, type 2 diabetes mellitus, cardiovascular disease, hypertension, arthropathy, and carpal tunnel syndrome.
  - *Cushing's disease*. The presence of hypercortisolism secondary to a pituitary tumor releasing unregulated excess ACTH is classified as Cushing's disease. The most common clinical manifestations include decreased libido, hypertension, plethora, round face (moon face), obesity, hirsutism, ecchymoses, lethargy, hyperglycemia, dorsal fat pad (buffalo hump), and abdominal stria.
  - *Hyperprolactinemia*. Prolactin producing tumors can cause a state of amenorrhea in women with frequent galactorrhea if the prolactin levels are significantly elevated.
- *Past medical and gynecological history*. Aside from the above-mentioned medical issues, bleeding disorders increase the risk of pituitary apoplexy due to the increased risk of hemorrhagic transformation of the tumor. Hemodynamic changes during pregnancy and postpartum period have been reported to cause pituitary apoplexy in the presence of a tumor. Infarction of the pituitary gland due to profound hypotension and resultant ischemia is referred to as Sheehan syndrome which can manifest in a similar fashion in postpartum women [3, 4].
- *Previous surgeries*. Various surgical procedures and surgeries have been implicated in precipitating pituitary apoplexy, some of which are related to hemodynamic fluctuations and changes in blood pressure. Cerebral angiography has been linked to cases of pituitary apoplexy within minutes to hours after the procedure. Orthopedic and cardiothoracic surgeries have been associated with pituitary apoplexy more than gastrointestinal, pulmonary, or thyroid surgery; this is thought to be related to prolonged periods of relative systemic hypotension, leading to tumor ischemia, compounded by intraoperative anticoagulation and blood loss [5]. Ictus after surgical intervention has been reported up to 48 h postoperatively.
- *Medication use*. Treatment of hormone-sensitive cancers such as prostate and other infertility conditions with GnRH agonists has been implicated with pituitary apoplexy in the acute and subacute phases of treatment [6]. Anticoagulants of various types have been shown to precipitate pituitary apoplexy during the initiation and maintenance phase as they expand the risk of hemorrhagic events [7].

- *Head trauma*. Traumatic brain injury, even minor, has been shown to increase the risk of pituitary apoplexy in the immediate and subacute phases after injury.
- *Recent diagnostic procedures and testing*. Dynamic testing of insulin, TRH, GnRH, GHRH, or CRH has been shown to precipitate the incidence of pituitary apoplexy immediately, during, or shortly thereafter due to a mismatch of demand and blood supply to the adenoma [8].

As is the case with all medical issues, it is imperative to evaluate the patient's vital signs. Profound cases of acute corticotropic deficiency can lead to loss of peripheral vascular resistance, with ensuing refractory hypotension, making the body nonresponsive to both endogenous and exogenous catecholamines [9]. Immediate recognition and treatment with cortisol replacement therapy, in conjunction with pressor support, is paramount. Pyrexia can be present in 15% of patients with pituitary apoplexy [10].

A succinct yet thorough neurological examination is necessary to localize the offending pathology and determine triage urgency. The objective examination should include standard mental status and Glasgow Coma Scale to assess the level of consciousness and rule out the presence of mass effect, increased intracranial pressure, and determine the need for supportive measures in severe cases causing stupor or coma.

Disturbances in visual acuity may present in more than 40% of patients while 10% will present with blindness [11]. This is due to the rapid expansion of the suprasellar component of the necrotic and hemorrhagic tumor causing compression of the optic chiasm and nerves. A thorough ophthalmological examination of visual acuity (with corrective lenses if applicable), color vision, and visual field testing for bitemporal hemianopsia or other field cuts is essential. It is imperative to test for acuity with a pinhole test to eliminate deficiencies in accommodation due to an oculomotor palsy rather than optic apparatus compression. Testing of extraocular movements is necessary as diplopia and disconjugate gaze is present 50% of the time—from increased intrasellar pressure compressing the adjacent cavernous sinus—affecting cranial nerves III (most frequent), IV, and VI [12].

A thorough motor and sensory evaluation of the face and all four extremities is necessary for the complete examination. Facial pain or anesthesia can occur from compression of the first branch of the trigeminal nerve. Cortical localizing signs such as hemiparesis, hemiplegia, aphasia, and hemianesthesia as a result of a hemispheric cerebral infarction have been reported secondary to the rapid expansion of sellar contents, causing mechanical occlusion of the cavernous or clinoidal carotid artery [13].

16.2 Differential Diagnosis

This patient presents with headache—a nonspecific symptom with a myriad of potential etiologies. The sudden, rather than insidious onset, coupled with nausea and emesis, directs us toward a possible vascular etiology. The absence of endocrinological issues at baseline might be reassuring. However, many hypopituitary conditions go unrecognized by the patient due to their subtle clinical course. The presence of a visual disturbance aids in narrowing down the diagnosis.

Meningitis. Bacterial meningitis may present with headache, nausea, emesis, and meningismus—all of which are likely to be present in a case of pituitary apoplexy. A detailed history and clues of a sudden-onset ictus with visual disturbance rather than isolated photophobia could help differentiate apoplexy from meningitis. Nonetheless, a CSF culture can rule out an infectious etiology and is thus required if a concern is present [14].

Subarachnoid hemorrhage. A sudden-onset, thunder-clap headache is a diagnostic characteristic of subarachnoid hemorrhage which is often intertwined with nausea, emesis, meningismus, and even ocular palsies in cases of posterior communicating artery aneurysms. A lumbar puncture may not be useful in differentiating it from a pituitary apoplexy event due to the presence of xanthochromia, pleocytosis, high RBC count and protein level in both conditions [15].

Cavernous sinus thrombosis. Thrombosis of the cavernous sinus can be multifactorial and can be either septic or aseptic due to a prothrombotic state, neoplasia, trauma, or surgery [16]. Headache is often present. Cranial neuropathies (CN III, IV, VI), potentially with associated visual disturbance, may occur. Patients may also complain of visual disturbance due to lack of lens accommodation from an oculomotor nerve palsy. Examination of the face and sinuses can be useful in delineating septic causes due to an infection spreading from the facial venous system or contiguous spread from the paranasal sinuses, as is the case for rhino-orbital cerebral mucormycosis [17].

Ophthalmoplegic migraine. Patients with a history of migraines may develop debilitating headache with ocular palsies. Although rare, signs and symptoms can vary, and patients may even present in extremis. Critical evaluation for other possible pathologies is warranted, as this is a diagnosis of exclusion [18].

Stroke. Cerebrovascular events in the posterior fossa can present with a headache and, in cases of brainstem infarction, can be associated with ocular palsies among other findings. Large vessel occlusion of the basilar artery can be life-threatening and catastrophic, requiring urgent identification and intervention.

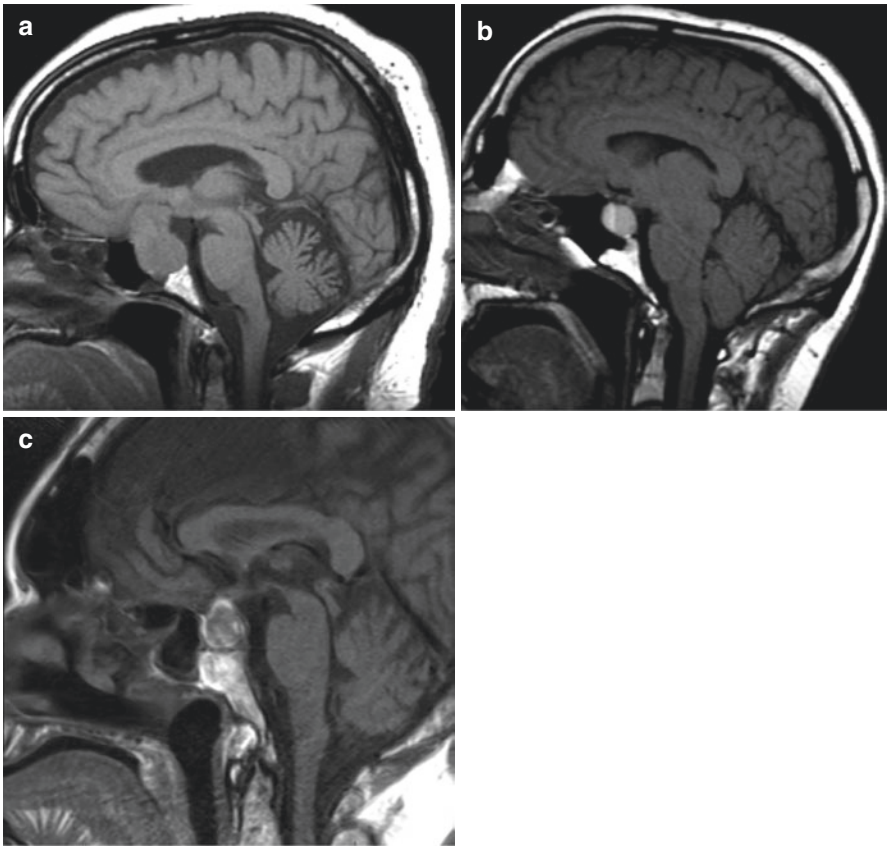

Fig. 16.1 (**a**–**c**) Pituitary apoplexy presents in a variable manner. The following are sagittal T1-weighted MRI sequences without the administration of contrast. (**a**) Infarction of a preexisting pituitary macroadenoma results in rapid expansion of the sella turcica with suprasellar extension and compression of the optic apparatus. (**b**) Hemorrhagic transformation of pituitary tumor with clear fluid levels within the sella turcica. (**c**) A heterogenous mass demonstrating infarcted, cystic, and hemorrhagic components with suprasellar extension compressing the optic apparatus

16.3 Diagnostic Evaluation

Head CT without contrast will provide the clinician with rapid and essential information to triage care for a patient presenting with a sudden-onset headache. The goal is to rule out life-threatening neurosurgical emergencies such as a subarachnoid hemorrhage, but it is also effective in detecting a sellar mass approximately 80% of the time [5]. It is important to note the histopathological, and hence radiographic, variability of pituitary apoplexy, as not all cases are due to hemorrhagic transformation but could be due to infarction of the tumor or a mix of both (Fig. 16.1a–c).

The mainstay radiographic modality to detect and characterize pituitary apoplexy is a brain MRI with and without contrast, ideally with specialized sella or pituitary slices. While a CT scan can be of limited value in detecting small or delayed apoplexy events, MRI has a high diagnostic yield with an ability to estimate the chronicity of the hemorrhage based on the T1- and T2-weighted sequences. The diffusion-weighted imaging (DWI) sequence is especially useful for identifying areas of ischemia representing infarcted tumor. Due to its high resolution, MRI is also useful in evaluating the relationship of the tumor to adjacent structures in cases of cavernous sinus invasion, suprasellar extension, or optic chiasm compression.

A lumbar puncture for cerebrospinal fluid analysis is not particularly useful in differentiating pituitary apoplexy from subarachnoid hemorrhage and should be avoided in cases of mass effect to prevent downward herniation.

The diagnostic evaluation should consist of a thorough evaluation of the patient's vital signs and aim to determine the presence of other metabolic and endocrinological derangements due to the presence of a pituitary tumor or as a direct result of a pituitary apoplexy event. A comprehensive metabolic panel is necessary to determine electrolyte and fluid status. A complete blood count, as well as a coagulation profile, is useful to detect thrombocytopenia or coagulopathy which could precipitate further hemorrhagic events or hinder surgical intervention. Urine analysis to measure urine specific gravity helps in diagnosing diabetes insipidus in patients with hypernatremia. Measurement of random serum cortisol and thyroid labs (TSH and free T4) can be helpful to establish the presence of corticotropic deficiency and thyroxine deficiency, respectively. The remainder of the endocrine evaluation can be performed but does not alter the acute management of this disease process.

16.4 Clinical Decision-Making and Next Steps

Pituitary apoplexy can behave in a myriad of ways leading to a variable disease presentation. It is thought that subacute and silent pituitary apoplexy occurs much more frequently than acute pituitary apoplexy as incidental findings are routinely found on imaging or autopsy up to 25% of the time [5].

The treatment of pituitary apoplexy is dependent on the clinical scenario. Expectant management is the mainstay form of therapy in the absence of acute visual changes. In severe forms, however, patients can develop blindness, drift into a coma, and/or have severe hemodynamic abnormalities. Establishing a diagnosis is of paramount importance, even in neurologically stable patients, especially to prevent the consequences of adrenal failure which may ensue.

For patients presenting in extremis, the ABCs of emergency care are a priority for patients in a coma or decreased level of consciousness. After the airway, breathing, and circulation are secured and resuscitated, further management can proceed. Patients with hemodynamic instability can be resistant to vasopressors; once myocardial infarction and shock of cardiogenic origin have been ruled out, corticosteroid replacement should be initiated intravenously with a bolus hydrocortisone

100–200 mg followed by 50 mg every 6 h is essential due to the wide prevalence of corticotropic deficiency after an acute pituitary apoplexy event [19]. This can be continued for up to 48 h and slowly tapered thereafter according to the clinical course and expert consultation. Thyrotropic deficiency is determined based on the free T4 level sampled earlier and can be replaced with levothyroxine if indicated. It is important to emphasize the need for hydrocortisone administration prior to any levothyroxine administration as the latter can unmask cases of subclinical hypoadrenalism and contribute to hemodynamic instability.

Suprasellar extension of the tumor alongside its now necrotic and hemorrhagic contents can produce visual symptoms, and the same is true with cavernous sinus extension and compression. The common complaint of blurry vision is due to compression of the optic chiasm or nerves but it can also be due to an oculomotor nerve palsy secondary to a disturbance in accommodation of the lens; a pinhole examination can differentiate between the two. Surgical decompression of the optic apparatus is indicated when there is an acute decrease in visual acuity or the presence of a visual field deficit, as it can provide remarkable results when done in a timely fashion. Monocular or binocular blindness portends a dismal prognosis, despite intervention [5]. Conservative management is otherwise equally beneficial when there are no acute visual acuity issues as cranial nerve palsies will gradually resolve over time [20].

The prognosis of endocrine function after pituitary apoplexy is poor, and the patient will require close monitoring and follow-up. An expert consultation to endocrinology is recommended. There have been reports of patients faring better after surgical intervention, but the data is controversial, and should not influence surgical decision-making.

In the case presented at the beginning of this chapter, the patient presented with sudden-onset headache and visual complaints. He appeared to be in stable neurologic and hemodynamic condition. Noncontrast CT imaging confirmed the diagnosis of pituitary apoplexy (Fig. 16.2). Complaints of “blurry vision” were initially

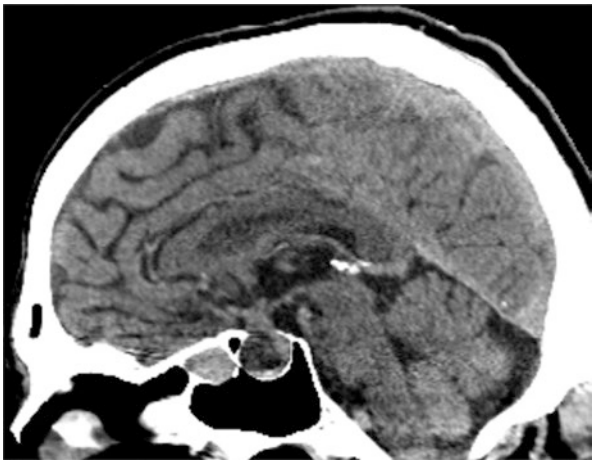

Fig. 16.2 Sagittal noncontrast CT image demonstrating pituitary apoplexy

falsely localized to the optic apparatus (optic nerves or chiasm), but correction with pinhole testing suggested that this was the result of a third nerve, or oculomotor, palsy secondary to inadequate accommodation of the lens on the affected side. More specialized endocrinological labs, such as thyroid labs and cortisol, were drawn but did not impact the first response as the patient was given hydrocortisone regardless (after the blood draw to check for cortisol levels). More specific labs investigating the entire pituitary axis were drawn after the patient was stabilized, and hormone replacements were prescribed at the discretion of the endocrinology specialist. A decision was made to defer surgical excision of the tumor and evacuation of the hemorrhagic content due to the lack of optic apparatus compression and acute visual compromise. The patient made a complete recovery at 3 months with conservative management. He remained on long-term hormone replacement therapy.

16.5 Clinical Pearls

- Pituitary apoplexy has a highly variable presentation and can range from mild headache and visual disturbance to critical hemodynamic compromise and coma.
- Rapid identification is a key to initiate proper treatment and remedy any damage to the optic apparatus.
- Hydrocortisone is a mandatory treatment for patients with pituitary apoplexy to prevent circulatory collapse.
- Surgery is warranted in cases of acute deterioration of visual acuity and loss of peripheral vision.

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Chapter 17
Hydrocephalus and Shunt Failure

Arthur Bartolozzi, Michael Zhang, and Gerald Grant

Clinical Scenario

A 17-year-old male presented to the Emergency Department (ED) with a 2-day history of headaches and vomiting. He described his headaches as frontal, without radiation, unrelated to position, and not associated with photophobia or phonophobia. The patient had a history of migraines that typically subside after one episode of vomiting. However, these headaches were different and persisted despite over-the-counter medications and sumatriptan. While in the ED, the patient experienced two episodes of bilateral arm numbness and tingling, slurred speech, and reported left lower facial droop that resolved without intervention.

His past medical history included GMFCS I cerebral palsy and a non-programmable ventriculoperitoneal (VP) shunt placed at 2 months of age for communicating hydrocephalus secondary to bacterial meningitis. He had never experienced shunt failure or undergone a shunt revision. He had no history of seizures. He took no other medications and had no prior surgeries.

17.1 History and Neurologic Exam

Ventricular shunts offer the primary outpatient instrumentation for managing elevated intracranial pressure due to hydrocephalus. Ventricular shunt placement is a common neurosurgical procedure in the United States, where 33,000 shunt

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_17

procedures are performed annually in adults and children; revisions comprise 48% of those procedures [1]. An analysis of the Pediatric Health Information System (PHIS) database included 1307 children who underwent shunt placement and were followed over a 5-year period. In this cohort, 37% of children required one shunt revision and 20% required 2 or more within 5 years [2]. In this study, high volume centers (>83 shunts per year) had the lowest likelihood of revision at 5 years (22%), relative to 39% at lower volume centers. These percentages have been validated in other large studies [3]. Given the high reported incidence of shunt revision, evaluating a patient for shunt failure is a critical clinical skill for emergency providers.

Proximal (ventricular) obstruction with tissue, clot, infection, kinking, or tip migration are the most common etiologies which can lead to shunt failure [4]. Cysts or loculations can also develop and obstruct flow at either end. Over-draining cerebrospinal fluid (CSF) or "siphoning" due to gravity induced drainage or inappropriate valve setting can lead to "slit ventricle syndrome" with resulting obstruction. This concern has been ameliorated somewhat with the introduction of secondary valves or antisiphon devices [5]. Tubing can fracture, which is more common along the extracranial, distal course of the shunt. Positioning errors of the proximal or distal end are most common in the immediate postoperative period but can also occur farther out from surgery as patients grow. There is a higher likelihood of shunt failure closer to surgery, driven by technical aspects of shunt function and increased likelihood of infection [6–8].

There are many studies delineating risk factors that can aid in identifying which patients should raise further concern for shunt failure. For patients presenting with common complaints without significant neurologic compromise—as in the case above—knowing certain risk factors can help expedite the diagnostic workup. In a series of 1015 patients with shunts placed for hydrocephalus, multivariate analysis identified patient age <17 years (OR 4.22), prior revision procedure (OR 9.01), and "high-risk" diagnosis including congenital/spinal dysraphism and obstructive hydrocephalus (OR 2.81) as significant predictors for shunt revision [9]. Intracranial pathology including tumors, intraventricular hemorrhages, post meningitis hydrocephalus, age <6 months at placement, and pediatric cardiac abnormalities are also associated with poor shunt longevity [10].

For a patient with known shunted hydrocephalus presenting with headaches and vomiting, the differential is quite broad. Depending on the severity of the presentation, more urgent action may be required (see below). It is also important to note that there is often significant reliance on caregiver report for pediatric and nonverbal patients. Lines of inquiry for the patient in this case may be as follows:

- Prior shunt failures and if so, prior presenting symptoms.
- Headache description, onset, precipitating factors, and association with neurologic findings like photophobia, phonophobia, dysarthria, weakness, seizures or paresthesias. Patients with headaches, particularly in shunt failures, may present repeatedly with similar symptoms.
- The positional nature of the headache has implications for the likely diagnosis. Headache that is worsened in the upright position may suggest intracranial hypo-

tension due to over-shunting, whereas a headache that is worse upon waking (or, that wakes the patient from sleep) after being supine all night suggests an increased pressure state likely due to obstruction.
- Constitutional symptoms such as fever, recent sick contacts, recent dental work or procedures may indicate an infectious cause for either shunt failure or intracranial pathology.
- Behavioral and mood changes, particularly in pediatric or nonverbal patients, can indicate subacute shunt failure.
- Specific shunt history including indication for placement, date of initial placement and any revisions; details about the shunt, if available, or the presence of a programmable valve or reservoir; recent changes to the drainage settings; and any symptomatology around prior adjustments.
- Head or body trauma of any variety, either as an explanation for headaches or as a mechanism to induce fracture of the tubing.
- History of bleeding disorders or active use of anticoagulants.

The most common symptom reported in a longitudinal study of shunted pediatric patients presenting to the ED of a single center was headache (79% of total visits over a 12-year study period). This was followed closely by nausea/vomiting (55%), and then, by visual deficits (37%), dizziness (10%), fever/chills (6%), and tinnitus (2%) [11]. These symptoms are relatively nonspecific. In a Nationwide Emergency Department Sample database study of over 74,000 ED visits, presenting complaints of headache, nausea/vomiting, seizures, or fever in shunted patients were more likely to be attributable to pathophysiological causes other than shunt malfunction [12]. This study highlights the importance of a complete workup, appropriate application of clinical suspicion, and the use of data-driven methods for localizing common chief complaints to shunt malfunction. From an emergency physician perspective, the culprit is the shunt until proven otherwise.

Other, more severe symptoms may include increased seizure frequency, diplopia, visual or pupillary abnormalities, or significantly altered mental status [13]. These presenting complaints are much more likely to be associated with increased intracerebral pressure (ICP). In certain circumstances, rapid or sustained increases in ICP can lead to decreased cerebral perfusion pressure, rapid deterioration of cognition and neurological function, and coma. If untreated, severe disability or death may result. Addressing acutely increased ICP requires a multilateral medical and surgical approach and is discussed at length elsewhere in this text [14].

Once pertinent history has been elicited, a comprehensive physical examination should be performed. The patient in the current clinical scenario was awake, alert, and interactive. However, he demonstrated delayed responses to commands for age. A left pronator drift—not previously documented (though records were patchy)—was present. Strength, sensation, reflexes, and cranial nerves were normal. Fundoscopic exam did not reveal papilledema or optic nerve swelling. His abdomen was benign, and there were no signs of additional surgical procedures. His scalp was notable for well healed shunt scars, without erythema, fluctuance, or induration or evidence of extensive scarring to suggest revisions.

The physical examination of this patient is remarkable for a contralateral pronator drift which had not been reported previously but is otherwise reassuring. In a multicenter trial of 248 failed pediatric shunts over a 2-year period, bulging fontanel (likelihood ratio 44.6), palpable fluid collection or fluid tracking along the tubing or reservoir (LR 20.1), depressed consciousness (26.2), irritability (LR 13.7), abdominal pain (LR 12.8), nausea/vomiting (LR 11.1), accelerated head growth (LR 6.02, subacute), and headache (LR 4.28) were strongly associated with shunt failure. In this study, fever was strongly associated with shunt infection (LR 39.3), as were gross signs of purulent drainage or dehiscence (but those were rare) [10]. Obesity has also been independently associated with a significantly shorter median shunt survival time [15].

It is important to examine all aspects of the patient that may be affected by shunt placement. In a study of a national database encompassing 74,552 ED visits by pediatric patients with a CSF shunt over a 9 year period (12.8% underwent revision), the strongest physical examination findings predictive of revision were peritonitis, papilledema or optic nerve swelling, and oculomotor palsies [12]. Papilledema generally requires a formal ophthalmologic examination for diagnosis, so if suspicion is high, such a consultation should be incorporated into the initial evaluation of the patient. Although the absence of papilledema is not sufficiently sensitive to exclude elevated intracranial pressure, the specificity may obviate the need for a potentially unsterile shunt tap. A patient with a cardiac or pleural distal shunt terminus may present with non-traditional symptoms reflecting distal failure. These may include tricuspid valve insufficiency, arrhythmia/atrial fibrillation, shortness of breath, pulmonary hypertension, pleural effusion, or even frank heart failure [16].

17.2 Differential Diagnosis

For this patient presenting with new onset frontal headaches, nausea/vomiting, and pronator drift on the side contralateral to his indwelling shunt—with a normal BMI and the only risk factor for failure being shunt placement for neonatal pathology—the differential diagnosis is broad. There are no signs localizing to the abdomen. There is a low suspicion for infection. Considerations in this setting should include:

- *Migraine*—presumed to be the most likely diagnosis at this stage.
- *Tension headache*—common, but in this case, unprecedented in the patient and usually not associated with nausea/vomiting.
- *Cluster headache*—the expected headache localization and acute severity are not present in this patient.
- *Shunt failure*—cannot be ruled out at this point and must be investigated further, as this is potentially actionable.
- *Infection* (including central nervous system infection/meningitis or more commonly experienced systemic/respiratory/gastrointestinal infection with similar

localizing symptoms) less likely in this patient given an absence of constitutional symptoms and exposures.
- *Seizure*—certainly can be associated with headaches, nausea, and vomiting but is not generally sustained over a period of days and is less likely in a young adult patient without a history of seizures.
- *Stroke*—pronator drift is present on neurologic exam, but functional strength, coordination, and sensation testing were normal, decreasing the likelihood of this diagnosis.
- *Subdural hemorrhage*—a severe consequence of over drainage that is less likely in a young patient.

17.3 Diagnostic Evaluation

The patient in this clinical scenario underwent a radiographic shunt series (X-rays) showing no disconnection, followed by a rapid sequence ("fast brain") MRI. No acute infarct was noted. The right frontal approach ventriculostomy catheter was in place, with the distal tip terminating at the medial aspect of the right lateral ventricle, near midline. Compared to a head CT two years prior, there was a mild increase in the caliber of the supratentorial ventricles, but without evidence for significant transependymal edema. The fourth ventricle was stable in size. Figure 17.1 depicts representative images from these studies. Standard labs were unrevealing. WBC (9.8 k/μL, neutrophil 81.5%) was within normal limits, hemoglobin (15.8 g/dL) was normal, BMP was unremarkable. COVID-1 PCR was negative.

A "shunt series"—consisting of AP and lateral radiographs along the length of the shunt from the skull, neck, chest, and abdomen—is routinely obtained. Traditionally, these x-rays have been used to identify specific areas of discontinuity or gross malalignment in an expeditious manner. They can also help identify valve type. Questions about ultimate usefulness and resource optimization have been raised in the current healthcare landscape where cross-sectional imaging is omnipresent.

CT is useful for identifying ventriculomegaly and catheter trajectory in an expeditious fashion. However, CT will not capture all causes of shunt failure and contributes significantly to radiation exposure. In a study of 461 separate ED visits for shunt evaluation, of the 71 (15.4%) patients who were diagnosed with shunt failure, 31% were judged to have a normal head CT. Of the patients with a normal CT head, 30% were identified to have an abnormal shunt series [1]. It is also important to note that in up to 15% of shunted patients, compliance of the brain and ventricles will have decreased to the point where increases in ICP due to shunt failure will not lead to increased size of the ventricles [17]. Some evidence describes a shunt series as a low-yield modality given poor sensitivity, imparted delay of care, and lack of impact without changing management [18]. However, if a patient needs to go to the operating room for shunt failure, an X-ray can be very important to map the shunt system

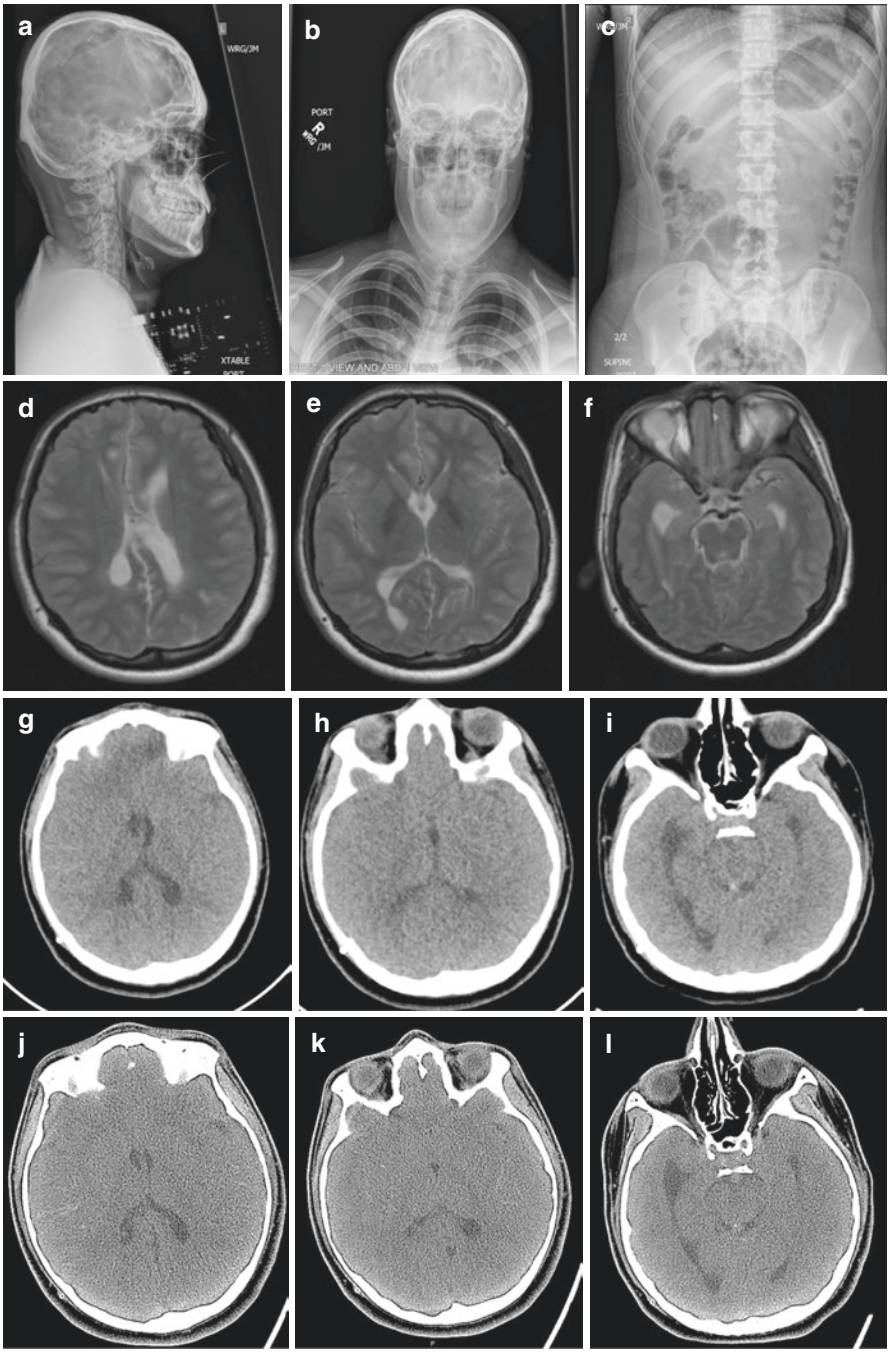

Fig. 17.1 (**a**–**l**) Selected images from X-ray shunt series (**a**–**c**) are included and do not show a disconnection. Fast MRI (T2, **d**–**f**) and CT scan in the ED (**g**–**i**) are included and demonstrate mildly increased ventricle size in both the lateral ventricles and temporal horns, as compared with a CT head from 2 years prior (**j**–**l**)

in advance of surgical intervention (particularly when there may be multiple systems and/or orphan catheter segments in place).

A standard MRI is a radiation-sparing, volumetric alternative to CT for detecting changes in ventricular size. Its longer acquisition times, need for sedation among pediatric cases, and availability (particularly on nights/weekends/holidays) limit its generalized use. These drawbacks have been addressed by the development of rapid acquisition sequences based on T2-weighted imaging. Such sequences can be acquired within 20 s, for a total scan time of under 3 min. This obviates the need for sedation in most cases for young children [19]. Additionally, rapid MRI has been shown to demonstrate reasonable visualization of the catheter except in cases of slit/small ventricles [20]. In a large case series of 698 ED visits among 286 unique patients, rapid MRI was noninferior to CT for diagnosing ventricular shunt malfunction as indicated by need for revision during that admission (81.8% MRI vs 82.4% CT) [21]. Rapid MRI is still more expensive than CT, but is the preferred modality when available. It remains important to confirm model and setting of shunt valves prior to MRI imaging, such that they can be reset to their desired setting after magnet exposure.

When a VPS demonstrates appropriate continuity, nuclear medicine imaging with a technetium-99 m diethylenetriaminepentaacetic acid radiotracer can be used to ensure patency. This is called a "shunt flow study." The tracer is injected into the reservoir and followed for flow at an appropriate rate toward the shunt terminus. It has been reported to have high sensitivity (92.6%) for detecting patients in shunt failure who will go on to have surgery. This improved to 96.3% sensitivity when combined with CT [22]. However, nuclear imaging is costly, entails radiation exposure, and requires coordination of staff and resources. These may preclude its incorporation into emergent workup, and its decreased selection as a diagnostic modality [21].

Nascent strategies focusing on faster, radiation free, point-of-care diagnostics are emerging. One such technique is ultrasound-measured optic nerve sheath diameter—a bedside procedure that does not require sedation, special equipment, or radiation. The diameter threshold correlating with increased ICP or shunt failure has not been defined, as there are differences across institutions and protocols [23]. Though there are currently few studies and experiences to substantiate recommendations for this modality, it exhibits a high negative predictive value and substantial cost-effectiveness [24, 25].

Another option is noninvasive thermal sensor designed to evaluate fluid flow based on temperature changes across ventricles. Current studies have low numbers and suggest specific, but not sensitive, shunt failure identification [26, 27].

The patient in our case was clinically stable and able to tolerate a rapid sequence MRI. A shunt series was also obtained. Neither was definitively diagnostic, and there were no signs of an overt infectious process. Given the sustained suspicion for shunt failure based on clinical symptoms, the patient was admitted for observation and a bedside shunt interrogation.

Figure 17.2 summarizes the typical diagnostic evaluation for suspected shunt failure.

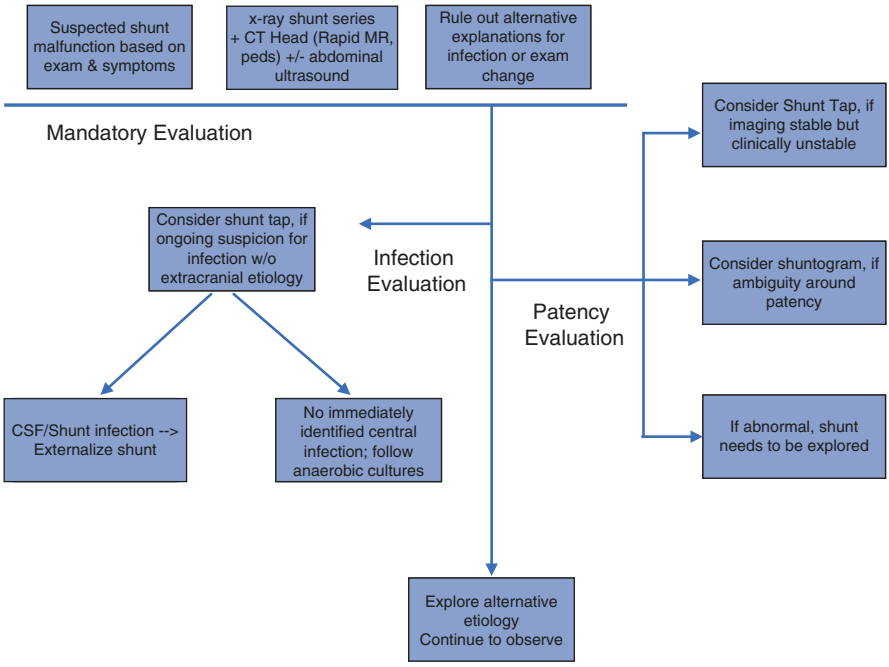

Fig. 17.2 Flow chart depicting the suggested evaluation process for suspected shunt failure

17.4 Clinical Decision-Making and Next Steps

Beyond medical management discussed below, any procedural steps must be approached with caution as the risk of infecting or obstructing an otherwise normally functioning ventricular shunt carries significant consequences. The shunt reservoir usually can be accessed with a 25 or 23 gauge butterfly needle to analyze flow/patency, check ICP, and permit drainage of CSF for routine analysis or culture [28]. Certain shunt valves can be reprogrammed noninvasively to adjust CSF flow rates to symptoms. However, this is generally performed in a planned fashion by neurosurgical care teams and would not be appropriate for emergency room presentations.

Lumbar puncture is rarely, if ever, indicated in evaluating shunt failure in the ED. If signs/symptoms of severely elevated ICP are present, the case is brought immediately to the OR. Operative indications include all methods of shunt failure. Revision is undertaken on an urgent basis in the absence of severe neurologic symptoms. In simple cases, the failing element is identified and replacements are limited to the defective components. These may include the proximal tubing, the distal tubing, the valve, or any combination including the entire system. In the setting of infection, the contaminated indwelling device and catheters must be entirely

removed. Since infectious processes can require days to weeks for adequate antibiotic therapy and clearance depending on organism and CSF culture, the ventricular drain would need to be externalized before definitive replacement. If an alternative infectious etiology can be identified and adequately explain the severity of presenting symptoms, a shunt tap can be deferred. At the authors' institution, a shunt tap is not pursued to primarily document negative CSF involvement when CNS infection is substantially lower on the differential.

In some cases, an endoscopic third ventriculostomy (ETV) is performed to allow CSF to drain through the base of the third ventricle without reimplanting the shunt. Originally described as a durable alternative to shunting in the developing world, this is now a procedure performed routinely for both children and adults if they are good candidates—either in the primary or revision setting. The ideal candidate has triventricular hydrocephalus, where the lateral and third ventricles are large and the fourth ventricle is small due to aqueductal stenosis. An acceptable success rate for ETV, whether elective or emergent, is 64–75% survival over 2 years, with higher failure rates reported in the setting of CNS infection [29, 30]. ETV success rates can be predicted with the ETV Success Score (ETVSS), which considers multiple factors including age, hydrocephalus etiology, and previous shunt placement [31]. Specific relative indications for a "secondary" ETV—as a conversion or adjunct to an existing shunt—include (but are not limited to) active infection, recurrent shunt failures, and post-hemorrhagic hydrocephalus [32].

In cases where the constellation of presenting symptoms suggests shunt failure, medical management is largely symptomatic: nausea and headache treatments and fluid resuscitation in the case of profound vomiting. Another clear, albeit sluggish target is the carbonic anhydrase mechanism that produces CSF. Acetazolamide decreases CSF production and can be used in infants prior to placement of a shunt. A recent study of 112 pediatric shunt failure patients treated with dexamethasone, acetazolamide, and ranitidine prior to revision demonstrated substantial improvements in headache, emesis, irritability, lethargy, blood pressure, and pain [33]. These medications are generally well tolerated and effective for cases of suspected shunt failure without severe features. Acetazolamide is thought of as a long-term medication for control of CSF production rather than as a treatment for acute elevation in ICP, but has been shown to lower opening pressures for shunted patients by as much as 69% in 4–6 h [34, 35]. It should be noted that acetazolamide is not to be used in cases of overdrainage and does not substitute for surgical revision.

Ultimately, the patient in this clinical scenario was admitted for further evaluation. ShuntCheck [25]—a temperature-based flow sensor—was applied and detected "no flow." Next, a bedside shunt tap of the reservoir was performed. This demonstrated only a very small amount of CSF into the syringe from the reservoir and no backflow, indicating a proximal obstruction. Given the constellation of clinical findings, including limited shunt flow despite stable appearing ventricles, the patient underwent a proximal shunt revision with endoscopic guidance which led to appropriate restoration of flow through the system and improvement in his symptoms.

17.5 Clinical Pearls

- Shunt failure may be acute or subacute. Patients in failure may present with a variety of symptoms—neurologic or systemic. Patient risk factors and clinical suspicion are key to drive further evaluation.
- Appropriate workup of a suspected shunt failure includes a shunt series, a fast-sequence MRI (preferred) or CT, and standard labs specifically to exclude infection. New noninvasive tools including optic nerve sheath diameter measurement and thermosensors continue to be evaluated as adjunct diagnostics.
- Judiciously applied medical adjuncts may provide a bridge to definitive surgery for patients who do not require emergent intervention.
- Surgery is almost always indicated in diagnosed shunt failure. The timing and extent of intervention are determined by suspicion for raised ICP, localization of the point of failure, and presence of infection.

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Chapter 18
Acute Intracranial Infection

P. B. Raksin

Clinical Scenario

A 34-year-old man presents to the Emergency Department with a complaint of progressive headache. Records indicate that he presented 2 weeks earlier with submental swelling and subjective fevers. Non-contrast CT head was unremarkable at that time. However, his WBC count was markedly elevated (180,000). A peripheral blood smear revealed 85% blasts, and subsequent bone marrow biopsy was consistent with acute lymphoblastic leukemia. The patient underwent two rounds of leukapheresis, followed by induction chemotherapy. He was discharged on ampicillin-sulbactam.

The patient reports onset of headaches shortly after discharge. Headache was initially diffuse, but now localizes to the right occipital area and radiates to the posterior neck. He admits nausea and dizziness, but denies emesis, vision changes, photophobia, seizure, neck stiffness, or weakness/numbness of his extremities. He is afebrile. His current WBC count is 0.4. His platelet count is 24,000. The previous submental fluid aspirate culture was negative.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_18

18.1 History and Neurologic Exam

The primary neurosurgical consideration for a patient—recently diagnosed with cancer and immunosuppressed—presenting with progressive headache would be intracranial pathology. It is unclear at this point, however, whether the process is diffuse or space-occupying. Nor is it clear whether the process is neoplastic or infectious in origin.

Therefore, it would be prudent to elicit history on several fronts. Relevant lines of inquiry may include:

- *Constitutional symptoms*. Establish whether the patient been experiencing symptoms suggestive of a systemic process. Inquire about recent fever, sweats, chills, and cough, as well as anorexia and/or weight loss.
- *Neurologic symptoms*. Start by eliciting more detailed history regarding the presenting complaint of headache. Document the quality, frequency, and duration of these episodes. Occurrence at a particular time of day (i.e., upon waking) might suggest raised intracranial pressure. Determine whether there are ameliorating or exacerbating conditions. Explore other symptoms—such as nausea/emesis, dizziness, or vision changes—that might accompany headache episodes. Inquire about potential signs and symptoms of meningitis—photophobia, nuchal rigidity, etc. Ask about events suspicious for seizure activity. Inquire about weakness and/or numbness of the extremities.
- *Recent head trauma*. Headache alone is a nonspecific symptom; however, if head trauma is reported, this should be followed by questions to exclude cerebrospinal fluid leak (clear, watery drainage; salty fluid in the oropharynx; positional headache; ring formation on the pillow) or possible open injury (a laceration not appreciated to communicate with a fracture, etc.).
- *Recent illnesses or sick contacts*. Document recent medical issues, as well as exposures to other ill individuals. We know that this patient recently was diagnosed with leukemia. It would be important to determine where he is with respect to his chemotherapy cycle to discern whether his pancytopenia is anticipated. The presence of leukopenia also influences the potential causative infectious agents. The presence of cancer, of course, broadens the differential diagnosis beyond the topic of this chapter.
- *Recent receipt of antibiotics*. This patient was treated empirically with ampicillin-sulbactam for his submental swelling (the final culture was negative). It is important to document both agent(s) and duration of therapy. Recent prior antimicrobial therapy may predispose the patient to harbor a resistant organism and may inform the choice of agents for broad-spectrum antimicrobial coverage.
- *Recent dental procedures and/or poor dentition*. Document any recent dental procedures. Transient bacteremia may predispose the patient to seeding with oral flora.
- *Recent hospitalization or residence in a long-term care facility.* This information is relevant to establish whether the patient has had a recent infection, is known to

be colonized with drug-resistant bacteria, and to inform the appropriate selection of broad-spectrum antimicrobial coverage.
- *Employment history and hobbies*. The patient's occupation and hobbies may provide additional clues regarding potential exposures.
- *Travel history and national origin*. Certain infectious processes may be endemic in the patient's country of origin. Likewise, travel to certain geographic regions may influence the differential diagnosis (such as the presence of fungal infections in the American Southwest).
- *Pets in the home*. An immunosuppressed patient, as in this example, may be at an elevated risk for infection from seemingly innocuous exposure to household pets (such as from toxoplasmosis).

A targeted neurologic exam may assist in localization of the process before diagnostic imaging is available. The objective exam should include standard mental status, cranial nerve, motor, sensory, and cerebellar elements. The presence of lateralizing signs should prompt concern for a space-occupying lesion and trigger expeditious imaging.

Given concern for an infectious process, the general systemic evaluation should include assessment for photophobia and signs of meningismus, as well as for the presence of rhinorrhea or otorrhea. The external ear canal should be visualized, both for the presence of discharge and to assess the integrity and appearance of the tympanic membrane. A quick survey of dentition during the cranial nerve exam may provide an indication of the likelihood of an oral flora source for infection. A patient with underlying endocarditis may present with cutaneous findings such as Osler's nodes or Janeway lesions, in addition to a new or changing heart murmur.

18.2 Differential Diagnosis

This particular patient presents a conundrum. The presenting complaint of headache is a notoriously nonspecific symptom. He does not describe exacerbation in the early morning to suggest raised intracranial pressure. Nor does he describe specific accompanying symptoms aside from the equally nonspecific nausea and dizziness. Nor does he describe lateralizing symptoms that might reasonably provide localization of the presumed lesion. The absence of fever might be reassuring. However, this is occurring in the context of pancytopenia. That only serves to broaden the diagnostic considerations. Fever, if present, will often be low-grade.

On the basis of the available data, the differential diagnosis remains quite broad. Progression of the patient's underlying neoplastic process is a distinct possibility. This might take the form of either a space-occupying lesion or carcinomatous infiltration of the cerebrospinal fluid and meninges. Leukopenia, of course, raises the specter of a central nervous system infectious process. Again, in the absence of lateralizing signs or focal deficit, the possibilities might include meningitis—more

likely fungal or granulomatous than bacterial, given the 2-week time course—as well as an extra- or intra-axial lesion.

Space-occupying intracranial infection may arise via contiguous spread from adjacent structures, through hematogenous dissemination, following operative neurosurgical procedures, or after head trauma. The same structural elements that define the various intracranial compartments—epidural, subdural, parenchymal, and ventricular—also dictate the pathways for spread of infection across those natural barriers.

18.2.1 Epidural Abscess

Infection within the space between the inner table of the calvarium and dura occurs most commonly as a complication of paranasal sinusitis, orbital cellulitis, mastoiditis, or chronic otitis media. It may also occur following traumatic fracture of the calvarium or following craniotomy. Rarely, epidural abscess may follow from fetal scalp monitoring or the application of halo pins to the skull [1]. Clinical presentation is often insidious. Headache may be accompanied by a relative paucity of other symptoms—unless mass effect is present or the infectious process extends to the subdural space as well. Periorbital edema occurs in conjunction frontal bone osteomyelitis or orbital cellulitis. (Pott's puffy tumor is the historical term applied to the clinical finding of forehead soft tissue swelling due to the presence of subgaleal fluid [2].) An infectious nidus adjacent to the petrous apex may present as Gradenigo's syndrome. Beta-hemolytic streptococci (*Streptococcus milleri* group) predominate, though post-traumatic and post-craniotomy infections are more commonly associated with staphylococcal infection [3]. Enterobacteriaceae (i.e., *Proteus*) and other anaerobes are also common isolates.

18.2.2 Subdural Empyema

Infection within the potential space between dura and arachnoid mater—arises either from the spread of infection via valveless emissary veins (in association with thrombophlebitis) or via extension of an osteomyelitis of the skull with an accompanying epidural abscess. Other predisposing conditions include skull trauma, infection of a pre-existing subdural hematoma, or prior neurosurgical procedure. A small number are metastatic (often from a pulmonary source). Subdural empyema may also occur in up to 10% of infants with bacterial meningitis, presumably as the result of infection of a previously sterile subdural effusion [4]. Clinical presentation is marked by rapid neurologic progression, with symptoms attributable to increased intracranial pressure, meningeal irritation, and focal cortical inflammation. Fever (greater than 102.2 °F (39 °C)) is present in most cases. Headache and vomiting are typical early findings. These symptoms may be accompanied by confusion, seizure,

and focal neurologic deficits (most commonly hemiparesis). Neurologic decline may be rapid following symptom onset. On the other hand, post-surgical subdural empyema may present in a delayed fashion—up to 8 weeks following initial intervention [3]. A less fulminant course is also seen in association with prior antimicrobial therapy, as well as in the setting of metastatic spread to the subdural space or infection of an existing subdural hematoma. Bacterial isolates are similar to those found in epidural abscess cases. Polymicrobial infection is common. The incidence of culture-negative (27–29% in one series) cases is greater in subdural empyema [5]; this may reflect the fastidious nature of many anaerobic organisms.

18.2.3 Intracerebral Abscess

Focal, encapsulated infection within the brain tissue may be single or multifocal. A single abscess typically arises by direct contiguous extension of a paranasal sinus, mastoid, or middle ear infection; a solitary focus may also arise following penetrating trauma. Multifocal disease more commonly results from hematogenous spread of primary cardiac, pulmonary, periodontal, abdominal, or dermatologic infection. Less than 50% of patients will present with the classic triad of headache, fever, and focal neurologic deficit [6]. In fact, patients may present with headache or nausea alone. Fever, when present, is typically low-grade; a temperature of greater than 101.5 °F (38.6 °C) should raise suspicion for a systemic infection. Focal neurologic symptoms reflect the location of the pathology. Hemiparesis is common [7]. New onset of meningismus, associated with sudden neurologic worsening, may indicate rupture into the ventricular space. Mortality in such cases is high [8]. Isolated pathogens are predominantly bacterial, commonly polymicrobial, and reflect the site of origin. Streptococci are isolated in up to 70% of cases (and frequently in mixed infections). *Staphylococcus aureus* is present in 10–15% of brain abscesses—usually post-trauma or in the setting of bacteremia and/or endocarditis—and is usually a solitary isolate. *Bacteroides* and *Prevotella* are present in 20–40% of cases and often occur in mixed culture. Enteric Gram negative bacilli are present in up to 22–33% of cases, often in association with otic foci, bacteremia, or post-craniotomy [9]. Diagnostic considerations must be expanded in cases of immunocompromise. Gram negative organisms and fungal isolates are common in cases of neutrophil deficiency, while *Listeria*, *Nocardia*, *Cryptococcus*, and *Toxoplasma* are encountered in the setting of T-cell deficiency.

18.3 Diagnostic Evaluation

CT head pre- and post-contrast will provide basic information regarding lesion location, the degree of associated edema/mass effect, and bony involvement. Cerebritis will appear as a nonspecific region of hypodensity, distinguished from acute

ischemia by the fact that it does not necessarily respect a known vascular territory. A more mature abscess will demonstrate peripheral enhancement, with associated perilesional edema. CT of the sinuses (with coronal and sagittal reconstructions) may be a necessary adjunct depending upon the relationship of intracranial findings to the sinus spaces.

Magnetic resonance imaging (MRI) brain pre- and post-gadolinium may provide additional information to assist diagnosis and therapeutic interventions. MRI is more sensitive than CT for the detection of focal intracranial infectious processes, offering earlier detection of cerebritis, cerebral edema, and inflammation at the level of the subarachnoid spaces and ependyma [10]. MRI may define the stage of abscess or cerebritis. On T1-weighted images, an abscess capsule may appear iso- to slightly hyper-intense with respect to the adjacent parenchyma. Post-gadolinium peripheral enhancement defines the abscess capsule. High T2 signal around a parenchymal abscess provides a qualitative measure of the degree of perilesional edema. The presence of restricted diffusion (with low apparent diffusion coefficient (ADC)) within an area of signal abnormality is suggestive of an infectious process. Diffusion weighted imaging (DWI) has demonstrated high sensitivity and specificity for distinguishing between abscess and a cystic or necrotic tumor (the latter typically demonstrating elevated ADCs). Sensitivity and specificity are upwards of 90% for distinguishing infection from tumor [11]. However, there is some evidence that DWI is less useful in the setting of postoperative infection, where postoperative changes may produce either false positive (in the case of hemorrhage) or false negative (in the case of temporary depressed immune response due to surgery or therapy) imaging results [12]. MR-spectroscopy (MR-SPECT), in combination with DWI, can increase the diagnostic accuracy of MRI for infection [13]. PET also may help distinguish an infectious from a neoplastic process. In cases of epidural or subdural empyema, magnetic resonance venography (MRV) will define the extent of sinus thrombosis, if present.

Lumbar puncture generally is not necessary and, when a mass lesion is present, may be contraindicated. Given physical separation from the subarachnoid space, cerebrospinal fluid should be sterile (perhaps with nonspecific inflammatory changes) in the setting of epidural or subdural empyema. Lumbar puncture plays a more essential role in the diagnosis of patients presenting with clinical signs and symptoms of meningitis or encephalitis. A discussion of cerebrospinal fluid indices relative to select infectious etiologies for meningitis is beyond the scope of this chapter.

More recently, procalcitonin has been investigated in the serum and cerebrospinal fluid (CSF) as a marker for infection, particularly in postoperative patients, where the distinction between infectious and non-infectious inflammatory states may be challenging [14]. The concentration of procalcitonin in healthy individuals is generally low; an elevated procalcitonin is thought to correlate with systemic inflammatory response.

The diagnostic evaluation should seek to determine the presence of a systemic process, as well as to define comorbid conditions that might provide etiologic

clues with respect to the observed intracranial pathology. Two sets of blood cultures should be drawn from different sites (preferably prior to initiation of antimicrobial therapy). HIV testing should be undertaken, as the spectrum of infectious pathology (and the approach to treatment) in the HIV-positive population may differ. A chest X-ray should be completed. A QuantiFERON-TB Gold (QFT) assay should be performed, or a PPD should be placed if tuberculosis is suspected. A Panorex X-ray may define an odontogenic etiology for intracranial infection. An echocardiogram may identify endocarditis as the source for intracranial infection.

18.4 Clinical Decision-Making and Next Steps

The indications for surgical intervention are dictated by size, anatomic location, and accessibility, as well as by known or presumed pathogen. In all cases, surgical intervention must be coupled with appropriate intravenous (and in certain cases, intrathecal) antimicrobial therapy. Formal infectious diseases consultation is appropriate to guide antimicrobial therapy. If infection arises from the sinuses or mastoid process, simultaneous management of the infectious pathology by otolaryngology may be indicated. Otolaryngology should be involved in the pre-operative planning for such cases.

18.4.1 Epidural Abscess

Most cases require open neurosurgical debridement. Burr hole drainage generally is ineffective given the consistency of the purulent material; however, in select cases where a very small collection is present, trial burr hole drainage may be attempted. The participation of otolaryngology may be necessary for simultaneous debridement of the affected sinus(es).

18.4.2 Subdural Empyema

The vast majority of cases require open neurosurgical debridement. More limited burr hole drainage may be considered in cases of early empyema (for which irrigation of liquid purulent material may be feasible), parafalcine empyema, critically ill patients in septic shock, and children presenting with empyema secondary to meningitis [15]. Repeated drainage and/or conversion to craniotomy may be necessary in such cases, particularly when maturation of the collection results in thickening of its contents and formation of loculations.

18.4.3 Intracerebral Abscess

Several factors dictate the indications for and extent of neurosurgical intervention. Primary considerations include size, location, and maturity of the capsule. Britt and Enzmann stratified brain abscesses into four categories based upon the observed enhancement pattern on CT following contrast infusion. These categories, in turn, were correlated with intra-operative findings to define stages in the maturation of the abscess capsule [16]. Early cerebritis (days 1–3) is marked by an initial inflammatory response with poor demarcation with respect to brain tissue. Progression to late cerebritis (days 4–9) occurs as pus formation enlarges the necrotic center and fibroblasts start to lay down the reticulin network that ultimately forms the capsule. During the early encapsulation phase (days 10–13), the developing capsule begins to demarcate abscess cavity from the surrounding parenchyma. The capsule continues to mature and a peripheral gliotic zone forms during the late capsule phase (days 14+).

Abscesses within the brain parenchyma may be approached either in an "open" or stereotactic manner. The location of the pathology will provide some guidance as to the most suitable approach. A large, lobar abscess may best be approached via open craniotomy, whereas a small abscess or one within a deep and/or eloquent area may best be approached by stereotactic means. In one series of 142 patients, no significant difference in outcome was observed for resection, open aspiration, or stereotactic drainage [17].

The decision to drain or resect a given lesion depends not only on the location, but also upon the presumed maturity of the capsule. A lesion in a deep subcortical or eloquent area may be better suited to aspiration than resection, whereas a superficial lesion may be appropriate for either intervention. Cerebritis, in general, is not a surgical disease. Abscesses may be amenable to cannulation and drainage during the early encapsulation phase—without attempted resection of the wall, which is typically thin and discontinuous at that time. This strategy may also be appropriate in the setting of a more mature lesion in a less accessible location. With maturity comes greater collagen deposition and consequently, a capsule more consistent with that of a metastatic lesion. Consideration may be given to drainage—with resection of capsule—in the case of an accessible lesion estimated to be at least 2–3 weeks of age. A combined approach may be necessary for debridement and obliteration of an adjacent air sinus if contiguous spread is suspected and may require the participation of otolaryngology.

The size of the lesion also may influence treatment strategies. It has been suggested that abscesses of a certain size (1.7 cm or less) may be treated by medication alone, while lesions of greater than 2.5 cm rarely resolve without surgical intervention [9, 18].

Medical therapy alone also may be considered in cases of multifocal disease, lesions in eloquent areas, concomitant meningitis, co-existent hydrocephalus where shunt placement risks contamination, or where medical contraindications to invasive intervention may exist [19]. In a patient with documented bacteremia and a

positive culture, consideration may be given to a trial of systemic antimicrobial therapy—provided the chosen agent(s) offers good central nervous system penetration. If the diagnosis is in question and/or there is a question of a polymicrobial infection in an immunocompromised host, consideration should be given to early biopsy to permit pathogen-directed therapy.

18.4.4 Suppurative Intracranial Thrombophlebitis

This is a feared complication of central nervous system infection. Suppurative thrombophlebitis may begin within the veins or venous sinuses or may occur after infection of the paranasal sinuses, middle ear, mastoid, or oropharynx. MRI of the brain, with MRV, is the test of choice. Surgical intervention, when undertaken, is generally directed toward debridement of infected air sinuses (and may be performed by an otolaryngologist). An extended course of intravenous antimicrobial therapy is recommended; the choice of agent(s) depends upon the presumed source— air sinus, odontogenic, or otologic—of the infectious process. Historically, the use of anticoagulation in this setting has been controversial [20]. However, there is growing evidence to support the use of anticoagulation (unfractionated heparin) to prevent propagation, particularly in the setting of cavernous sinus thrombosis [20, 21]. It is also important to note that relapse may occur within 6 weeks—after apparent clinical resolution—and abscess formation has been reported up to 8 months later [22].

Regardless of the suspected intracranial compartment involved, empiric, broad-spectrum antimicrobial therapy should be initiated at the time of presentation. The source, and therefore likely pathogens, should be considered. For de novo presentations, the author prefers a regimen of vancomycin, ceftriaxone, and metronidazole, bearing in mind that the specific clinical circumstances of a given case may dictate modification of this regimen and/or the addition of antifungal or antituberculous coverage. In the case of a patient with a suspected nosocomial process or immunocompromise, a cephalosporin with anti-pseudomonal activity (cefepime or ceftazidime) or a carbapenem should be substituted for ceftriaxone. (Metronidazole is not necessary if a carbapenem is selected.) Empiric therapy should be continued pending culture results and then narrowed accordingly to provide targeted therapy for the identified pathogen(s). Generally, a 4–6 week course of intravenous antimicrobial therapy is prescribed. Some advocate a 6–8 week course for intracerebral abscess [23]. Longer-term therapy may be indicated for select organisms (i.e., *Mycobacterium tuberculosis*). In cases where the pathogen is known, targeted antimicrobial therapy should be continued.

Corticosteroid therapy may be considered on an individual case basis for management of accompanying vasogenic edema. While the use of corticosteroids has been shown to be of some benefit in the setting of meningitis [24], there exists no similar established role for steroids in the primary medical management of abscess.

If employed, steroid therapy should be tapered rapidly in accordance with evolving clinical exam and evidence of resolving edema/mass effect per serial imaging.

Seizures are common in the setting of intracranial infection. Anti-epileptic drug prophylaxis should be initiated upon presentation. If no documented seizure activity, AEDs may be tapered off in the postoperative period.

Patients with evidence of increased intracranial pressure may require additional medical therapies for management.

In this particular case, the presenting complaint of headache, coupled with the absence of fever and a non-focal neurologic exam, provided little diagnostic direction. The observation of neutropenia aroused suspicion for an infectious process. Non-contrast CT imaging (Fig. 18.1) obtained at the time of initial presentation demonstrated a small, rounded region of hypoattenuation within the superficial right parietal lobe (measuring 1.5 × 2 × 1.6 cm). MRI brain pre- and post-gadolinium was obtained upon the patient's return to the hospital. This study revealed wispy peripheral enhancement of the lesion (measuring 1.5 × 1.8 × 1.6 cm), with associated perilesional edema (Fig. 18.2a, b). Restricted diffusion was present (Fig. 18.2c); however, this finding does not necessarily distinguish infection from neoplasm. Therefore, MR-SPECT was performed; this study demonstrated prominent lipid and lactate peaks with decreased NAA, favoring abscess.

Despite the relatively small size (<2.5 cm) of the lesion in question, the patient's immunocompromised state dictated prompt intervention and therapy. Stereotactic

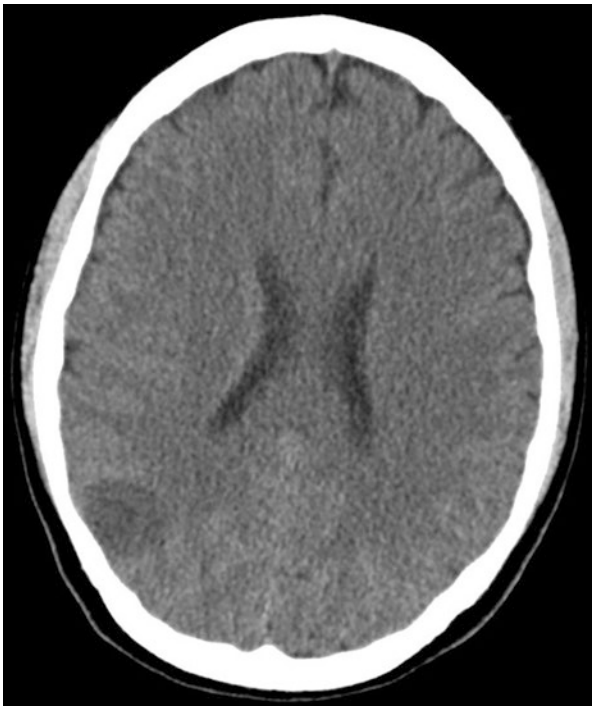

Fig. 18.1 Non-contrast CT head obtained at initial presentation demonstrated a superficial, rounded region of hypoattenuation within the right parietal lobe

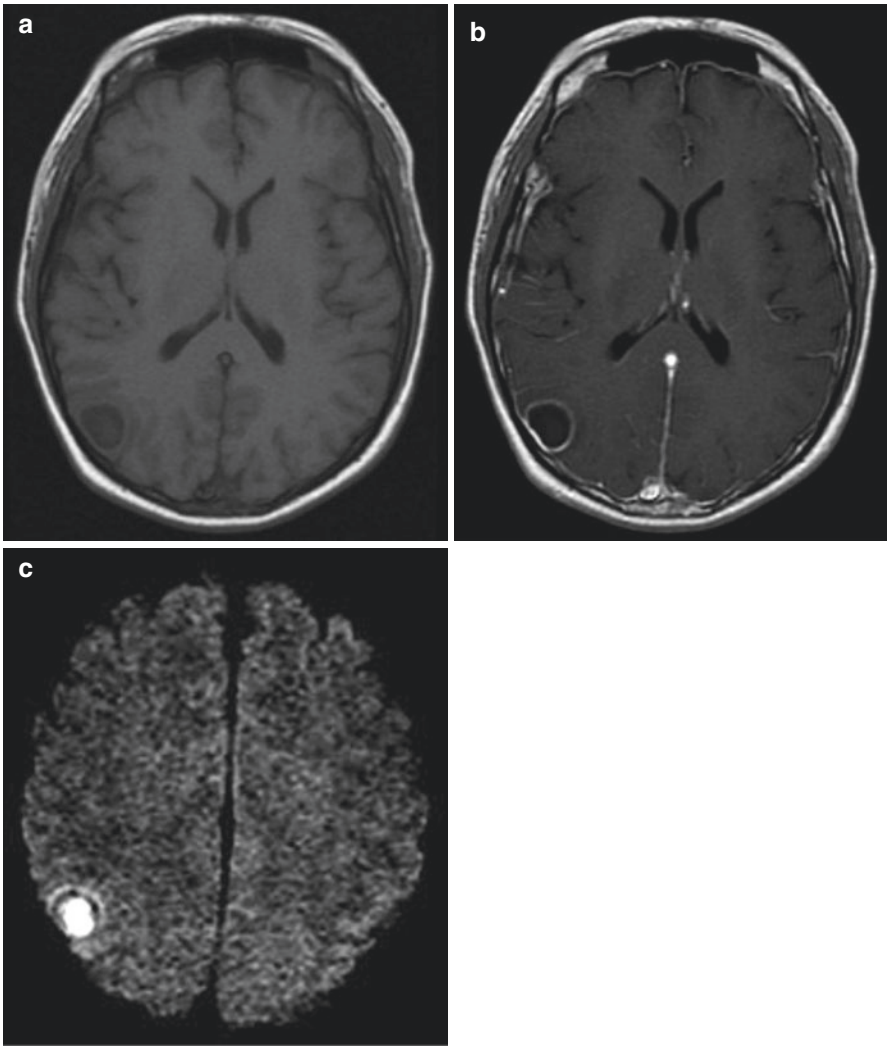

Fig. 18.2 (**a**–**c**) MRI brain pre- and post-gadolinium was obtained at the time of the patient's return to the hospital. (**a**) Axial T1 image demonstrating a rounded region of centrally hypointense signal, with an isointense capsule, within the superficial right parietal lobe. (**b**) Gadolinium infusion results in wispy peripheral enhancement of the area in question. (**c**) The DWI sequence reveals restricted diffusion (hyperintensity) within the area of the abscess

aspiration of the lesion was elected due to its presumably immature capsule—by imaging and reported time course—as well as a desire for minimally invasive intervention in the setting of multiple comorbidities. Empiric, broad-spectrum antimicrobial therapy was initiated at presentation. Antifungal coverage was included due to neutropenia. Cultures ultimately grew *Klebsiella pneumoniae*. The patient received a 6-week course of appropriate antimicrobial therapy, in consultation with the infectious diseases specialist.

18.5 Clinical Pearls

- The classic triad of headache, fever, and focal neurologic deficit occurs in a minority of patients presenting with brain abscess.
- MR-based modalities of imaging—post-gadolinium, DWI, and SPECT—assist in the characterization of pathology present as well as to distinguish it from neoplasm.
- Size, location, and the maturity of the abscess capsule dictate the options for invasive intervention.
- Medical treatment for suppurative intracranial infection generally demands an extended (4–6 week) course of antimicrobial therapy, targeted to culture data.

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Chapter 19
Nontraumatic Spinal Cord Compression

Vikas Parmar and Daniel Resnick

Clinical Scenario

A 55-year-old female with a history of IV heroin use and poor dental hygiene presented to the Emergency Department (ED) approximately 4 months ago with difficulty in breathing and chest pain. Patient was found to be tachycardic. Spiral CT of the chest demonstrated a segmental pulmonary embolism. The patient was initially put on a heparin drip and clinically improved over the course of a week, with no further pleuritic chest pain or dyspnea. The patient was switched over to oral anticoagulation, specifically warfarin, with a target INR of 2.5–3.0. The patient was discharged home.

The patient now presents to the ED with a new constellation of symptoms. She reports mid-thoracic back pain for several weeks. The pain is significantly worse when standing up and is relieved when lying down flat. She also has had multiple falls from standing and progressive weakness in her bilateral lower limbs. She denies sensory, bowel, or bladder changes. She is afebrile. WBC is 7.0, INR is 4.0, ESR is 110, and CRP is 55.

19.1 History and Neurologic Exam

A patient with progressive lower limb weakness, frequent falls, and mid-thoracic back pain directs a clinician to compression of the thoracic spinal cord. The patient's presentation is complicated by ongoing anticoagulation, with a supratherapeutic

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_19

INR, as well as elevated inflammatory markers. These features suggest a broad differential, including infectious, hemorrhagic, or neoplastic conditions.

Often, a careful history can help one pinpoint the etiology of the nontraumatic spinal cord compression prior to imaging. Essential elements to explore when obtaining a history include:

- *Neurologic symptoms*. It is important to determine specific details regarding neurologic changes. The *timing* of the weakness (i.e., acute or subacute, progressive) provides information regarding etiology, whereas the *location* of the weakness (i.e., bilateral versus unilateral, lower limbs versus both upper and lower limbs) helps to localize the lesion. The *degree* of weakness is important. Is the patient now bedridden, or is she still ambulating with a walker? Frequent falls, particularly at night, can imply an issue with proprioception and the dorsal columns of the spinal cord. Balance is defined by input from three fundamental systems: vision, vestibular, and proprioception. A loss of any two of these three systems can lead to balance problems and frequent falls. Questions about altered sensation can help determine a potential sensory level. Lhermitte's sign is often seen in cervical cord compression. The presence of bowel or bladder incontinence in the setting of cord compression may reflect spasticity or overflow incontinence. Incomplete emptying of the bladder after attempted micturition may be measured by checking a post void residual (PVR). Rectal examination is also important, especially for more rapidly presenting pathologies.
- *Pain*. The patient in this example presents primarily for evaluation of midthoracic back pain. Surprisingly, pain is more likely than weakness to prompt a patient to seek medical attention. While localization of pathology is crucial, questions regarding the onset, quality, radiation (i.e., radiculopathy), severity, provoking and palliating factors, and current treatments employed shed substantial light on etiology. This particular patient has pain that is provoked almost immediately upon standing and is alleviated when lying flat. This suggests mechanical instability.
- *Constitutional symptoms*. Elicit history regarding the presence of fever, sweats, chills, weight loss, poor appetite, and malaise; these are signs and symptoms of a systemic process. Past history of neoplasia or infection is also important.
- *Past medical/surgical history*. The patient has a history of an unprovoked pulmonary embolism, This pulmonary embolism could be a result of a hypercoagulable state from an underlying neoplastic process.
- *Drugs*. A thorough evaluation of the patient's drug history should be done. This includes prescription, homeopathic, and illicit drugs. Various homeopathic remedies can also have antiplatelet and anticoagulant properties. Certain illicit drugs (heroin, cocaine, methamphetamines, etc.) may play a role in vascular spinal cord pathologies, such as nontraumatic epidural hematoma or spinal cord stroke. Intravenous drug use carries a significant risk of systemic infections such as sepsis, endocarditis, and pneumonias. Hematogenous spread of bacteremia to the spine system may manifest as discitis, osteomyelitis, epidural abscess, or meningitis. Besides illicit drug use, prescription drugs are equally important. Here, the

patient was taking warfarin but was supratherapeutic at admission. Remember the patient presented with back pain and could also have been taking naproxen, which has cytochrome P450 dependent clearance and can increase the serum level of warfarin.

- *Poor dental hygiene*. Periodontal abscesses can occur in patients with poor dentition. This can lead to hematogenous spread of certain oral pathogens.

In terms of the neurologic examination, a complete motor, sensory, and reflex exam are crucial for the evaluation of spinal cord compression. Myelopathy can be diagnosed based on hyperreflexia, positive Hoffman's sign, upward going Babinski's sign, crossed adductor reflex, clonus in the lower extremities, and numbness in bilateral hands. The distribution of pathologic reflexes may suggest localization to the cervical (upper and lower) or thoracic (lower only) segment. For instance, a T4 sensory level would cause decreased sensation below the nipple line and a T10 sensory level would be below the umbilicus. Proprioceptive function is crucial to determine integrity of dorsal columns. Be sure to document perineal sensation and rectal tone as well.

This patient was found to have 4/5 weakness symmetrically in all major motor groups of lower extremities. She had 3+ patellar and Achilles reflexes, with 2+ biceps, triceps, and brachioradialis reflexes; crossed adductor reflexes were present. Two beats of clonus were observed. Proprioception was impaired. No sensory level or issues with rectal tone were present.

19.2 Differential Diagnosis

This patient has quite a few symptoms and physical exam findings that suggest spinal cord compression. The patient has obvious myelopathy, as evident from hyperreflexia, clonus, lower extremity weakness, and difficulty with proprioception. Frequent falls may reflect these findings as well.

However, the differential for the cause of the progressive cord compression is broad: infectious, hemorrhagic, and neoplastic processes must be considered. In addition, pathological fractures may cause spinal cord compression with no history of trauma. Table 19.1 lists the parts of the patient's history that support a diagnosis of cord compression and might reasonably fall into one of those three broad etiologic categories.

19.2.1 Spinal Cord Compression Secondary to Infection

Infectious etiologies for cord compression may include discitis/osteomyelitis, epidural abscess, subdural empyema, and rarely, intramedullary spinal cord abscess.

Table 19.1 Summary of the features of this patient's presentation that might suggest an infectious versus hemorrhagic versus neoplastic etiology for cord compression. While a preponderance of features in one column might influence the plan for diagnostic evaluation, the clinician should remain open to the possibility of an alternate etiology or even, multiple etiologies

Infectious	Hemorrhagic	Neoplastic
IV heroin use	Supratherapeutic INR of 4.0, on warfarin	Progressive symptoms
Poor dentition		Potential hypercoagulable state with hx of unprovoked PE
Elevated ESR and CRP		
Progressive symptoms		

19.2.1.1 Discitis/Osteomyelitis

Infections of the disk space (discitis) and bone (osteomyelitis) most commonly affect the lumbar spine (58%) [1]. The average age of affected patients is between 50 and 60 [2]. Approximately 55–80% of discitis/osteomyelitis is caused by *Staphylococcus aureus*, and spread is primarily via the hematogenous route. Contiguous spread of infection from adjacent soft tissue structures—such as from a retropharyngeal abscess to the cervical spine—is possible, but rare. In the lumbar spine, infections can spread from pelvic organs along Batson's venous plexus but again, occurs only rarely via that route. The more common cases of hematogenous origin primary discitis/osteomyelitis (i.e., not related to postoperative complications) have a notable mortality between 2% and 20% [2].

It is important to differentiate if the disk space is involved. Because the pathogen spreads hematogenously and the segmental arteries of the spine supply the lower portion of the rostral vertebral body and the upper portion of the caudal vertebral body and the disk space, discitis/osteomyelitis affects contiguous vertebral body segments and the in-between disk space. If pathology appears to involve contiguous vertebral bodies but spares the disk space, tuberculosis (Pott's disease) or a neoplastic process should be considered.

Risk factors include immune compromise (prolonged steroid use, HIV, etc.), IV drug use, obesity, other concurrent infections (endocarditis, septic joints, sepsis), diabetes mellitus, travel to endemic areas, and poor nutritional status.

The most common clinical symptom of patients with discitis/osteomyelitis is back pain. Pain when standing upright with axial loading could suggest instability. Less commonly, but certainly of greater importance, patients can present with neurologic issues such as myelopathy or radiculopathy.

Workup includes CBC, ESR, CRP, HIV status, and blood cultures. If the blood cultures do not demonstrate a pathogen, a fluoroscopic or CT-guided biopsy of the disk space or vertebral body by an interventional radiologist should be performed. The specimen is sent for Gram stain and culture, fungal culture, and acid-fast bacillus (AFB), if tuberculosis is suspected.

19.2.1.2 Epidural Abscess/Subdural Empyema

Spinal epidural abscess (SEA) is rare, but can have life-threatening consequences. Mortality can range from 5% to 16%, and less than 50% of surviving patients achieve full recovery [3]. Most often, patients are older than age 50 [3].

Spinal epidural abscess can be either primary or secondary. Primary SEA is most often a result of hematogenous spread from osteomyelitis/diskitis via epidural veins. Secondary SEA is essentially directly related to a surgical procedure, such as laminectomies or even spinal injections. Clinically, patients are often more likely to develop neurologic compromise with SEA than with chronic osteomyelitis/discitis. CRP is often more elevated than ESR, and even WBC count can be increased. Systemic signs such as fevers or night sweats are common.

In terms of imaging, it is recommended to obtain a MRI of the spine with gadolinium. A focal MRI based on patient history and exam is recommended initially. For, instance, a patient with signs of cord compression and mid-thoracic pain warrants a MRI of the thoracic spine. The MRI should visualize the entire epidural abscess as it can track through the epidural space and often affect multiple levels.

Subdural empyema, like SEA, is typically a consequence of adjacent osteomyelitis/discitis. Patients with subdural empyema can present with similar neurologic compromise. They can also present with a clinical picture of meningitis. However, infection tracking through the dura and into the subdural space is very rare, with only a handful of case reports.

19.2.1.3 Intramedullary Spinal Cord Abscess

True intramedullary spinal cord abscess (SCA) is a very rare entity, with only a limited number of cases reported. Patients seem to mostly present with acute onset myelopathy. Patients can also present with posterior neck pain, fevers, or urinary incontinence [4]. These infections tend to arise from a congenital dermal sinus tract in children and pulmonary, urinary infections, or endocarditis in adults.

19.2.2 Spinal Cord Compression Secondary to Hemorrhage

19.2.2.1 Spinal Epidural Hematoma

Spinal epidural hematoma (SEH) can be spontaneous or traumatic. Spontaneous SEH can present with acute onset severe back or neck pain with associated radiculopathy or weakness. Most often, no true etiology is discovered, but other times, use of anticoagulants, undiagnosed coagulopathy, or an arteriovenous malformation (AVM) have been linked to SEH. The pattern of bleeding is most often along the dorsal surface of the dura.

Traumatic SEH are fairly frequent and are often associated with fractures. SEH results from either cancellous bone bleeding or epidural venous bleeding adjacent to the fracture site.

CT imaging may be the first imaging performed if SEH is associated with a trauma. In the absence of defined trauma, MRI with and without contrast of the affected spine segment should be obtained. On MRI imaging, blood can be seen well on gradient echo (GRE) sequences and can be graded for chronicity based on T1 and T2-weighted images. Acute SEH will be isointense on T1 and bright on T2-weighted images.

19.2.2.2 Spinal Subarachnoid Hemorrhage (SAH) or Subdural Hematoma (SDH)

Spinal SAH and SDH are rare entities for hemorrhagic spinal lesions. Most often they are the result of trauma, coagulopathy, or iatrogenic events such as a spinal puncture [5]. According to a 1999 review of 106 spontaneous spinal SDH cases, 70% involved the thoracolumbar or lumbar region and 47% were linked to a recent spinal puncture [5].

MRI imaging is used to determine if the blood products are, in fact, intradural. If a true spontaneous spinal SAH or SDH is found, further imaging such as a spinal angiogram may be warranted to rule out spinal arteriovenous malformation.

19.2.2.3 Intramedullary Spinal Hemorrhage

Intramedullary spinal hemorrhage is just as rare as spinal SAH or SDH. Like spinal SAH, SDH, or SEH, it is often associated with coagulopathy. However, it differs from the other pathologies by being even more closely associated with an intramedullary tumor or vascular lesion (cavernous angioma, arteriovenous malformation, or dural arteriovenous fistula) [6, 7]. In fact, only a few cases of an intramedullary spinal cord hemorrhage without a definitive cause have been reported.

MRI with and without contrast is an important first imaging step. Imaging of the entire spinal axis may be considered if an oncologic etiology is suspected. If a neoplastic process is, indeed, high in the differential, imaging the brain and chest, abdomen, and pelvis for metastatic lesions is crucial as it can alter management decisions. If MRI is not revealing, a spinal angiogram should be performed.

19.2.3 Spinal Cord Compression Secondary to Neoplasm

Spinal cord compression may result from neoplastic processes that are extrinsic or intrinsic to the spinal canal. Spinal tumors may be distinguished by compartment: extradural, intradural (extramedullary), and intramedullary.

19.2.3.1 Extradural Tumors

Extradural tumors include primary tumors of the bone and soft tissue, as well as secondary tumors such as metastases. Benign primary bone lesions include osteoid osteoma, osteoblastoma, osteochondroma, vertebral hemangioma, and giant cell tumor. Of note, giant cell tumor is of benign histology but can be locally aggressive. Malignant primary bone tumors include osteosarcoma, chordoma, teratoma, plasmacytoma, lymphoma, fibrosarcoma, and Ewing's sarcoma. The bony aspects of the spine can be infiltrated by metastasis from lung, breast, prostate, kidney, colorectal, multiple myeloma, germ cell, and thyroid tumors. Pediatric extradural tumors can include neuroblastoma and germ cell tumors in the differential.

19.2.3.2 Intradural, Extramedullary Tumors

Intradural, extramedullary tumors arise inside the dura but outside of the spinal cord. Benign primary intradural tumors include meningioma, schwannoma, neurofibroma, paraganglioma, and ganglioneuroma. Malignant tumors include malignant peripheral nerve sheath tumor (MPNST) and hemangiopericytoma. The tumors originating from the nerve root sheath, schwannoma, neurofibroma, and MPNSTs can often have a "dumbbell" appearance on axial MRI or CT as the tumor extends out the exiting foramen, reflecting both intradural and extradural components. Rarely, malignant tumors, such as glioblastoma, lymphoma, and lung and breast metastasis, can spread via leptomeninges.

19.2.3.3 Intramedullary Tumors

Finally, spinal cord compression can be caused by intrinsic compression from an intramedullary tumor. These tumors arise from the parenchyma of the spinal cord tissue and cause mass effect on descending and ascending fiber tracts. Tumors include primary tumors such as ependymoma, astrocytoma, oligodendroglioma, lipoma, and hemangioblastoma. Metastasis from lung, breast, renal, melanoma, and lymphoma can also rarely present as intramedullary lesions. MRI with and without gadolinium will demonstrate contrast-enhancing intramedullary tumors and is, without a doubt, the primary way to image such pathology.

Regardless of the location of the spinal tumor, most patients present with pain prior to symptoms of spinal cord compression. Tumors, especially bony metastasis or primary bone tumors, elicit mechanical back pain for weeks or months prior to neurologic symptoms. Instability in the form of a pathologic compression fracture or focal kyphosis may also be present. Various scoring systems have been designed to evaluate spinal instability related to spinal tumors such as the Spine Instability Neoplastic Score (SINS) [8]. SINS incorporates location (rigid, semirigid, mobile, junctional), mechanical pain, type of bony lesion, sagittal

alignment, vertebral body collapse, and posterior spinal involvement. Scores between 12 and 18 indicate gross instability, suggesting a need for fusion at the time of surgical decompression.

19.3 Diagnostic Evaluation

If the patient presents as a trauma or with acute neurologic changes, initial CT imaging may be appropriate. Neurologic deficits that assist anatomic localization—such as a sensory level—may allow for more targeted imaging by spine segment. CT permits visualization of fracture, hematoma, and some aspects of soft tissue involvement.

More often than not, an MRI of the spine—with and without gadolinium—is necessary to fully understand the nature of the compressive process and to provide diagnostic clues as to etiology. If a neoplasm is visualized, then imaging of the entire neuroaxis (brain and total spine) is needed, in addition to CTs of the chest, abdomen, and pelvis to evaluate for metastasis. MRI of the spine will help differentiate between infectious (if bone or disk involvement), hemorrhagic, or neoplastic causes.

If an infectious source is suspected, additional testing to consider may include a Panorex (for odontogenic source), chest X-ray, transthoracic echocardiogram (for endocarditis), blood cultures, ESR, CRP, CBC, and HIV testing. An infectious diseases consultation may be helpful to assist diagnosis and to guide medical therapy. Interventional radiology consult may be helpful for biopsy of the infected disk space/vertebral body. If a hemorrhagic source is suspected, vascular imaging—MR angiogram, CT angiogram, or formal spinal angiogram—should be undertaken. Diagnostic evaluation for coagulopathy should be completed if appropriate. Finally, further evaluation for neoplastic processes should include MRI of the entire neuroaxis (brain and total spine) with and without contrast, CT of the chest, abdomen, and pelvis to evaluate for metastasis, PET scan, lumbar puncture if leukemia or lymphoma is suspected, and a carefully planned preoperative biopsy if concerned for chordoma, sarcoma, malignant peripheral nerve sheath tumor (MPNST), or giant cell tumor. Medical oncology and radiation oncology consults are necessary as well.

In this case, an MRI thoracic spine with and without contrast demonstrated a T8–9 contrast enhancing extradural soft tissue lesion with associated disk space involvement as demonstrated in Fig. 19.1a–e. It is often very difficult to distinguish liquid purulence and phlegmon on imaging. T8 and T9 also have pathologic compression fractures. Of note, there is significant thoracic cord compression from the contract enhancing lesion that likely represents a spinal epidural abscess. CRP was 4.6 and ESR was 65 – both elevated. Blood cultures, echocardiogram, chest X-ray, Panorex, and HIV testing were negative.

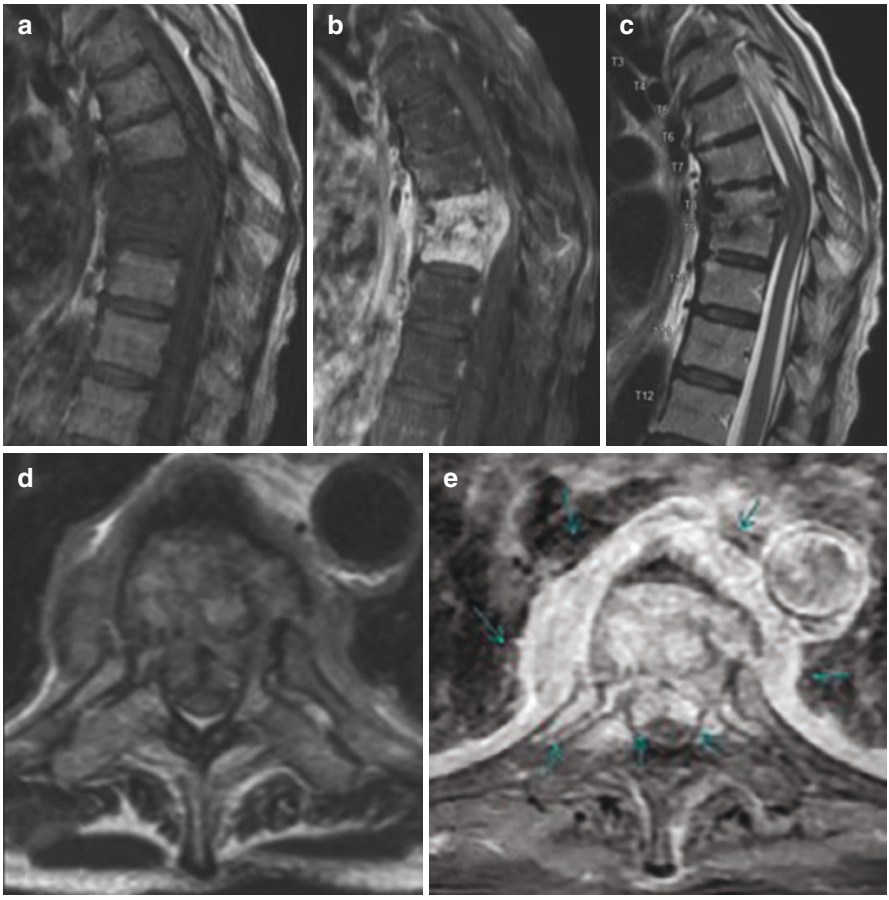

Fig. 19.1 MRI lumbar spine sagittal T1-weighted precontrast (**a**), sagittal postcontrast (**b**), sagittal T2-weighted (**c**), axial T2-weighted (**d**), and axial T1-weighted postcontrast (**e**) images. Together, the selected images demonstrate a contrast-enhancing lesion that obliterates the T8–9 disk space and involves T8 and T9 vertebral bodies. This pattern is concerning for osteomyelitis. There is also significant ventral compression from an epidural abscess. The overall picture is one of severe spinal cord compression, with accompanying T2 signal change within the thoracic spine cord suggestive of myelomalacia

19.4 Clinical Decision-Making and Next Steps

In general, most patients with true spinal cord compression will need surgical intervention. However, the etiology (infectious, hemorrhagic, and neoplastic) plays a large role in this decision-making process.

19.4.1 Infectious Pathology

19.4.1.1 Discitis/Osteomyelitis

For patients with discitis and osteomyelitis – without spinal cord compression—a 6–12 week course of highly bioavailable (IV or oral) antibiotics may be appropriate [9]. A duration of 6 weeks of parenteral or bioavailable oral antimicrobial is the recommendation of the 2015 IDSA guidelines as well. Surgery is considered for patients who have neurologic compromise and spinal cord compression, instability, progressive deformity, or unresponsiveness or progression of disease through conservative measures. Often a diagnosis is needed, and interventional radiology can perform a vertebral body or disk biopsy. Surgery can vary in terms of an only anterior approach, only posterior approach, or a combination. Regardless of approach, the goals of surgery are to decompress neural elements and establish stability with fusion. At times, these patients can present with delayed kyphotic deformity, necessitating a fusion for correction.

19.4.1.2 Spinal Epidural Abscess/Subdural Empyema

Treatment of SEA should be started immediately. An organism should be obtained whether from a biopsy of a disk space or bone or from blood cultures. Surgical decompression, where appropriate, and systemic antibiotics is the gold standard of treatment. However, conservative management with only antibiotics can be attempted in patients with no neurologic symptoms and relatively small SEA. Conservative management alone is also reasonable for patients with complete paralysis greater than 72 h, with significant comorbidities, or with a SEA that spans the numerous or noncontiguous segments for which surgery is not feasible. It is vital that if conservative management is pursued that these patients are followed vigilantly [10]. Up to 49% of patients can demonstrate worsening neurologic symptoms if managed conservatively [11]. Thrombophlebitis with ischemic injury could be a possible reason for neurologic progression and sometimes failure of decompression.

In general, surgical decompression is pursued for patients with neurologic deficits, sizable focal SEA that antibiotics alone would not penetrate, or for failure of conservative management. Some risk factors for failure of conservative management are age greater than 50, diabetes mellitus, and MRSA infection [12]. If surgery is performed, special care to avoid durotomy during surgical decompression is warranted so as to prevent infection spread into the central nervous tissue.

Subdural empyemas, like SEA, are treated as surgical urgencies with drainage and antibiotics being the primary treatment options [13]. Patients with subdural empyemas can worsen rapidly, and mortality is directly related to treatment delay [14].

19.4.1.3 Intramedullary Abscess

Because of the relative infrequency of intramedullary abscesses, management is determined on a case-by-case basis. Children with a congenital dermal sinus tract will usually require surgery for resection of the dermal sinus tract and are considered as distinct from adults with SCA with respect to treatment and prognosis. A review by Kurita et al. in 2009 advocates for rapid treatment with broad-spectrum high-dose ampicillin and third-generation cephalosporin for adults [4]. They reported complete recovery after 2 months in their case report. There is, however, evidence for improved prognosis with surgical drainage within 5 days of symptom onset and IV antibiotics [15]. Surgery should be considered in patients with SCA large enough for surgical drainage or with progressive neurologic worsening despite proper antibiotics. SCA should also be considered in the differential diagnosis for a patient presenting with spontaneous spinal cord infarction [15].

19.4.2 Hemorrhagic Pathology

19.4.2.1 Spinal Epidural Hematoma

Urgent surgical decompression via laminectomy and evacuation of hematoma is the mainstay of treatment for symptomatic patients or enlarging hematomas. If dealing with a spontaneous SEH, it can be useful to get an MRI or angiogram to verify that there is no underlying AVM or tumor prior to surgery. Patients with small traumatic SEH without neurologic problems can be managed conservatively with close observation. If there is a fracture present, post-laminectomy stability must be taken into account.

19.4.2.2 Spinal Subarachnoid Hemorrhage/Subdural Hematoma

Surgery for patients with spinal subarachnoid hemorrhage or spinal subdural hematoma is certainly warranted for patients with neurologic compromise, evidence of spinal cord compression, or progressive symptoms. Surgery includes bony decompression, opening of the dura, evacuation of the SDH, and visualization of the spinal cord for tumors or vascular lesions. If a patient has no neurologic impairment, conservative management and repeat imaging after the blood has cleared should be considered.

19.4.2.3 Intramedullary Spinal Hemorrhage

Surgery is reserved for patients with progressive worsening neurologic symptoms as surgery could risk damaging eloquent spinal tracts. Patients often have some degree of initial neurologic compromise and weighing the risks and benefits of

surgery is often difficult. If a neoplastic or a vascular lesion is found on workup, resection should be considered. Most lesions can be resected safely. However, aggressive resection should be avoided if the lesion border is ill-defined. If a tumor is indeed incorporated within the spinal cord with no clear distinction between tumor and parenchyma, biopsy and an expansile duraplasty can be performed. These patients should be watched carefully as they have a notable risk of rebleed. Likely, this high risk of rebleed is associated with inadequate resection of a neoplastic or vascular lesion. Again, patients with no neurologic compromise should be watched conservatively.

19.4.3 Neoplastic Pathology

19.4.3.1 Extradural Neoplasms

Treatment for extradural neoplastic lesions causing spinal cord compression depends on quite a few factors. The NOMS (neurologic, oncologic, mechanical, systemic) system describes a framework to treat these tumors on case-by-case basis. "Neurologic" involves grading the degree of epidural spinal cord compression based on a 6-point grading scale developed by the Spine Oncology Study Group (SOSG). "Oncologic" refers to the histology of the tumor and its sensitivity to radiation. Patients with truly radiosensitive tumors, such as lymphoma, seminoma, and myeloma, may (in the absence of instability) be treated with conventional external beam radiation regardless of the degree of spinal cord compression. Radiosensitive solid tumors include breast, ovarian, prostate, and neuroendocrine tumors, whereas radioresistant solid tumors include renal, melanoma, non-small cell lung carcinoma, colon, and hepatocellular carcinoma. Radioresistant tumors with no spinal cord compression can be treated with stereotactic radiosurgery (SRS), whereas radioresistant tumors with cord compression need surgery with adjuvant SRS postoperatively. At times, some tumor resection in the form of "separation surgery," to allow at least 2 mm between the tumor and the dura, will allow adequate radiation doses to the tumor without negative consequences to the spinal cord [16].

The "mechanical" aspect of NOMS is purely a determination of the need for stabilization or fusion. Again, the SINS scoring system is reliable in this regard. Low SINS scores (0–6) do not need any instrumentation, whereas high SINS scores (13–18) need instrumentation and stabilization. Intermediate scores (7–12) are in between and up to surgeon choice.

Finally, "systemic" refers to tumor burden, expected life expectancy, and overall medical comorbidities. If a given patient already has a significant tumor burden and life expectancy is less than a few months, surgery may not be the apt approach. Similarly, if a patient has significant cardiac and pulmonary comorbidities that make surgical risk high, a more palliative approach may also be beneficial. Various scoring systems such as Tokugashi, Tomita, and Bauer grading systems have tried to evaluate life expectancy with these cancer patients.

Additional considerations apply in the management of chordoma, sarcomas, MPNSTs, and giant cell tumors. These tumors often require *en bloc* resection, if possible, without causing significant neurologic or vascular injury, as they demonstrate malignancy (with the exception of benign giant cell tumor) and high recurrence rate. If a biopsy is performed for these pathologies, the biopsy tract should be resected as well.

19.4.3.2 Intradural, Extramedullary Neoplasms

Treatment for intradural, extramedullary tumors with spinal cord compression is decompression, with intradural exploration and resection. Most commonly, these tumors are schwannomas, meningiomas, or neurofibromas with low risk of recurrence. Thus, intratumoral, piecemeal resection is often performed.

19.4.3.3 Intramedullary Neoplasms

Intramedullary tumors are difficult surgically as they are surrounded by eloquent tissue. If these tumors extend to the dorsal surface or demonstrate signs of growth on imaging, surgery for resection may be indicated. Entry zones into the spinal cord, if the tumor is not exophytic, include the posterior median sulcus and the posterolateral sulcus. Intraoperative frozen pathology should always be obtained. The ultimate factor guiding surgical resection is the presence or absence of a plane of dissection between the tumor and the surrounding spinal cord. If astrocytoma is suspected based on frozen pathology, gross total resection is unlikely due to its close association with parenchyma; however, if ependymoma is suspected, gross total resection should be attempted as there is often a demarcation between tumor and spinal cord. These patients have a longer survival with a gross total resection. Radiation oncologists may also start adjuvant radiation, no earlier than 2–3 weeks postoperatively, pending the degree of resection and the grade of the tumor.

In this particular case scenario, the patient, indeed, had thoracic spinal cord compression from a SEA, as well as discitis/osteomyelitis with vertebral body collapse and some kyphotic deformity. The patient underwent T8–9 laminectomy and a bilateral T8–9 transfacet, transpedicular approach for debulking/evacuation of the spinal epidural abscess to create space ventral to the cord. A bilateral transfacet/pedicular approach, superimposed upon T8/9 pathologic fractures and focal kyphotic deformity, would most certainly produce mechanical instability; as such, the patient had instrumented fusion with pedicle screws from T6 to T11. Postoperative CT imaging is shown in Fig. 19.2. Intraoperative cultures demonstrated Gram positive cocci that eventually grew methicillin-sensitive staphylococcus aureus (MSSA). The patient was started on IV antibiotics and was discharged with IV oxacillin and oral rifampin for 6 weeks, with repeat imaging upon the completion of antibiotics. It is worthy to note that improvement of radiographic measures of infection often lags behind improvement of clinical course (symptoms, ESR, and CRP).

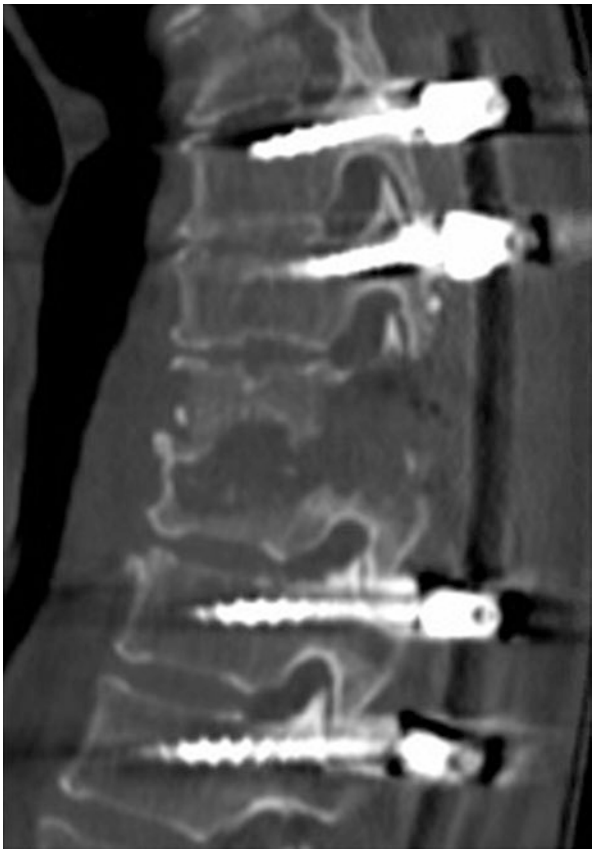

Fig. 19.2 Postoperative CT sagittal image demonstrates the decompression of T8–9 via laminectomy and bilateral transfacet approach. Instrumentation has been performed with pedicle screws at T6, T7, T10, and T11, with good correction of the preoperative focal kyphosis as well

19.5 Clinical Pearls

- Patients with spinal cord compression most commonly present with back pain, but should be examined carefully for signs of myelopathy, deficits in proprioception, and/or a sensory level.
- Potential infectious processes that might produce cord compression include discitis/osteomyelitis, spinal epidural abscess, subdural empyema, and intramedullary spinal abscess.
- Potentially compressive hemorrhagic pathology includes spinal epidural hematoma, spinal subarachnoid hemorrhage/subdural hematoma, and intramedullary spinal hemorrhage.
- Neoplastic processes may be benign or malignant and may occupy extradural, intradural/extramedullary, or intramedullary compartments.
- If the patient presents as a trauma, a CT of the spine is indicated. Otherwise, MRI with and without contrast is the most important diagnostic test to distinguish among potential etiologies for cord compression.

- Discitis/osteomyelitis without neurologic compromise can be managed with pathogen-directed antimicrobial therapy (or, empiric broad-spectrum therapy if no pathogen is isolated) for 6 weeks.
- Patients presenting with spontaneous spinal hemorrhage need vascular imaging, such as an CT angiogram or formal angiogram, prior to surgery.
- The NOMS (neurologic, oncologic, mechanical, systemic) system describes a framework to treat spinal tumors on case-by-case basis.
- Management is dependent on etiology. Surgery is indicated for most patients with spinal cord compression. Surgery typically involves a decompressive laminectomy though certain patient and imaging factors may also necessitate fusion.

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Chapter 20
Cauda Equina Syndrome

Robert J. Rothrock and Allan D. Levi

Clinical Scenario

A 63-year-old man with a history of right lower extremity radiculopathy and right L4–L5 microdiscectomy 2 years prior presents to the Emergency Department (ED) with new, severe low back pain and left lower extremity radiculopathy. His symptoms began a few hours ago after leaning down to pick up his mobile phone from the ground. He endorses left thigh numbness and weakness in his left foot. In addition, he notes that he has increased urinary urgency and new numbness in his groin, left greater than right. On physical examination, he has 2/5 weakness in left dorsiflexion and great toe extension, but otherwise has full 5/5 strength. He has numbness of the left thigh and lateral leg, as well as left groin and perianal anesthesia; his rectal tone is intact. After being asked to void, an indwelling urinary catheter is placed and reveals 800 mL of post-void residual.

20.1 History and Neurologic Exam

Based on the patient's acute clinical presentation with sensory and motor deficits, as well as the presence of bowel/bladder symptoms, a significant spinal pathology is suspected. Neurologic localization can be honed based on the clinical history and focused neurological exam.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_20

Key elements of clinical history include:

- *Constitutional symptoms*. Back pain or discomfort is present in up to 97% of patients with cauda equina syndrome [1]. In addition, the presence of radiculopathy helps to localize a cauda equina lesion, since a compressive spinal cord lesion without spinal instability will usually present with a painless neurological deficit. Constitutional symptoms such as fever or malaise may signal underlying infection and/or spinal epidural abscess. Unintended weight loss and fatigue may signal underlying metastatic disease.
- *Distribution of symptoms/deficits*. The distribution of symptoms and deficits also helps to localize the neurological lesion. A sudden pop or pain the lower back followed by sudden, unilateral leg weakness and numbness with bowel/bladder incontinence favors a traumatic disc herniation with cauda equina syndrome [2]. Bilateral radiculopathy should raise greater concern for cauda equina syndrome. Isolated bowel/bladder incontinence without numbness or weakness in the extremities suggests an unrelated genitourinary process or involvement of the conus medullaris or sacral plexus [3]. A gradual onset of symmetric symptoms in a painless fashion favors an insidious lesion of the spinal cord such as epidural metastatic disease. Subacute, unilateral leg weakness, and numbness without lower back symptoms may suggest a lesion of the lumbar plexus or large lower extremity peripheral nerve [4].
- *Trauma*. Given the acute nature of the symptoms, a preceding history of trauma may suggest disc herniation or spinal fracture as the etiology of the neurological deficit. Asking the patient to point to the main area of pain with one finger can help to localize the level of injury. The mechanism of injury is also important—for instance, a restrained driver or passenger presenting with a lumbar burst fracture.
- *Cancer history*. The spinal column is the third most common site of metastatic disease from systemic cancer [5]. A seemingly insignificant spinal trauma can lead to sudden neurological deficit in the setting of underlying metastatic epidural disease or pathological fracture.
- *Infectious history*. Lumbar epidural abscess due to discitis/osteomyelitis may follow from a prior, recent or remote, unrelated infectious process [6]. For instance, a patient who had septic urinary tract infection or cellulitis months ago may now present with symptomatic epidural abscess. Other possible etiologies include dental abscess, soft tissue infection, and septic arthritis.
- *Coagulopathy*. Spinal extra-axial hematoma can cause an acute, compressive lesion of the cauda equina or conus medullaris [7]. A history of coagulopathy or use of anticoagulant/antiplatelet agents predisposes patients to formation of spontaneous spinal epidural hematoma, especially in the setting of invasive procedures such as lumbar puncture.

The classic symptoms of cauda equina syndrome include back pain/discomfort, sensory changes in the lower extremities, motor weakness in the lower extremities, bladder dysfunction, bowel dysfunction, saddle anesthesia, and/or sexual dysfunction [8]. When several of these symptoms are present, there should be a high degree of clinical suspicion for cauda equina syndrome. Motor and/or sensory

deficit—when present—is characteristically asymmetric, distinguishing it from a conus medullaris or a spinal cord-level lesion.

Focused physical examination should assess for point tenderness of the spine, motor weakness, sensory deficits, lower motor neuron signs (such as areflexia) in the lower extremities, saddle anesthesia, decreased or absent rectal tone, and urinary retention (bladder scan or urinary catheterization following attempted voiding). With conus medullaris syndrome—since this is a spinal cord lesion—upper motor neuron signs such as spasticity and hyperreflexia may be present. Loss of perianal sensation is a more specific physical exam finding to acute cauda equina syndrome and an important time-stamp regarding the onset of symptoms, since patients operated on after 48 h from this physical exam finding have significantly worse clinical outcomes [9].

Another important differentiating prognostic feature regarding cauda equina syndrome is the presence of complete versus incomplete urinary retention. With incomplete urinary retention, the patient will still feel urinary urgency and be able to urinate with effort, whereas with complete urinary retention, the patient will experience painless urinary overflow incontinence [10]. On physical examination, the trigone sensitivity test can be used to assess for complete retention if the patient has an indwelling urinary catheter. With this maneuver, gentle traction on the catheter balloon should produce the urge to urinate; if not, there is loss of trigone sensation and likely complete urinary retention (poor prognostic indicator) [2]. Proper assessment of bowel/bladder function is important as these are the least reversible deficits and among the most impactful to quality of life [11].

20.2 Differential Diagnosis

In the present case, the patient has history of previous lumbar disc herniation at L4/L5 and now has a clinical history and exam findings that are concerning for a new, larger mass lesion at the same level. The symptom onset was sudden and occurred immediately upon bending to pick up an item from the ground. The clinical findings concerning for cauda equina syndrome include sudden back and leg pain, new motor and sensory deficits, and saddle anesthesia in tandem with urinary retention. The differential diagnosis favors acute cauda equina syndrome in this case, likely from a new, larger disc herniation.

20.2.1 Cauda Equina Syndrome

As noted above, the classic symptoms of cauda equina syndrome include back pain/discomfort, sensory changes in lower extremities (often asymmetric), motor weakness in the lower extremities (often asymmetric), bladder dysfunction, bowel dysfunction, saddle anesthesia, and/or sexual dysfunction. Cauda equina syndrome merely describes this constellation of symptoms, which localizes to compression of

the neural elements within the L2 to S1 segment. The extent of symptoms is often proportional to the amount of the spinal canal that is occupied by the lesion, but also due to the sensitivities of the affected nerve roots [12]. Hence, the symptoms are often asymmetric between the two lower extremities, since lesions of the lumbar spinal canal are often eccentric (i.e., lumbar disc herniation). The underlying cause of the cauda equina syndrome is important to the exact surgical treatment strategy, since some pathologies (disc herniation, epidural hematoma, spinal epidural abscess) require decompression alone, whereas others (erosive discitis/osteomyelitis, erosive tumor, unstable fracture) may require spinal instrumentation and fusion.

Approximately 45% of cases of acute cauda equina syndrome are due to lumbar disc herniation [1]. Spontaneous epidural hematoma is an extremely rare cause of cauda equina syndrome; most cases occur in patients with significant coagulopathy [7]. Lumbar metastatic disease or epidural tumor is also a rare cause of cauda equina syndrome, and more typically presents with mechanical radiculopathy, where spinal instability leads to mechanical compression of the dorsal root ganglion, causing radiculopathy with movement [13]. Lumbar epidural abscess from discitis/osteomyelitis is a particularly important potential surgical emergency, since the mechanism of neurologic injury is thought to be thrombophlebitis and not direct compression of the neural elements [14]. Evacuation of the local pus, in conjunction with administration of systemic antibiotics, is important to successful treatment and potential reversal of neurologic deficits.

20.2.2 Conus Medullaris Syndrome

Conus medullaris syndrome is a rarer clinical syndrome involving compression at the thoracolumbar junction and conus medullaris of the spinal cord (T11–L1) [8]. The same differential diagnosis of underlying causes applies as regards cauda equina syndrome, and both entities are often considered together. Conus medullaris syndrome, however, is an upper motor neuron syndrome, and the presence of spasticity or hyperreflexia helps differentiate it from cauda equina syndrome on physical exam. It also can involve more symmetric symptoms of the lower extremities for this same reason. Ultimately, MRI is the most important localizing tool. Surgical decision-making in this case more frequently involves use of instrumentation and fusion given the higher risk for iatrogenic instability with wide decompression of the neural elements [15].

20.2.3 Sacral Disease/Compression

Isolated sacral disease usually involves primary or metastatic cancer. In cases presenting with isolated bowel/bladder incontinence without lower extremity weakness, imaging of the sacrum should also be performed. This especially in

cases where spinal imaging is otherwise reported as negative, but the full extent of the sacrum is not visualized on imaging [3]. In cases of erosive metastatic disease of the sacrum, treatment is usually oriented towards palliative radiation, given that extensive surgical intervention is highly morbid. In cases of primary sacral tumor, such as chordoma or sarcoma, sacrectomy and radical resection are considered.

20.2.4 Peripheral Nerve Lesion

In cases where weakness involves multiple nerve distributions, without accompanying bowel/bladder symptoms, a peripheral nerve injury or lesion should be considered. This can be further evaluated with MRI of the lumbar plexus or the leg as indicated [4].

20.2.5 Non-compressive Lesions

Non-compressive lesions of the spinal cord such as cord infarct, transverse myelitis, and multiple sclerosis can mimic cauda equina syndrome with asymmetric neurologic deficits and findings [16]. Such lesions may be visible on MRI spinal survey and do not necessitate emergent spinal decompression.

20.3 Diagnostic Evaluation

Definitive diagnostic evaluation is performed with magnetic resonance imaging (MRI) of the spine. Early neurosurgical or orthopedic spine consultation/evaluation is advised in patients with physical exam findings concerning for cauda equina syndrome [17]. In cases where spinal cord compression is also on the differential diagnosis, MRI spinal survey (faster protocoled, full spinal scan) can be useful, since cases of spinal cord compression and cauda equina syndrome are time sensitive to surgical decompression [18]. If spinal infection or spinal tumor is suspected, the MRI imaging ideally should be performed with and without gadolinium contrast. In patients with non-MRI compatible instrumentation or foreign bodies, CT myelogram can be performed. This provides detailed assessment of spinal anatomy but can be practically more difficult to obtain since it requires lumbar puncture and injection of contrast directly into the spinal subarachnoid space.

Since cauda equina syndrome is a surgical emergency, diagnostic evaluation should also include blood work to assess surgical risk with complete blood cell count with platelets, basic metabolic panel, calcium, magnesium, prothrombin time/international normalized ratio (INR), activated partial prothrombin time (PTT). In

cases with suspected infection, it is recommended to obtain a baseline erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level to trend treatment response [19].

20.4 Clinical Decision-Making and Next Steps

Cauda equina syndrome is an overall rare clinical entity with estimated annual incidence around 2 per 100,000 people, and compromising about 3% of all lumbar disc herniation surgeries [20]. Approximately half of patients with acute cauda equina syndrome will present with complete urinary retention at the time of hospital admission [21].

Timing to surgery is an important consideration in acute cauda equina syndrome. For patients with an incomplete acute cauda equina syndrome, surgery is ideally performed within 24-h of clinical deficit [22]. Urgent surgery is defined herein as intervention performed within 12–24 h of hospital arrival and emergent surgery as within 2 h. Patients with surgical decompression at greater than 48 h after symptom onset have significantly worse prognosis [23]. Furthermore, of patients with complete bowel/bladder incontinence at presentation, 20–25% will never recover function [24]. The need for chronic urinary self-catheterization has a major negative impact on quality of life for patients, even in the setting of complete motor recovery [11]. Surgical timing greater than 48 h from symptom onset also negatively impacts medico-legal cases involving cauda equina syndrome, having been shown to be significantly associated with unfavorable rulings for treating physicians [2, 25]. In fact, in many of the cases reviewed by Daniels et al., the timing to surgery determined the verdict over the actual degree of functional loss [25].

If a compressive lesion is seen on MRI scan, prompt surgical decompression of the lesion is indicated. In the case of a very large lumbar disc herniation in a patient with bowel and bladder deficits, bilateral laminectomy allows for safer removal of the herniated disc fragment to accommodate further retraction of the thecal sac [26]. Although this may require more significant medical facetectomy, which in turn may elevate future risk of need for spinal fusion, the benefits of safer discectomy outweigh these potential risks [27]. Tubular microdiscectomy or endoscopic discectomy is generally not recommended in the setting of massive disc herniation with cauda equina syndrome given the higher risk for direct nerve root injury, leakage of cerebrospinal fluid, and incomplete removal of the herniated disc fragment [28].

Rarely is emergent posterolateral fusion performed for a large lumbar disc herniation causing cauda equina syndrome. In the case of thoracolumbar junctional disc herniation, though (T11–L2), posterolateral fusion is sometimes performed given the higher risk of iatrogenic instability with significant medial facetectomy [15]. In cases of compressive lumbar metastatic epidural disease, separation surgery sometimes necessitates transpedicular approach or facetectomy (i.e., mechanical radiculopathy), and thus, posterolateral fusion [13]. In cases of isolated sacral

metastatic disease, treatment is often nonsurgical and relies on regional radiation therapy given the high degree of surgical morbidity in this population [3].

In the present case, MRI of the lumbar spine revealed a massive L4/L5 disc herniation causing near complete obliteration of the central canal (Fig. 20.1a–d). Gadolinium enhanced MRI can help differentiate new disc herniation from prior surgical scarring (the latter should enhance). This was at the level of the patient's prior lumbar discectomy, which correlated with the suspected etiology and findings on clinical history and examination. Treatment was with urgent surgical intervention in the form of bilateral laminectomy and spinal decompression at L4/L5 with

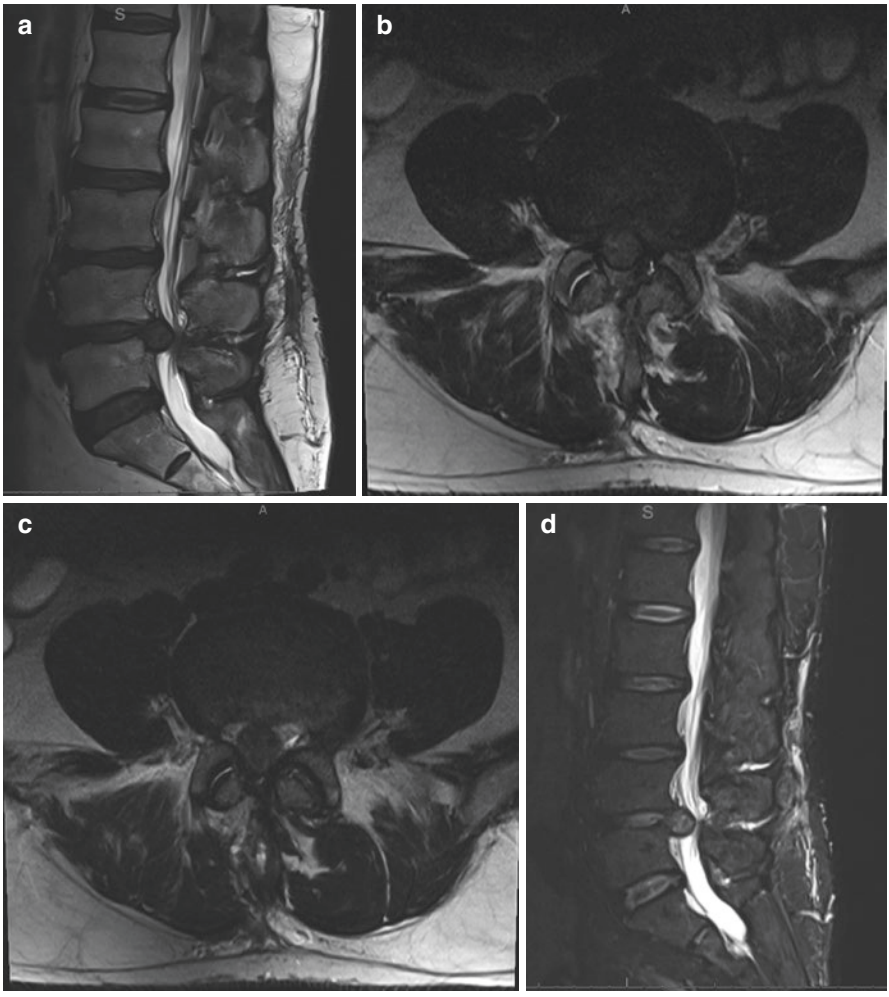

Fig. 20.1 (**a–d**) MRI of the lumbar spine without contrast demonstrating large disc herniation at L4–L5, occupying greater than 95% of the lumbar spinal canal. (**a**) Sagittal T2-weighted image. (**b**) Axial T2-weighted image. (**c**) Axial T2 weighted image. (**d**) Sagittal STIR sequence

discectomy. Postoperatively, the patient recovered his lower extremity strength, as well as bladder function, but had some residual lower extremity numbness. When counseling patients about expected recovery of function, it is important to advise them that even with prompt surgical intervention, restoration of full bowel/bladder function can be difficult. Approximately 20–25% of patients have persistent deficits in bowel/bladder/sexual dysfunction [2]. These deficits also take the longest to recover, however, and continued improvement can be seen several years following injury and surgical intervention.

20.5 Clinical Pearls

- The classic symptoms of cauda equina syndrome include back pain/discomfort, sensory changes in lower extremities (often asymmetric), motor weakness in the lower extremities (often asymmetric), bladder dysfunction, bowel dysfunction, saddle anesthesia, and/or sexual dysfunction.
- Prompt diagnostic imaging is critical and a limiting step to rapid surgical intervention for cauda equina syndrome.
- Time to surgical intervention is an important prognostic indicator for recovery of neurologic function.
- Even with prompt surgical decompression, bowel/bladder dysfunction can persist and be a significant driver of decreased quality of life for patients.

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Part III
In the ICU

Chapter 21
Sudden Neurologic Worsening in the Postoperative Patient

Francis J. Jareczek and J. Christopher Zacko

Clinical Scenario

The discussion of sudden neurologic worsening in the postoperative patient can be an extended and complex one, not only because the differential for sudden neurologic worsening may be broad, but also because there exists considerable diversity of postoperative neurosurgical patients—from those undergoing an open cranial procedure, to those undergoing an endovascular procedure, to those presenting to the Intensive Care Unit (ICU) after a prolonged spine operation. The following discussion will highlight some of the more common pathologies to anticipate in the care of postoperative neurosurgical patients.

Case 1: Status Post-Craniotomy for Supratentorial Tumor Resection
A 68-year-old man was brought to the ICU after undergoing an awake left-sided craniotomy for tumor resection. The case had gone without complication, and the lesion had been resected safely, without change in the patient's neurological exam or intraoperative neurophysiological monitoring.

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_21

Approximately 3 h after his admission to the ICU, his nurse comes to you with the concern that he is no longer following commands. The nurse additionally notes that he is not speaking and is exhibiting a forced gaze to the right, as well as some twitching of his left upper extremity. Your assessment is similar.

Case 2: Status Post-Craniotomy for Clipping of a Ruptured Intracranial Aneurysm

A 44-year-old woman was admitted to your ICU 6 days ago after undergoing a right pterional craniotomy for successful clipping of a ruptured anterior communicating artery aneurysm (Hunt and Hess grade 3, Fisher grade 2 subarachnoid hemorrhage). Her external ventricular drain (EVD) was working well. Recorded intracranial pressure (ICP) was consistently low. She experienced occasional episodes of hypotension, addressed by a reduction in nimodipine dose. Oral intake was adequate. Therefore, intravenous fluids were discontinued on post-bleed day 3. She was participating well with PT and OT and was hopeful for a short rehab stay at the time of discharge. During ICU morning rounds, the patient reports that she has been unable to lift her legs off the bed since she woke up an hour or two prior. You quickly scan through her data, and you note that her urinary output has been increasing and her serum sodium levels have been trending down over the preceding days.

Case 3: Status Post Suboccipital Craniectomy for Evacuation of Posterior Fossa Hematoma

You are caring for a 57-year-old man brought to your ICU that morning after undergoing an emergent suboccipital craniectomy overnight for evacuation of a 4-cm spontaneous cerebellar hemorrhage. He did well immediately postoperatively, but the nurse notes that he has been complaining of a terrible pounding headache and has been growing increasingly somnolent over the past hour. As you assess him, he reports the sudden onset of extreme nausea and has two episodes of projectile vomiting. His vital signs are notable for a blood pressure of 254/108. His heart rate has been stable, in the range 80–87 bpm.

Case 4: Status Post Long Segment Spinal Decompression and Fusion

A 32-year-old man, with a history of multiple spinal surgeries for back pain and spinal instability at an outside institution, was brought to your ICU after a 10-h procedure during which he underwent removal and replacement of hardware, with extension of his prior fusion from T5 to pelvis. The surgeon reported 2000 mL of blood loss; the patient received 3 units of packed red blood cells in the operating room and was on vasopressor support for most of the case. The patient was a bit drowsy from anesthesia immediately postoperatively but appeared to have a nonfocal neurological exam and was able to move all four extremities to command. When you return to re-examine the

patient after an hour, he is more awake but reports that he is unable to elevate his bilateral lower extremities. He had full strength in his legs preoperatively.

21.1 History and Neurologic Exam

The differential diagnosis for acute neurological worsening in a patient who has recently undergone neurological surgery can be narrowed based on a number of key elements from the patient's history, the details of the operation itself, and the types of symptoms exhibited by the patient. Inherent to each type of surgery, whether open or endovascular, supratentorial or infratentorial, cranial or spinal, is a set of potential complications with which the practitioner should be familiar. Any time the cranial vault is opened and the dura manipulated away from the inner table of the skull, the potential exists for an epidural hematoma to develop. With the opening of the dura, postoperative subdural hematomas and pneumocephalus find a place in the differential. Manipulation of the brain tissue—whether by the pathology to be treated or in accessing that pathology in the process of treating it—creates the potential for intraparenchymal hematomas and seizures. When the vessels are accessed, vasospasm, stroke, and acute bleeding enter the list of considerations. In the context of a normal preoperative exam, discerning the cause of an acute change in the neurologic exam after a prolonged spinal surgery requires an attention to the details of the operation itself, as well as the perioperative and immediate postoperative management of factors such as patient hemodynamics.

Each of these potential diagnoses is, of course, impacted in part by the patient's medical history and the history of their disease; thus, it is prudent to first inquire into these elements in developing a differential diagnosis for the cause of an acute neurological change in a postoperative neurosurgical patient.

Pertinent elements of the patient's medical history include the following:

- *Underlying coagulopathy*. Patients with hemophilia or other clotting factor deficiencies are at increased risk of hemorrhage in general, as well as in the perioperative period [1, 2]. In most cases, a thorough preoperative assessment has been performed and the patient optimized prior to proceeding with surgery; however, surgical stressors can alter bleeding and clotting dynamics.
- *Iatrogenic coagulopathy*. Presumably, the patient would have been instructed to hold any home antiplatelet (e.g., aspirin, clopidogrel) or anticoagulant (e.g., apixaban, warfarin) medications preoperatively, but be sure to verify with the patient or patient's family. The use of antiplatelet and anticoagulant agents is presumed to increase the risk of postoperative bleeding events after elective surgery [3–5], though interestingly, a recent study demonstrated no difference in postoperative bleeding events in patients undergoing emergency surgery for traumatic intraparenchymal hemorrhage (IPH) or traumatic brain injury (TBI) [6, 7].

- *History of TIAs or strokes*. Patients with a history of stroke or transient ischemic attacks (TIAs) are at risk for additional ischemic events, and this risk may be increased in the perioperative period [8, 9]. Furthermore, patients who had been on antiplatelet therapy for stroke prevention are often asked to hold those medications prior to neurological surgery. In delineating a patient's likelihood of a perioperative stroke, it is also helpful to investigate other risk factors for stroke, e.g., smoking status, use of oral contraceptive pills, or of other pro-thrombotic medications [10, 11].
- *History of preexisting respiratory conditions*. Patients with a history of pulmonary conditions such as obstructive sleep apnea (OSA) or chronic obstructive pulmonary disease (COPD) may exhibit postoperative alterations in mental status secondary to hypoxemia or hypercapnia as a consequence of their respiratory disorder [12, 13]. Even with excellent intraoperative management, upper airway obstruction or carbon dioxide retention after extubation may contribute to an acute deterioration in a patient's neurological examination after he has arrived to the intensive care unit.

The history of the patient's disease course, both prior to admission and during his or her hospital stay, can also be quite informative. Specific aspects to consider are as follows:

- *History of trauma*. Coagulopathy is common in the trauma setting, whether secondary to thromboplastin release, hemodilution after fluid resuscitation, hypothermia, or acidosis [14]. A phenomenon known as trauma-induced coagulopathy can also occur independently of these factors [15], further increasing the risk of hemorrhagic complications that may affect an acute change in neurologic examination.
- *History of seizures or antiepileptic use*. Seizures can be a common symptom associated with brain tumors, especially those that involve cortical structures [16–18], and may appear de novo in the postoperative period [19]. Patients with seizures as a tumor-associated symptom will typically be on antiepileptic medications at presentation. Determine when the patient last took his or her antiepileptic drug (AED) prophylaxis.
- *Timing and progression of symptom appearance*. Were the new symptoms noted immediately postoperatively, or did they appear a few days after the procedure? Did the symptoms progress rapidly, or did the patient exhibit a gradual decline in his or her level of arousal? Symptoms that appear early after surgery and progress rapidly suggest a more acute pathology, perhaps related to the operation itself, that may need to be addressed in an urgent fashion. In contrast, the delayed onset of more gradually progressing symptoms infers a broader differential, one that also includes non-structural causes such as metabolic derangements.
- *Balance of intake and output, trend in sodium levels, trend in transcranial Doppler (TCD) velocities*. Vasospasm, a phenomenon that is not unique to but may be most commonly seen in the setting of aneurysmal subarachnoid hemorrhage, is associated with and can be suggested by other clinical observations, such as an increase in urinary output [20], the development of hyponatremia (i.e., cerebral salt wasting) [21, 22], and an increase in TCD velocities over time [23–25].

In patients with a ventricular drain, a decrease in cerebrospinal fluid (CSF) output may also be suggestive of developing vasospasm [26].

- *Trend in ICP*. An increase in ICP preceding the acute neurological change may be suggestive of a mass lesion such as a hemorrhage [27–29].
- *Use of vasospasm prophylaxis*. In patients with a diagnosis of subarachnoid hemorrhage, was nimodipine (or alternative vasospasm prophylaxis agent) reduced or discontinued for any reason?
- *Changes in blood pressure around the time of symptom appearance*. The role of systemic blood pressure (or, conceptually, organ perfusion pressure) and its association with or prediction of an acute neurological change will differ depending on the pathology under consideration. Episodes of relative hypotension may precede the appearance of stroke-like symptoms or weakness of the extremities due to hypoperfusion of the brain and spinal cord [30–32]. Severe hypotension may also beget altered mental status, especially in elderly patients. In contrast, uncontrolled hypertension may contribute to the development or worsening of a postoperative intracranial hemorrhage [33, 34]. However, it must also be noted that a significant alteration in blood pressure is often a symptom of the process underlying the acute neurological change rather than a cause of the change. In the setting of subarachnoid hemorrhage or traumatic brain injury, patients developing vasospasm may "autopress" in an attempt to counteract relatively decreased perfusion secondary to the vasospasm [35]. In the case of acutely elevated ICP and impending brain herniation, hypertension may develop as part of the "Cushing's triad" of hypertension, bradycardia, and irregular respirations [36]. Thus, significant changes in blood pressure must be investigated promptly to identify the causative factors, as the appropriate intervention may change based on the underlying etiology.
- *Presence of radiographic ventriculomegaly or threatened obstructive ventriculomegaly on initial imaging*. Review pre- and postoperative imaging for any potential impact on CSF pathways—whether due to impaired absorption (e.g., from diffuse subarachnoid blood) or mechanical obstruction (e.g., from a posterior fossa mass lesion).
- *Considerations unique to spine procedures and pathologies*. In patients with an acute neurologic change thought to be due to spinal cord pathology, it is important to note the preoperative neurological examination and whether any preoperative deficits were present. In the setting of both elective intervention and acute spinal cord injury (SCI), the degree of radiographic compression and presence of intrinsic spinal cord signal change on MRI are important factors to consider. The details of ongoing intensive care management are also crucial, such as whether the patient was requiring vasoactive medication to support mean arterial pressure (MAP).

Key questions to be asked of the surgeon or to be reviewed in the operative report include:

- *Location of and surgical approach to the pathology of interest*. Was the lesion (blood clot or tumor) cortically based or deep-seated? Did the operative trajec-

tory pass through cortical tissue? Did the surgical procedure compromise any major vascular structures—either intentionally or inadvertently?

- *Maintenance of hemostasis*. Was it difficult to achieve hemostasis during the case? Was the tumor bed "oozy"? Was a particular vessel found to be associated with the evacuated blood clot?
- *Nature of closure*. Was a watertight dural closure achieved? Were dural tack-up sutures placed? Did the brain seem "full" at the time of closure?
- *Medical interventions in the OR*. Was the patient given an antiepileptic before or during the case? Did the patient receive mannitol or any other interventions to decrease ICP? Were steroids given intraoperatively? If so, were they given for reasons of cerebral edema or as part of the anesthesia plan to reduce postoperative nausea and vomiting?
- *Other surgical considerations*. Was there any difficulty with obtaining adequate exposure to facilitate safe manipulation of the normal neural tissue (brain or spine)? If neurophysiological monitoring was used during the case, was there a significant change in signals?
- *Anesthesia considerations*. Was there any difficulty maintaining blood pressure during the case? Were any blood products required in response to surgical blood loss or due to coagulopathy, baseline hematologic derangement, or preoperative antiplatelet or anticoagulant therapy? What anesthetic agent(s) was used?
- *Considerations unique to spine procedures*. In a patient with concern for cervical spine instability, was an awake fiberoptic intubation used? Was spinal cord perfusion optimized by avoiding hypotension and large variation in MAP? Was the anesthesia team able to adequately resuscitate in the setting of large volume blood loss?

When assessing the patient, it is important to complete a thorough neurological examination to best delineate the etiology of the acute worsening:

- *Level of consciousness*. Is the patient lethargic, or alert and engaged with a more focal deficit? Whereas somnolence suggests a more global or brainstem-level structural process such as elevated ICP or a post-ictal state, a more focal finding may assist localization within the cranium or spine. Non-structural causes of somnolence are also common and include toxic-metabolic insults, hypoxia or hypercapnia, and iatrogenic phenomena such as over-narcotization, among others.
- *Presence of forced gaze, aphasia, or twitching/tremoring of face or extremities*. Note any epileptiform activity, whether this activity is focal or generalized, and whether there is any evolution of symptoms. Determine whether depressed consciousness or any focal weakness (i.e., Todd's paralysis) had been preceded by seizure-like activity.
- *Presence of pupillary abnormalities*. Anisocoria of up to 1 mm is physiologic in up to 20% of the population [37, 38], whereas a unilateral "blown pupil" (i.e., fixed and dilated) tends to portend a more significant pathology such as brain herniation [39, 40], though it may also be seen in the setting of seizure [41].
- *Presence of speech deficits*. New-onset aphasia could suggest seizure, stroke, or vasospasm in the middle cerebral artery (MCA) territory on the left.

- *Presence of isolated cranial nerve deficits*. Isolated cranial nerve deficits tend to suggest a brainstem pathology.
- *Presence of isolated extremity motor abnormalities*. Focal weakness isolated to one extremity may suggest a small focal stroke, whereas hemiplegia suggests large vessel (e.g., MCA) involvement. Weakness of the bilateral lower extremities with preserved strength in the bilateral upper extremities would typically be more consistent with a spinal cord stroke but could also reflect bilateral venous infarction due to sinus injury or thrombosis [42]. New weakness in the deltoid and/or biceps after cervical spine surgery may be due to C5 palsy, a known but incompletely understood complication of cervical decompression [43].
- *Associated nausea/emesis beyond what is expected as a post-anesthetic effect.* Whereas global elevations in ICP can present with nausea and emesis, some studies suggest that these symptoms are also commonly seen in the setting of posterior fossa pathology and after surgical access of the posterior fossa [44–46].
- *Patterns of neurological findings suggestive of spinal cord pathology.* The anatomic organization of the spinal cord facilitates fairly stereotypic manifestations of injury. Hemicord injury is characterized by ipsilateral weakness, ipsilateral loss of proprioception and vibration sensation, and contralateral loss of pain and temperature sensation. An anterior spinal cord infarction classically presents with paralysis and loss of pain and temperature sensation with preservation of proprioception and vibration sensation.

21.2 Differential Diagnosis

Generating a comprehensive, yet appropriately focused differential diagnosis for sudden neurologic worsening in the postoperative neurosurgical patient can be challenging. A good starting point is to consider the nature of the procedure itself, focusing on which intracranial or spinal structures were manipulated over the course of the operation, and how manipulation of neural tissue could lead to a change in the neurologic exam.

In **Case 1**, the patient had undergone a left-sided craniotomy for tumor resection. In the first few hours of the postoperative period, he developed an acute change in his level of consciousness and no longer followed commands. One consideration for a depressed level of consciousness in a patient with recent surgery would be a mass lesion—in this setting, a hematoma or stroke. Several types of hematomas could develop in the postoperative setting, including epidural (EDH), subdural (SDH), and intraparenchymal (IPH, either into the tumor bed or remotely) and are discussed in detail elsewhere in this text. If the tumor was located in close proximity to the venous dural sinuses or large veins, local tissue manipulation could lead to venous infarction and associated hemorrhage [47–49]. Studies identify the first 6 h after surgery as a “critical period” for the development of postoperative hematomas that will become clinically apparent [34, 50, 51], but hemorrhages can also occur in a delayed fashion [52, 53]. The likelihood of a hematoma forming is altered by

various patient factors such as the presence of an underlying coagulopathy, whether genetic, pathologic (as in the setting of hemorrhagic TBI [54]), or iatrogenic. Surgical factors also play a role: subtotal tumor resection and the presence of a large resection cavity have been associated with hemorrhage into the tumor bed [34], and failure to place epidural tacking stitches in patients with difficult to control epidural bleeding may increase the risk of developing a postoperative epidural hematoma [55].

Generalized seizures are another entity that can lead to an alteration in a patient's level of consciousness. In this particular case, the patient's additional symptoms of forced gaze deviation and extremity twitching suggest that this may be a more likely diagnosis. Seizure is often the presenting complaint for a new brain lesion [56–58], and for these patients, a preoperative history of seizures predicts postoperative seizures as well [16, 18]. In other patients, seizures may not occur until the postoperative period. Certain tumor types, such as meningioma, are more commonly found to be associated with seizures [18]. Seizures are also associated with other pathologies such as TBI, with an incidence of up to 10% [59]. This risk may be compounded if operative intervention is pursued for these patients.

An infrequent but serious complication after cranial procedures is tension pneumocephalus. It is not uncommon for a small amount of air to be seen in the cranial vault after craniotomy. However, when air continues to enter through a dural defect and becomes trapped via a ball-valve mechanism, it can begin to exert mass effect on the brain tissue [60, 61]. While seizures and focal neurological deficits can be seen with tension pneumocephalus, a perhaps more common presentation is a declining level of conscious. Prompt recognition of this complication will prevent progression to herniation and death.

In **Case 2**, the patient had also undergone a craniotomy—in this instance for clipping of a ruptured aneurysm. The differential diagnosis for this patient should also include both hematoma and seizure; however, the particular pathology of aneurysmal subarachnoid hemorrhage raises concern for an additional set of potential complications. Direct manipulation of blood vessels intraoperatively—for dissection and treatment of the aneurysm—risks direct injury, vasospasm, and/or occlusion (thrombotic or iatrogenic due to clip placement) resulting in stroke [62–64]. This complication would manifest with acute neurological findings attributable to the brain region supplied by that vessel, e.g., an infarct in the left MCA territory could cause aphasia, whereas a similar event in the left ACA territory would cause right leg weakness. Ischemia or infarction secondary to surgical manipulation of the vessels would typically be apparent in the immediate postoperative period.

Vasospasm is an entity somewhat unique to subarachnoid hemorrhage, presenting several days after the initial insult and potentially resulting in delayed cerebral ischemia. Blood in the subarachnoid space is irritating to the blood vessels and leads to arterial narrowing via incompletely understood mechanisms [65, 66], effectively producing acute stroke-like symptoms in the territory supplied by the vessel experiencing vasospasm [67, 68]. The risk of vasospasm is generally highest from postbleed day 5–10 [69]. A number of studies have attempted to predict which patients will develop symptomatic vasospasm. One classic association is presentation with

symptomatic vasospasm in conjunction with an increase in urinary output and concomitant decrease in serum sodium, consistent with a diagnosis of cerebral salt wasting (CSW) [20, 70]. While the mechanism of CSW remains poorly understood, the polyuria associated with CSW may lead to hypovolemia and worsen vasospasm. The syndrome of inappropriate antidiuretic hormone (SIADH) has also been associated with aneurysmal SAH [71]. In the ICU setting, transcranial Doppler sonography (TCDs) of the large vessels is often performed daily to assess for changes in blood flow that may suggest developing vasospasm [23, 72]. An acute increase in TCDs, or an absolute value of >120 cm/s in the MCA (with >200 cm/s suggesting severe vasospasm), is consistent with the diagnosis [23]. It should be noted that while aneurysmal subarachnoid hemorrhage is perhaps the most common setting in which vasospasm is found, it may also occur in the setting of traumatic brain injury [73].

Of note, endovascular treatment of intracranial aneurysms carries its own unique set of potential complications that will not be discussed in detail here. Briefly, these may include the development of focal cerebral edema [74], post-intervention hemorrhage (secondary to aneurysm rupture [75, 76] or vessel perforation [77]), or thromboembolic or thrombo-occlusive events [78]. The catheters themselves may physically disrupt and cause embolization of atherosclerotic plaques, or they may create a dissection within the vessel wall [79]. The nuances of diagnosing and managing these complications is beyond the scope of this chapter and has been reviewed elsewhere [80–82].

Case 3 addresses considerations specific to pathologies involving the posterior fossa. The posterior fossa is a confined space containing the brainstem, the cerebellum, and the fourth ventricle. Mass lesions, whether tumor or hematoma, can manifest with a variety of symptoms secondary to compression of the exiting cranial nerves or of the brainstem itself. The ability of posterior fossa lesions to cause obstructive hydrocephalus through occlusion of the fourth ventricle is well known [83, 84]. Symptomatic posterior fossa pathology may manifest as nausea and emesis, similar to any post-craniotomy patient [85]. However, these symptoms in a patient with posterior fossa pathology are more likely to reflect increased ICP—whether due to direct compression from hematoma or swelling, or due to secondary obstructive hydrocephalus. Another phenomenon, thought to be secondary to medullary compression, is accelerated refractory hypertension [86–89]. The constellation of worsening somnolence, extreme nausea and emesis, and accelerated hypertension in this patient are concerning for re-hemorrhage. The normal heart rate is not consistent with the bradycardia seen in "Cushing's triad," which, if present, would be more concerning for obstructive hydrocephalus causing an acute elevation in ICP.

Case 4 is unique in its focus on acute neurologic worsening in the postoperative spine patient. Many of the general classes of pathology (e.g., infarction, hemorrhage) are the same, but the anatomy and surgical approaches to this part of the central nervous system merit a more focused discussion. In most individuals, the spinal cord terminates with the conus medullaris at approximately the L1 vertebral body. Thus, spine procedures at levels above L2 carry the additional risk of direct

injury to the spinal cord, either at the time of surgery or in a delayed fashion secondary to recurrent disc or bone fragment impingement [90, 91] or hardware subsidence [92, 93]. Postoperative spinal epidural hematomas are rare but can also cause compression of the cord and cauda equina [94–96].

Another somewhat unique feature of the spinal cord, secondary to its vascular supply, is its relative susceptibility to ischemia, and hypotensive infarction is a well-known entity [32, 97]. The region from T4 to T8 is at greatest risk as it lies in a "watershed zone" between the territories of the anterior spinal artery (supplying the cervical and high thoracic segments) and the great radicular artery of Adamkiewicz (supplying the lower thoracic segments) [98]. Another consideration in the setting of a decompressive procedure is reperfusion syndrome, also known as "white cord syndrome" due to its characteristic MRI finding of T2 hyperintensities. It is believed that reperfusion of a chronically ischemic spinal cord causes worsening neurologic deficits [99]. In the case presented above, the prolonged surgery, significant blood loss, and blood product and vasopressor requirements suggest that hypotension and consequent cord ischemia may underlie the patient's new weakness.

21.3 Diagnostic Evaluation

In the case of most cranial pathologies, a non-contrast head CT is often a good first step to assess for any acutely operative complications: it is a relatively rapid diagnostic test that will readily reveal clinically significant hemorrhage, hydrocephalus, or edema. However, clinical judgment must be exercised to ensure hemodynamic stability and to promptly manage other urgent conditions, such as seizure, prior to sending the patient for imaging.

In **Case 1**, seizure is the most likely cause of the patient's acute neurologic change. His symptoms should be managed medically (e.g., with intravenous lorazepam) and promptly, prior to pursuing further diagnostic testing. While EEG could be helpful for localizing the seizure, or if subclinical status epilepticus is suspected, a general idea of the cortical regions involved can be gleaned from the clinical picture, and the diagnosis remains a clinical one. Once the seizures are controlled, cranial imaging can be obtained.

Non-contrast head CT will reveal any areas of acute hemorrhage, whether into the tumor bed, or in the subdural or epidural space associated with cranial access. Acute blood will appear hyperdense, or bright, on this study. The CT will also provide some information about the degree of perilesional edema that may be contributing to the patient's symptoms. This imaging modality will be similarly useful for assessment of the posterior fossa in **Case 3**, not only for revealing any potential rehemorrhage, but also for demonstrating the development or progression of acute hydrocephalus.

In **Case 2**, where there is concern for potential vasospasm and resultant ischemia, non-contrast head CT remains a reasonable first step to exclude space-occupying lesions or hydrocephalus. If brain ischemia or infarction is suspected,

this may be supplemented by CT angiogram, with or without CT perfusion [100, 101]. These studies may demonstrate narrowing of the affected vessels, in conjunction with decreased perfusion of the territories supplied by those vessels and would provide the most expedient route to urgent endovascular therapy, if appropriate. Alternatively, MRI brain with "stroke protocol" may be performed to confirm the diagnosis; however, in most settings, MRI is less time-efficient to obtain. The "gold standard" study for diagnosing vasospasm is digital subtraction angiography (DSA), an endovascular procedure that additionally enables the interventionalist to attempt treatment. DSA will demonstrate regions of vasospasm and permits "real time" assessment of relative blood flow through the major intracranial vessels [69, 102, 103].

In **Case 4**, non-contrast CT imaging of the spine is helpful for rapidly ruling out bony pathology, hematoma, or hardware complication that may require an emergent return to the operating room. With appropriate windowing of the images, CT can also give limited information about compressive soft tissue lesions; however, MRI is more helpful for assessing soft tissue structures. Furthermore, MRI is the imaging of choice for diagnosing spinal cord ischemia or infarction. As in brain MR imaging, areas of cord infarct will restrict on diffusion sequences and will appear hyperintense on T2 and STIR sequences and isointense on T1 [104]. The involved tissue will not enhance until it has become a subacute infarction.

Any decline in neurologic exam warrants an appropriate expedited workup, such as described above, to look for new pathology or quickly reversible etiologies. The patient's medications should be reviewed, with specific attention to any recent administration of sedative or analgesic agents. A metabolic workup should be pursued early and may reveal abnormalities contributing to an acute change in the neurologic examination of a postoperative neurosurgical patient [105, 106]. Electrolyte dyscrasias can elicit confusion, somnolence, or generalized weakness, and hyponatremia specifically must be ruled out as a cause of seizure. Acute respiratory failure may manifest with confusion or somnolence. An arterial blood gas will help classify the respiratory failure into hypoxic or hypercapnic, a distinction that will guide further treatment. Endocrinological abnormalities such as hypothyroidism can also present with a depressed mental status, though typically in a more subacute fashion. If a structural or metabolic cause does not declare itself, there is accumulating evidence to suggest considering ICU-related delirium in the differential diagnosis [107].

21.4 Clinical Decision-Making and Next Steps

Arriving at an accurate diagnosis for the cause of the acute neurologic worsening is crucial, as some entities may be managed medically, whereas others require operative intervention. For potentially operative pathologies, the indications for surgical intervention are dictated by the nature, size, and anatomic location of the pathology.

21.4.1 Seizure

In the acute setting, antiepileptics are the mainstay of treatment. Seizures may be treated with intravenous lorazepam initially, while a loading dose of another antiepileptic such as levetiracetam is prepared. Primary medical control of seizure and airway control, if necessary, are imperative to obtain prior to pursing imaging. An EEG should be obtained if subclinical status epilepticus is suspected. Potential operative intervention is dictated in part by the presence of a culprit lesion, if identified, on subsequent imaging. Subdural hematomas, intraparenchymal hematomas, and residual tumor may all be responsible for seizures [16]. If the seizures are difficult to control with antiepileptics, surgical intervention may be required. The management of seizure and status epilepticus is discussed in further detail in Chap. 23.

21.4.2 Intracranial Hematoma

Small subdural hematomas or a small amount of hemorrhage into the tumor bed are not uncommon after craniotomy for tumor or other pathology, despite the surgeon's efforts to maintain meticulous hemostasis throughout the case. Many of these hematomas do not cause significant mass effect or become symptomatic. Postoperative hematomas causing clinical deterioration tend to occur within 6 h of surgery [108, 109]. Risk factors for these hematomas include intraoperative and immediately postoperative hypertension, as well as coagulopathy [33]. If a postoperative patient develops sudden neurologic worsening and a hematoma is identified and thought to be the cause of this neurologic worsening, surgical intervention is indicated. Longer delay to reoperation is associated with poor outcome; thus, intervention should be prompt [110]. General indications for the surgical management of extra-axial hematomas are discussed in Chap. 1.

21.4.3 Tension Pneumocephalus

Urgent surgical intervention is required for symptomatic tension pneumocephalus [61]. Bedside needle decompression through an existing burr hole could be considered if the pocket of air is accessible via this route [111–113]. Trace pneumocephalus commonly seen after most cranial procedures does not require intervention and will resorb spontaneously. Large but relatively asymptomatic (e.g., mild headache) pneumocephalus may also be managed expectantly, and some recommend the use of a nonrebreather mask with 100% oxygen for 24–48 h to aid in resorption [114, 115]. The amount of pneumocephalus over time can be monitored with serial skull X-rays [116]. If the cause of the pneumocephalus is not readily apparent, it must be identified and appropriately addressed to prevent recurrence.

21.4.4 Infarction

The management of cerebral infarction typically focuses on the prevention of further strokes and addressing any post-infarct edema that may result. In the case of iatrogenic small vessel occlusion sustained in the process of clipping an aneurysm, often no further management is required. In contrast, in the setting of a vascular injury such as a small dissection, the initiation of antiplatelet therapy could be considered; however, the evidence for this intervention is limited [117, 118]. Infarcts sustained in the process of vessel manipulation tend to be small and would not exhibit much swelling; however, large, full territory infarctions can subsequently develop a significant amount of edema [119, 120]. The use of hypertonic saline is often employed to augment serum sodium levels and combat this edema; alternatively, mannitol may be employed [121–123]. In some cases, operative intervention in the form of a decompressive hemicraniectomy may be pursued as a lifesaving measure [124, 125].

21.4.5 Vasospasm/Delayed Cerebral Ischemia

At the initial appearance of symptoms, permissive hypertension or even blood pressure augmentation may be trialed [126]. In mild cases, this intervention may be sufficient. If symptoms persist, return to the neurointerventional suite may be considered for angioplasty [127–129] or intra-arterial injection of a spasmolytic agent, such as verapamil, or a vasodilator, such as milrinone [130–133]. In some cases, a single intervention is sufficient. With recurrent symptomatic vasospasm, repeat intervention may be pursued. Other studies have found that a milrinone infusion following intra-arterial treatment may reduce the recurrence of vasospasm [134, 135].

21.4.6 Obstructive Hydrocephalus

Symptomatic obstructive hydrocephalus warrants urgent intervention. Two broad approaches may be taken as dictated by the etiology: addressing the cause of the hydrocephalus (e.g., removing an obstructive lesion), and thus secondarily treating the hydrocephalus, or addressing the hydrocephalus directly via placement of an external ventricular drain.

21.4.7 Spinal Epidural or Subdural Hematoma

Symptomatic spinal epidural hematoma typically requires urgent surgical exploration and evacuation, both to relieve the mass effect on the spinal cord and identify and address the source of the bleeding to prevent recurrence [95, 136]. This entity is described in further detail in Chap. 19, Nontraumatic Spinal Cord Compression.

21.4.8 Spinal Cord Ischemia or Spinal Cord Reperfusion Syndrome

Whereas infarcted spinal cord tissue is not salvageable, ischemic tissue may recover if perfusion is restored. Maintenance of perfusion is typically attained through blood pressure augmentation with a MAP goal of 85–90 mmHg for a duration of 5–7 days [137, 138]. Some patients may respond well to fluid boluses but many will require pharmacological augmentation, typically with a norepinephrine infusion to reduce the risk of reflex bradycardia seen with alpha-selective agents [138].

21.5 Clinical Pearls

- The differential for sudden neurologic worsening in the postoperative patient is broad and is heavily dependent on the type of procedure performed.
- Acute changes in vital signs, specifically blood pressure, may precede but are often the consequence of an underlying process and must be investigated promptly, as the appropriate intervention may actually be counter-intuitive.
- Important complications after craniotomy resulting in an acute neurologic change include postoperative hematoma, seizure, and, uncommonly, tension pneumocephalus.
- Sudden neurological worsening in the postoperative spine patient can occur due to direct injury to or compression of the spinal cord or due to spinal cord ischemia; the former is typically managed surgically, whereas the latter is typically managed medically.
- Particularly in the ICU setting, it is important to consider non-structural causes of sudden neurologic worsening; these are multiple and include electrolyte derangement, as well as metabolic, respiratory, and endocrine abnormalities.

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Chapter 22
Fever in the Neurocritically Ill Patient

Perry A. Ball

Clinical Scenario

A 27-year-old, 74 kg male was involved in a bicycle accident. He was intubated by paramedics at the scene of the accident. On arrival to the Emergency Room, he is noted to have Glasgow Coma Scale (GCS) of 6T. He is evaluated by the trauma surgical team who find no evidence for significant injury outside the central nervous system. He undergoes a head computed tomography (CT) that demonstrates a right sided acute subdural hematoma (Fig. 22.1). He is taken promptly to the operating room for craniotomy and evacuation of the hematoma with placement of a left frontal ventriculostomy. He undergoes placement of right internal jugular central venous catheter for volume infusion. He is given one dose of cefazolin prior to incision and started on phenytoin for seizure prophylaxis. Intraoperatively, the estimated blood loss is 750 mL, and he is transfused two units of cross matched packed red blood cells. On arrival to the ICU, his temperature in 36.5 °C (Celsius); he has a pulse of 75 beats per minute (BPM), with mean arterial pressure (MAP) of 75 mmHg, an intracranial pressure (ICP) of 15 mmHg, and a cerebral perfusion pressure (CPP) of 60 mmHg. Electrolytes are Na+ 139 mmol/L, K+ 3.7 mmol, HCO3− 18 mmol/L, Cl− 97 mmol/L. The BUN is 10 mg/dL, Cr is 1.1 mg/dL, and lactate is 1.2 mmol/L. White Blood cell (WBC) count is 10.5 × 103/mcL, hemoglobin (Hgb) is 13 g/dL, and international normalized ratio (INR) is 1.4. He is ventilated by volume control mode, with an inspired oxygen of 40% and a resulting arterial blood gas (ABG) of 7.40/39/95/99%. His admission chest X-ray shows acceptable endotracheal tube and central venous line positioning, with clear lung fields (Fig. 22.2). On the second

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_22

postoperative day, he develops a fever to 38.4 °C which resolves spontaneously over an hour.

On the fourth postoperative day, he develops a sustained fever to 39 °C, with a pulse of 90 BPM and MAP of 80 mmHg. The ICP is 20 mmHg, and the resulting CPP is 60 mmHg. His GCS score remains 6T. He has made 40–50 mL of urine per hour for the past 8 h. There has been no diarrhea. He is now requiring FiO2 50%; the ventilator remains in volume control mode, with ABG7.35/35/85/97%. The WBC is 15.1 × 103/mcL, Hb 12 g/dL, Na+ 140 mmol/L, lactate 1.0 mmol/L, and Cr 1.0 mg/dL.

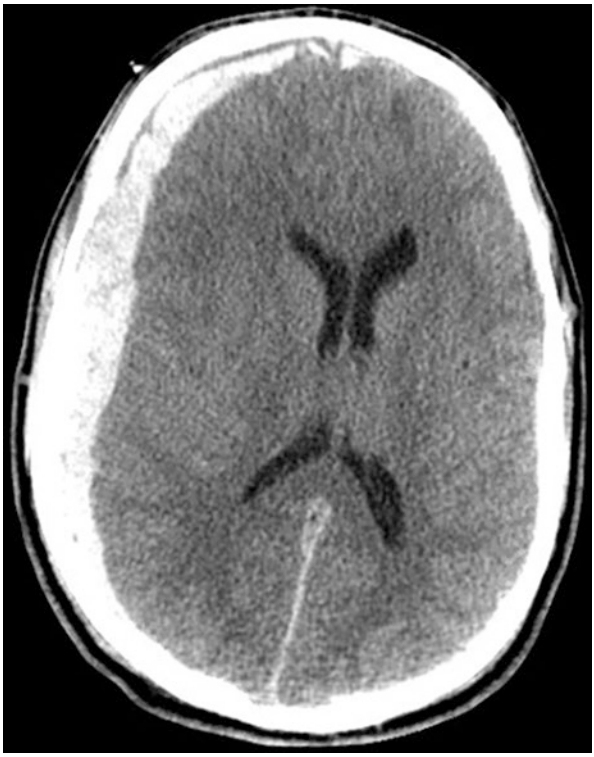

Fig. 22.1 Noncontrast CT head axial image demonstrating an acute right subdural hematoma

22.1 History and Neurologic Exam

The timing of onset and the magnitude of the temperature elevation are the most important factors in the initial evaluation of fever. The American College of Critical Care Medicine and the Infectious Diseases Society of America (IDSA) define fever as temperature greater than 38.3 °C [1]. Fever has been reported to occur in more

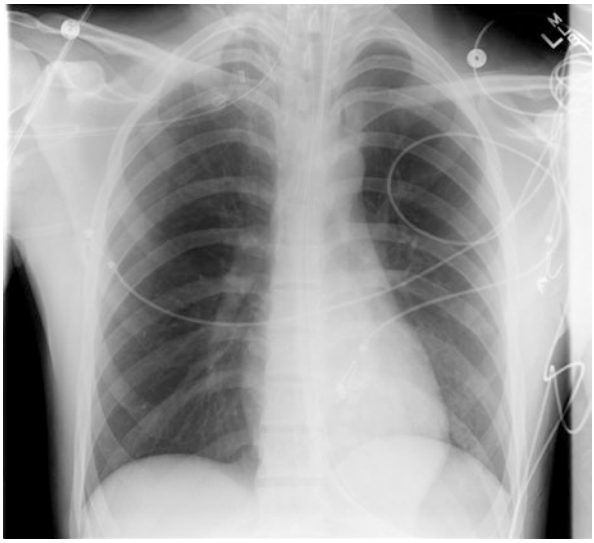

Fig. 22.2 Admission chest X-ray showing clear lung fields

than 40% of patients admitted to an ICU [2] and can be due to both infectious and non-infectious causes. This patient had a fever to 38.5 °C on the second postoperative day. Temperature elevations between 38 and 38.8 °C can be either infectious or non-infectious in etiology. Fevers occurring less than 48 h following surgery are rarely infectious [3]. This is often attributed to lung atelectasis; there is, however, little evidence to support atelectasis as a source of fever [4], and early fevers following surgery probably represent inflammatory response to the surgical procedure. This initial temperature elevation, therefore, is almost certainly non-infectious, and it resolved spontaneously. On the fourth postoperative day, he develops a fever to 39 °C. Temperatures between 38.9 and 41 °C are most likely to be infectious in origin [4]. In this patient, the temperature of 39 °C occurring more than 48 h following surgery strongly suggests an infectious origin. Temperatures greater than 41 °C, however, are usually non-infectious in origin and can be due to central fever, drug reactions, transfusion reactions, adrenal insufficiency, malignant hyperthermia, serotonin syndrome (SS), or neuroleptic malignant syndrome (NMS) [5].

An element of the history that would valuable to know is if the patient has had exposure to intravenous antibiotics in the previous 3 months as this increases the likelihood of colonization with multi-drug resistant (MDR) organisms. It would also be important to determine if there is a history of alcohol or drug use or exposure to anti-depressant or anti-psychotic medications as these raise the possibility of SS, NMS, or withdrawal symptoms. A history of recent intravenous drug use raises the possibility of endocarditis. It should be determined whether the central venous catheter and the ventriculostomy were placed under sterile conditions, with full barrier precautions, as these measures have been shown to reduce the rate of infection [6, 7].

The surgical incision should be inspected to look for signs of infection. The sites of the ventriculostomy and the subclavian central venous catheter should be inspected

for redness or purulence. The appearance of secretions from the endotracheal tube should be inspected to see if they are thin and clear or tenacious and cloudy. The chest, abdomen, and extremities should be examined for any signs that might point to an injury that was missed at the time of initial trauma evaluation or any skin breakdown that has occurred. A general neurological exam should be performed looking for signs of increased motor activity including rigors, rigidity, or posturing.

22.2 Differential Diagnosis

The timing and magnitude of the temperature elevation strongly suggest an infectious origin. This patient is mechanically ventilated, has an indwelling central venous catheter, and has a ventriculostomy; these would be the most likely sources of the fever. A surgical site infection is also possible, but unlikely if the wound has a benign appearance. An intra-abdominal source could be considered if a bowel or retroperitoneal injury was missed at the time of the initial trauma evaluation. The lack of diarrhea argues against *Clostridium difficile* colitis.

A non-infectious source could also be considered. Deep venous thrombosis can cause fever, but the temperature elevation usually does not reach the level seen in this patient. The lack of muscle rigidity would argue against SS or NMS. A transfusion reaction is possible, but the fever in this setting typically occurs less than 72 h [5] following transfusion. A drug reaction could also be possible, but this is largely a diagnosis of exclusion.

22.3 Diagnostic Evaluation

In weighing the potential sources of infection and treatment decisions, the first step is to assess for hemodynamic stability and the presence of sepsis. The diagnosis of sepsis is a clinical one, based on blood pressure measurement and assessment of tissue perfusion. If vasopressor agents are required to keep the MAP above 65 mmHg, oliguria is present, and the whole blood lactate is elevated, there should be strong suspicion of sepsis. If this is the case, broad spectrum antibiotics should be initiated and fluid resuscitation started. The central venous catheter should be removed and placed at an alternate site [1]. Some clinicians measure procalcitonin, as it is often elevated in the presence of infection and can be used as a component of the diagnosis of sepsis [1, 8], but it has a poor sensitivity and specificity for ventilator-associated pneumonia [9] and infections in neurosurgical patients [10]. Serial procalcitonin measurements, however, can be used to guide the length of antibiotic therapy [11].

This patient has a stable blood pressure, no significant acidosis, a normal lactate, and is making urine (with a stable creatinine)—all suggestive that sepsis is not present.

Blood cultures should be obtained from two separate sites, preferably through venipuncture. If it is not possible to obtain blood cultures peripherally due to poor

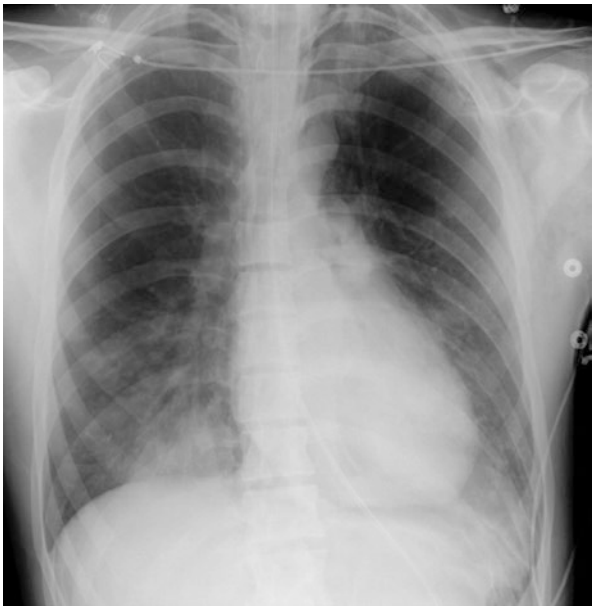

Fig. 22.3 Chest X-ray on postoperative day 4 demonstrating bibasilar infiltrates

venous access, one set of blood cultures could be drawn from the central venous catheter. This should be done with strict aseptic technique; higher rates of contamination have been reported from this strategy.

The next step would be to obtain a chest X-ray (CXR) and a sputum sample. The CXR (Fig. 22.3) demonstrates new bibasilar infiltrates. The method of obtaining the sputum sample could be through a non-invasive technique such as blind endotracheal sampling or an invasive one such as bronchoscopy, bronchial alveolar lavage (BAL), or mini BAL. There does not appear to be a difference in mortality, ICU length of stay, or duration of mechanical ventilation between the use of non-invasive and invasive sampling methods [12], and so, in most situations, blind endotracheal sampling is sufficient. In the situation of a focal infiltrate or non-diagnostic blind sampling, invasive sampling could be considered. This patient had a blind endotracheal sample demonstrating many WBCs and few Gram negative rods.

Sampling of cerebrospinal fluid (CSF) can be performed from the ventriculostomy. The CSF has 10 WBC/mm^3, glucose of 60 mg/100 mL, and total protein of 50 mg/100 mL. The Gram stain demonstrates no organisms.

22.4 Clinical Decision-Making and Next Steps

As this patient does not have signs of hemodynamic instability, proceeding to assess the most likely sources of infection would be appropriate.

If the central line insertion site looks clean and the patient is hemodynamically stable, the line may be left in place while awaiting blood culture results [13]. A central line-associated bloodstream infection (CLABSI) refers to a blood stream infection diagnosed with positive blood culture in the presence of a central venous line. The more narrow definition of a catheter-related bloodstream infection (CRBSI) is present if the same organism is cultured from a peripheral site and through the catheter [14]. In general, if the blood cultures are positive, empiric antibiotics should be started, and the line should be removed and replaced at a new site—particularly if the organism is *Staphylococcus aureus*, an enteric Gram negative, or Enterococcus. A difficulty arises if the organism growing in the blood culture is coagulase-negative Staphylococci (CoNS), as differentiating true infection from skin contamination can be challenging. If two or more blood cultures are positive within 48 h for identical strains of CoNS, then a true bloodstream infection is likely [15]. The length of antibiotic treatment should be 5–7 days for CoNS, 7–14 days for Enterococcus and Gram-negative bacilli, and 4–6 weeks for *Staphylococcus aureus* [16].

The ventriculostomy presents another potential source of infection. Ventriculostomy catheters, however, can become colonized with bacteria and without infection; interpretation is complicated further by the issue that is difficult to compare results across studies where differing definitions for infection are common [17]. The IDSA has proposed that if the patient has a positive cerebrospinal fluid (CSF) culture—accompanied by an elevation in the protein or low glucose in the CSF—this should be considered a *ventriculostomy-related infection* (VRI). If a single CSF culture is positive, but the CSF cell count and glucose are normal, this should be considered *contamination*, and if multiple CSF cultures are positive—with normal protein and glucose—this should be considered *colonization* [18]. If the CSF is strongly suggestive of ventriculitis based on the CSF cell count and chemistry indices, empiric antibiotics should be started while awaiting culture results, using vancomycin and an antipseudomonal beta-lactam agent such as cefepime, ceftazidime, or meropenem. The IDSA recommends removal and replacement of the ventriculostomy catheter due to risk of formation of biofilm along the catheter [18]. However, in a retrospective review of treatment of VRI, replacement of the catheter was not associated with a difference in poor outcome or mortality compared to leaving the catheter in place [19]. In general, the recommended length of treatment is 10-14 days, but some favor 21 days if the infection is due to Gram negative organisms [18]. The CSF should be monitored for response to infection, with an expectation of a decrease in the protein and pleocytosis and sterilization of the cultures [19]. This patient had a mild pleocytosis in the CSF, consistent with recent trauma, but normal protein and glucose, so there is insufficient evidence for a VRI.

The diagnosis of VAP is a source of longstanding controversy. During a period of endotracheal intubation, there is often colonization of the tracheobronchial tree by bacteria aspirated from the oropharynx; distinguishing this colonization from true infection is not always straightforward. The dilemma is that timely identification and treatment of VAP reduce mortality [20], but the overuse of antibiotics can

promote the emergence of antibiotic resistance and the development of *Clostridium difficile* colitis. The American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) have published guidelines for the diagnosis and treatment of VAP [21, 22]. These guidelines specify that the clinical diagnosis of VAP is dependent on the presence of new or progressive infiltrates on CXR and that these infiltrates are due to infection. The infectious nature of the infiltrates is indicated by two of the following: fever, leukocytosis, and/or purulent sputum (the presence of WBC and bacteria on Gram stain). If the CXR does not show new or progressive infiltrates, then according to these guidelines, the diagnosis of VAP could be excluded, and antibiotics should not be started.

Ventilator-associated tracheobronchitis (VAT) refers to a clinical syndrome associated with fever, leukocytosis, and purulent sputum—without a change in the CXR. The concern is that some patients with VAT can progress to VAP; treatment with antibiotics may decrease this risk [23]. The ATS/IDSA guidelines, however, recommend against treatment with antibiotics in this situation, as they feel the potential benefits do not exceed the potential costs in terms of additional antibiotic exposure [22]. The decision to initiate antimicrobial therapy in this setting should be individualized, as some patients may be quite unstable in terms of pulmonary function or some baseline infiltrates on CXR might make demonstration of progression difficult.

In this case, the CXR demonstrates a new infiltrate, and the patient is febrile and has leukocytosis. Therefore, the patient meets the criteria for VAP by ATS/IDSA guidelines, and it would be appropriate to initiate antibiotic therapy. In deciding what agents to use, the ATS/IDSA guidelines specify that the first considerations should be the likelihood of the patient having been colonized with multi-drug resistant (MDR) organisms and the incidence of antibiotic resistance in the particular ICU where the patient is being treated. Risk factors for MDR organisms include current hospitalization greater than 5 days, acute respiratory distress syndrome (ARDS), septic shock, acute renal replacement therapy, or exposure to intravenous antibiotics within the past 3 months [22]. In this case, the patient has been hospitalized for less than 5 days and does not have risk factors for MDR organisms or methicillin-resistant *Staphylococcus aureus* (MRSA), and so, monotherapy for coverage of Pseudomonas with a beta-lactam agent such as piperacillin-tazobactam, cefepime, imipenem, or aztreonam would be appropriate. If risk factors for MDR organisms and MRSA were present, double coverage for *Pseudomonas aeruginosa* with a fluoroquinolone or aminoglycoside and coverage with vancomycin would be recommended. The usual length of treatment is 7 days [22].

This patient has an indwelling urinary catheter, so the possibility of a urinary tract infection could be considered. The IDSA guidelines stress the distinction between catheter-associated bacteriuria (CAB) and catheter-associated urinary tract infection (CAUTI). The presence of bacteria ($>10^5$ colony forming units/mL in culture) is part of the definition of both conditions, and pyuria can be present in CAB. The presence of an indwelling urinary catheter predisposes to both conditions. The diagnosis of CAUTI is based on symptoms referable to the urinary tract and exclusion of other all other sources of infection [24]. This patient has an

alternate source of infection and explanation for fever. Many studies that have demonstrated high CAUTI rates in ICU patients have probably been reporting CAB [25], and, in fact, the urinary tract is an uncommon source of fever in the Neuro ICU [5, 26]. The presence of CAB in the ICU is unlikely to lead to urosepsis and usually does not warrant treatment [25].

The patient is started on piperacillin-tazobactam, but remains febrile over the next 12 h; the issue of fever control should be addressed. Fever control can be achieved with antipyretics such as acetaminophen, external cooling, or intravascular cooling. Fever in the presence of traumatic brain injury has been shown to be associated with worsened outcome [27, 28]. Trials of therapeutic hypothermia compared to normothermia have failed to demonstrate a benefit in patient outcome [29, 30]. The use of targeted temperature management via intravascular cooling to achieve normothermia has been associated with a reduction of intracranial pressure burden in patients with traumatic brain injury [31]. Given the potential adverse effect of elevated temperature on outcome, a goal of normothermia in the setting of brain injury is reasonable.

22.5 Clinical Pearls

- Temperatures between 38 and 38.8 °C can be infectious or non-infectious; temperatures between 38.9 and 41 °C are usually infectious; temperatures greater than 41 °C are usually non-infectious.
- The first step in evaluating fever is to assess for hemodynamic stability and the presence of sepsis.
- The most common sources of fever in the Neuro ICU are VAP, CLABSI, and VRI. UTI is rarely a source of fever in the Neuro ICU.

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Chapter 23
Seizure and Status Epilepticus

Liesl N. Close, Daniel Samano, and Kristine O'Phelan

Clinical Scenario

A 66-year-old male—with a past medical history of hypertension and tobacco use—presents following a car versus bicycle collision. According to a witness, the helmeted patient was impacted from the back, hitting his handlebars and ultimately striking the ground with his face. EMS reported positive loss of consciousness and recorded an initial Glasgow Coma Scale (GCS) score of 11. In route, he was intermittently responsive and bleeding profusely from the face. Upon arrival to the trauma bay, physical examination revealed blood in the oropharynx and deformities of the nose and left arm, along with abrasions over the body. He had a decreased level of consciousness and was intubated for airway protection. On initial evaluation by neurosurgery, his pupils were 3 mm and reactive bilaterally. He did not open his eyes to pain; he localized briskly on the right and weakly on the left. He was given a GCS of 7T.

Initial head CT without contrast (Fig. 23.1) *showed multifocal intracranial injury, including multiple frontal and temporal contusions, a large right frontotemporal intraparenchymal hemorrhage, and subdural hematomas along the bilateral convexities and falx cerebri. Extensive subarachnoid hemorrhage was present. A left frontal bone fracture was present, extending into the*

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_23

greater wing of the left sphenoid and across the anterior cranial fossa to involve the bilateral orbital roof. The left ambient cistern was effaced, and there was 2 mm of midline shift from right to left. His initial laboratory evaluation was unremarkable.

He was taken emergently to the operating room for a right hemicraniectomy with evacuation of the right subdural hematoma and temporal intraparenchymal hemorrhage. A left frontal external ventricular drain was placed through a burr hole. Postoperatively, the patient remained intubated and was admitted to the neurosurgical ICU. On postoperative examination, his right pupil was noted to be 4 mm and nonreactive, while his left pupil was 2 mm and reactive. He localized briskly on the right and was hemiplegic on the left. His flap was full, but not tense. Imaging findings showed expected postoperative changes (Fig. 23.2). *His vital signs and laboratory values were all within normal limits. He was treated with routine perioperative antibiotic prophylaxis and was placed on seizure prophylaxis with levetiracetam 1000 mg IV BID.*

On postoperative day 2, the patient was noted to have periods of elevated ICP with documented pressures of 25–28 mmHg. He was also noted to have periods of left gaze deviation lasting several minutes and was no longer localizing.

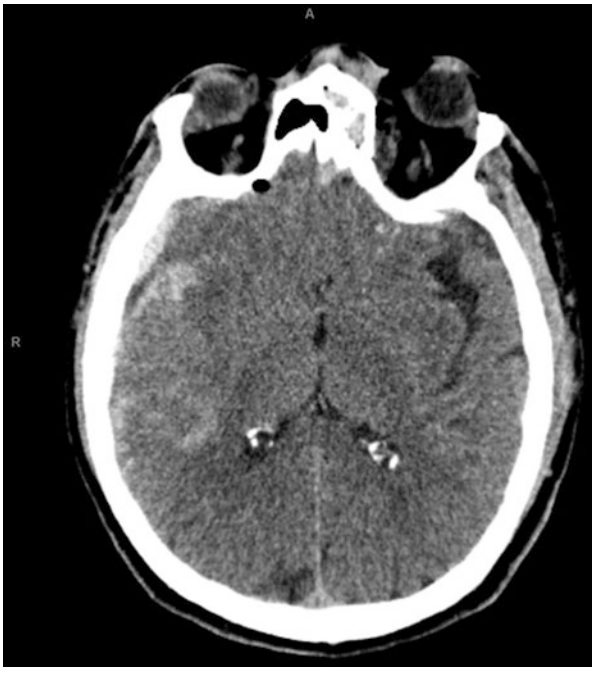

Fig. 23.1 Initial CT head without contrast, axial view

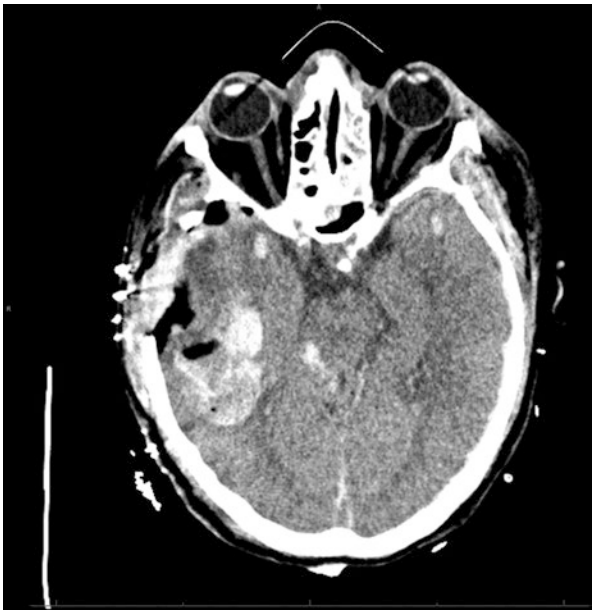

Fig. 23.2 Post-operative CT head without contrast, axial view

23.1 History and Neurologic Exam

A complete past medical and social history is often difficult to obtain in the acute setting following an acute brain injury. Friends and family should be interviewed as soon as practical. It is relevant to obtain past neurological history (i.e., history of seizure disorder, trauma, neurological interventions, or chronic conditions). In the meantime, laboratory evaluation and ancillary studies, including evaluation of alcohol, illicit drug use, and medication levels, ECG, echocardiogram, and findings on a trauma "pan-scan" can also provide clues about the patient's medical and social history.

A thorough history should be obtained to identify the potential risk factors for seizures. In a patient with a known history of epilepsy, AED levels should be checked to optimize levels for seizure control. A patient with a history of alcoholism may be suffering withdrawal seizures that respond well to benzodiazepine medications. Physical exam findings may also help to guide the workup. A fever and elevated white blood cell count could be suggestive of meningitis or other infectious process. New onset seizures in a patient with a history of metastatic cancer could suggest intracranial metastasis. Derangement of serum sodium, magnesium, and calcium can precipitate or exacerbate seizures; these electrolytes should be aggressively repleted.

Initial evaluation should follow the basic principles of advanced trauma life support [1] and emergency neurological life support [2]: airway, breathing, circulation, and neurological assessment, including pupillary response, brainstem function, and

motor response. A detailed neurologic exam is important not only for the initial assessment of the patient but also serves as a baseline objective measure to evaluate neurologic exam improvement and/or decline through the patient's clinical course. For this patient, the fluctuations in his postoperative neurologic exam are critically important. Episodic left gaze deviation with associated ICP elevations is highly suggestive of seizures.

23.2 Differential Diagnosis

Based on this patient's presentation and initial management, the differential diagnosis for his decreased level of consciousness remains broad (Table 23.1). Anisocoria, however, raises concern for a focal or lateralizing process in a patient with multifocal intracranial injury. In the immediate postoperative period, he may have suffered a new or worsening hemorrhage at the site of injury or remote to his primary injury. This, in turn, could lead to increased cerebral edema and an increase in intracerebral pressure (ICP), resulting in the pupillary asymmetry on physical examination. He may have suffered a stroke due to undiagnosed vascular injury or evolution of his primary injury, resulting in worsening cerebral edema. This might represent progression of focal, pericontusional edema, or global cerebral edema. These structural abnormalities can be detected on noncontrast CT imaging, which would be the next step in evaluating this patient postoperatively.

Once CT imaging is performed and a new structural lesion has been ruled out (i.e., worsening of localized edema, new or worsening hemorrhages) or the imaging study is found to be stable, other potential etiologies for a globally depressed level of consciousness should be considered. Gaze deviation is suggestive of new onset seizure activity [3]. This patient had episodes of elevated ICP accompanied by gaze deviation, which should be evaluated for a possible structural focus [4]. In the absence of a new structural lesion in the frontal lobe, episodic gaze deviation suggests seizure activity. Seizures increase the metabolic demand of the involved cortex, and local cerebral blood flow will be increased. This, along with increased cerebrospinal fluid (CSF) production, will further increase the ICP [5].

Table 23.1 Causes of decreased level of consciousness

Structural	Electrical	Metabolic
(Re)expanding hemorrhage	Seizures	Uremia
Focal or global edema	Status epilepticus	Hyponatremia
Ischemic stroke		Liver dysfunction
Hydrocephalus		Medication side effects

This patient is at risk for seizures both because of his TBI and his surgical procedure. Clinical post-traumatic seizures are present up to 12% of the time, whereas subclinical seizures may be diagnosed in 20–25% of patients by EEG [6]. Vespa et al. found evidence of a 22% prevalence of seizures following acute TBI, of which only 48% were clinical [7]. Recent neurological surgery has also been associated with the development of seizures [8].

The location of TBI-associated structural pathology is increasingly recognized as an important variable in the development of post-traumatic epilepsy (PTE). It has been shown that injuries affecting the temporal lobe (57%) and frontal lobe (35%) are frequent causes of PTE [9]. Temporal lobe damage has been associated with epileptogenesis [10, 11]. This patient's injury location is a reason to have a high index of suspicion for the development of seizures in the acute period, as well as PTE in the future.

Although less likely, one must also consider a metabolic abnormality leading to encephalopathy or coma. This may include uremia, elevated ammonia, hyponatremia, medication side effects (iatrogenic), or withdrawal syndromes. Post-ictal changes must be considered since the neuroendocrine system releases catecholamines and prolactin under maximal neuronal excitation. This can lead to acute hypertension and cardiac stress with accompanying elevation of serum troponin. Serum lactate is often elevated acutely postictally, as is prolactin level [12].

According to Neurocritical Care Society guidelines, status epilepticus (SE) is defined as 5 min or more of continuous clinical and/or electrographic seizure activity, or recurrent seizure activity without recovering to baseline between seizures [13]. SE can be subdivided further into convulsive, nonconvulsive, and refractory subtypes. *Convulsive* SE is marked by rhythmic jerking of the extremities—consistent with generalized tonic-clonic movements—as well as impairment of mental status. *Nonconvulsive* status epilepticus (NCSE) is seizure activity seen on EEG, without the associated clinical finding of tonic-clonic movements. *Refractory* status epilepticus (RSE) occurs when patients do not respond to standard treatment regimens and continue to have either clinical or electrographic seizures despite adequate doses of an initial benzodiazepine and a second antiepileptic drug. *Super-refractory* status epilepticus refers to seizures that break through aggressive anticonvulsant therapy—specifically, recurrent seizures occurring in patients who are on continuous infusions of anticonvulsant medications such as midazolam, pentobarbital, or propofol.

Although convulsive SE does not require EEG for diagnosis, nonconvulsive seizures and NCSE are common after cessation of generalized convulsions (48% and 14% [14, 15]). In order to evaluate for NCSE, occult, or subclinical seizures, continuous EEG is recommended in patients whose depressed level of consciousness exceeds what might be expected by imaging or those who do not return to normal neurologic function. Patients with TBI are at risk for post-traumatic epilepsy, including NCSE, despite routine use of AED prophylaxis [16–18]. Risk factors include depressed skull fractures, penetrating brain injuries, and large cortical contusions or hematomas [17]. Nonconvulsive seizures are often associated with increases in ICP and other subtle findings such as fluctuations in the neurological exam [19, 20].

23.3 Diagnostic Evaluation

Initial workup for this patient's worsening exam and decreased level of consciousness can be done expeditiously, and several elements can be performed concurrently. Seizures can be life-threatening; therefore, identifying and treating the underlying cause are essential. In this example, the primary goal should be to identify a structural problem amenable to surgical therapy. Additionally, identification of a new or worsening hemorrhage, or stroke, might direct one down a different management pathway. Once these have been ruled out, workup can proceed to assess for other causes of seizures including toxic, metabolic, and electrical abnormalities.

Specific elements of the initial evaluation may include:

- *Head CT*. A noncontrast head CT should be obtained expeditiously to identify any new or worsening findings. New or worsening hemorrhage, areas of ischemia, or worsening edema are all readily diagnosed on a head CT. These can be identified while the patient is in the CT scanner. In this patient, a follow-up head CT showed expected post-operative changes of decompressive hemicraniectomy and subdural hematoma evacuation (Fig. 23.2). There was improvement in the midline shift, but persistent effacement of the right lateral ventricle. There was improvement in the mass effect on the temporal lobe following evacuation of the temporal contusion. Upon review of the head CT, no additional surgical interventions were deemed necessary.
- *Labs*. Laboratory evaluation of patients with an altered level of consciousness should include a complete blood count, basic metabolic panel, blood glucose, and arterial blood gas. All were within normal limits.
- *ICP monitor.* This patient qualifies for an ICP monitor [5, 6]. An external ventricular drain was placed at the time of surgery to follow the patient's ICP. Although the patient was noted to have transient spikes in ICP over the first several days following surgery, these were not sustained and did not require any additional treatment.
- *MRI*. More advanced imaging modalities can be used for diagnosis of stroke, traumatic axonal injury, and disruptions to areas of the brain that play a role in consciousness. It is important to consider the appropriate timing of such a study. An unstable patient should not be sent to the MRI scanner.
- *EEG*. EEG is essential for evaluation of a patient with coma or with fluctuations in the neurological examination. EEG can detect nonconvulsive seizures or status epilepticus (SE), burst suppression, and patterns consistent with encephalopathy. Current recommendations are to continue EEG monitoring for at least 24–48 h to detect 3–19% of events [14].

Diagnostic evaluation for the underlying cause of status epilepticus should occur concurrently with stabilization and treatment. Initially, a fingerstick glucose should be obtained to rule out hypoglycemia. Once IV access has been obtained, basic laboratories should be sent, including complete blood count, basic metabolic panel,

calcium level, and magnesium level. Additional lab studies that may be important to obtain include liver function tests, toxicology screen, pregnancy test, arterial blood gas analysis, and anticonvulsant medication levels. In the outpatient or emergency room setting, serum biomarkers are sometimes useful diagnostic tools for seizure evaluation; these include serum ammonia, lactic acid, and prolactin levels [12]. However, in the ICU setting, the availability of continuous EEG monitoring renders the use of serum biomarkers less useful for seizure detection.

Furthermore, a thorough evaluation should be performed to determine if there is an occult infection, including intracranial abscess, meningitis, or viral infection such as herpes encephalitis. Routine bacterial cultures, as well as CSF studies, should be collected. A noncontrast head CT should be obtained in all patients suspected of SE in order to rule out intracranial pathology such as hemorrhage or mass lesion. EEG should be initiated as quickly as possible to detect and characterize electrographic seizures and to assess response to treatment. In the trauma setting, the cause is often more apparent (i.e., cortical contusion); however, an MRI of the brain and a lumbar puncture (LP) should be performed in any patient without a clear cause for new onset seizures. Again, it must be emphasized that treatment of status epilepticus should not be delayed for a diagnostic study.

23.4 Clinical Decision-Making and Next Steps

Continuous video EEG was connected to the patient. Rhythmic spike and wave activity were detected over the right frontal and temporal regions (Fig. 23.3). Upon identification of electrographic seizures, the patient was given a loading dose of levetiracetam, and the scheduled dose was optimized. He continued to have electrographic seizure activity, so a second agent was added. In this case, lacosamide was used at a dose of 100 mg IV BID. After initiation of dual antiepileptic drug (AED) therapy, the seizures resolved. His EEG returned to focal slowing over the right frontal area with some increased amplitude and frequency, consistent with a breach rhythm—a benign EEG pattern that is caused by a skull abnormality and is often difficult to differentiate from epileptiform activity [21]. Because this patient had a hemicraniectomy, this might be expected. His neurological exam stabilized; he

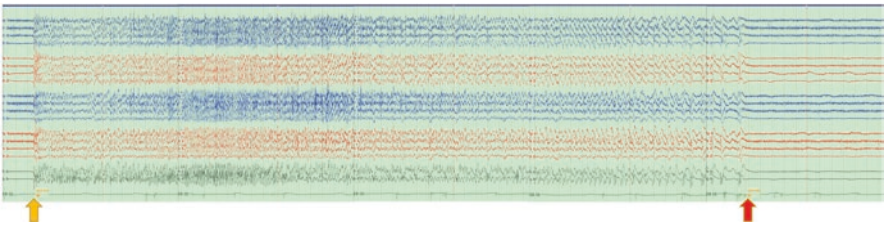

Fig. 23.3 Continuous EEG. The beginning of the seizure is indicated by the yellow arrow. The end of the seizure is indicated by the red arrow

continued to localize on the right and remained plegic on the left. During his hospital stay, he underwent placement of a tracheostomy and percutaneous endoscopic gastrostomy. At the time of discharge to a rehabilitation facility, he remained seizure-free and had regained some movement in the left lower extremity.

Primary seizure management in the setting of status epilepticus is geared toward stopping both clinical and electrographic seizure activity as quickly as possible, while maintaining the airway, breathing, and circulation of the patient. Steps that are suggested for the management of status epilepticus are outlined in Fig. 23.4. Upon recognition that a patient is seizing, the hemodynamic and respiratory stability of the patient should be considered. Emergent initial therapy should then be initiated with a benzodiazepine as an abortive therapy. Intravenous lorazepam (0.1 mg/kg) in doses of 4 mg IV is the preferred first-line treatment. Lorazepam will terminate approximately 70% of seizures prior to arrival to the emergency department [22]. However, midazolam is often the preferred prehospital abortive agent due to its more accessible administration options. Midazolam can be administered via intramuscular, nasal, or buccal routes. Diazepam may be administered rectally if no other access is available [15]. Each of these medications has been proven effective as an anticonvulsant in the emergency setting [22].

Most patients will tolerate IV lorazepam and the IV loading dose of an anticonvulsant without losing the ability to maintain their airway. In fact, untreated seizures

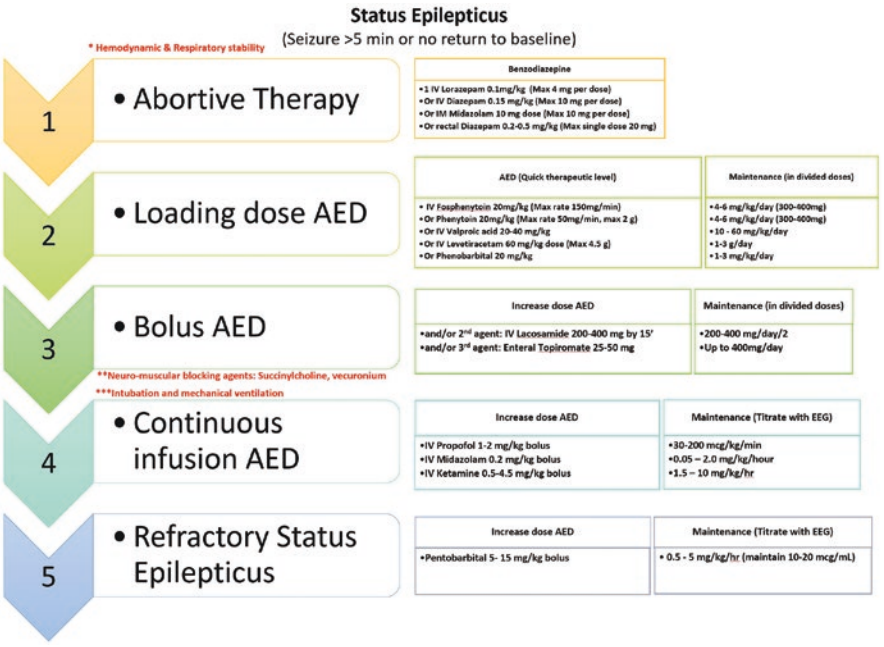

Fig. 23.4 Status epilepticus treatment flow chart. *Primary seizure management requires maintaining the airway, breathing, and circulation. **Neuromuscular blocking agents DO NOT stop the seizure. ***Intubation and mechanical ventilation are needed when anesthetics are used

pose a greater risk for aspiration, respiratory distress, and need for intubation than does benzodiazepine administration. While administering the first-line treatment, the patient's airway should be monitored, the head of the bed elevated, and suctioning used judiciously in order to prevent aspiration. Endotracheal intubation may be necessary to maintain oxygenation and ventilation if repeated doses of sedating medications are needed or if a continuous infusion of an anticonvulsant is necessary. All patients who receive continuous infusion midazolam, propofol, or pentobarbital will need to be intubated and may need fluids and vasopressors for hemodynamic support. An IV access should be secured for administration of medications and fluids for resuscitation. Blood pressure should be maintained, with a goal mean arterial pressure greater than 65 mmHg.

While administering a benzodiazepine, an IV loading dose of a maintenance antiepileptic drug (AED) should be given, with the goal of achieving a therapeutic level as quickly as possible. So called urgent control therapy is considered the second step in management. Preferred medications include fosphenytoin, levetiracetam, valproate, or phenobarbital. Levetiracetam is favored by many because of its minimal side effects, lack of drug interactions, and the fact that it does not require monitoring of therapeutic levels. In addition to documented efficacy for treatment of status epilepticus [23–26], levetiracetam has also been investigated for off-label use in the treatment of bipolar disorder [27]. Escalation of management should be based on the clinical exam and the EEG. If an abortive therapy plus an urgent control therapy fails to control seizures and return the patient to baseline, then escalating bolus doses of the AED should be initiated to optimize serum levels. Addition of a second or third agent should also be considered, as necessary. Additional AEDs that can be used include lacosamide (IV formulation) and topiramate (enteral route).

Patient characteristics should be considered when selecting an initial AED. These include the mechanism of drug metabolism, available routes of administration, and common side effects (Table 23.2). Phenytoin or fosphenytoin may cause hypotension and arrhythmias, including severe bradycardia and cardiac arrest. In a 2017 study, fosphenytoin was significantly correlated with hypotension in SE patients [28]. PR prolongation may occur with lacosamide, and valproate may cause severe hepatotoxicity and thrombocytopenia. Many frequently used anticonvulsants are metabolized through renal and hepatic pathways. Phenytoin, fosphenytoin, phenobarbital, pentobarbital, and valproic acid are all predominantly metabolized by the cytochrome P450 system in the liver and can cause elevation of serum transaminases and interfere with metabolism of many medications [29]. Valproic acid should be used with caution in patients with acute traumatic brain injury and in those with significant intracranial hemorrhage due to potential for antiplatelet effect.

If emergent and urgent treatments fail to control seizures, continuous infusion of an anticonvulsant medication must be initiated. If a continuous infusion is necessary, the patient should be intubated and mechanically ventilated due to expected respiratory depression. Similarly, hemodynamic monitoring should be employed, as most of these agents cause hypotension which can sometimes be severe. Propofol and midazolam are used commonly, while pentobarbital is often reserved for refractory status epilepticus. Propofol is an excellent choice due to its rapid onset and

Table 23.2 Pharmacologic agents for the management of status epilepticus, with available routes and common side effects

Drug	Route	Common Side effects
Benzodiazepines		Respiratory depression
- Lorazepam	IV	
- Diazepam	IV, Rectal	
- Midazolam	IM, Nasal, Oral	
Anticonvulsants		
- Phenytoin	IV	Cardiac arrhythmias: AV block
- Fosphenytoin	IV	Hypotension
- Valproate	IV	Hepatotoxicity, thrombocytopenia
- Lacosamide	IV	Cardiac: PR prolongation
Anesthetics		Respiratory depression
- Propofol	IV	Metabolic; Triglycerides. Infusion Syndrome
- Midazolam	IV	
- Ketamine	IV	

rapid recovery from drug effects. However, caution should be used when administering high doses (>5 mg/kg/h) for prolonged periods of time (>48 h) as patients are at risk for developing propofol infusion syndrome. This dreaded and potentially deadly complication is characterized by metabolic acidosis, rhabdomyolysis, renal failure, and cardiac failure. Of the 1% of patients who develop propofol infusion syndrome, mortality can be as high as 20% [30]. All patients who are treated with prolonged propofol infusions should be monitored for metabolic acidosis and hypertriglyceridemia. If serum bicarbonate is noted to decrease, a lactic acid level and serum creatine phosphokinase (CPK) should be measured.

The use of continuous EEG in comatose patients with acute brain injury and unexplained, persistent altered level of consciousness is necessary to detect electrographic seizures and evaluate the response to therapy. In a group of comatose patients undergoing continuous EEG in the ICU setting, 3–19% had nonconvulsive seizures that would not have been diagnosed if not on continuous EEG [14]. Of these comatose patients, 20% needed longer than 24 h to record their first seizure. Continuous EEG should be initiated as soon as possible and continue for as long as seizures are being treated. If initial EEG recordings are negative and clinical suspicion exists, continuous monitoring should be performed; 80% of seizures are detected within 24 h and 87% can be detected with 48 h of monitoring [31]. Other studies have shown that 93% of seizures are detected during the first 48 h [32].

Typically, anticonvulsant infusions are titrated for seizure control and then maintained at that dose for a period of time. No current data exists to determine the optimal duration of seizure suppression needed to resolve status epilepticus. Many practitioners will ensure control of electrographic seizures for 24–48 h prior to slow de-escalation of treatment. No data exist to guide duration of AED treatment following resolution of SE. Generally, once seizure control has been achieved,

maintenance therapy should be initiated and continued for the immediate future. Most patients who develop post-traumatic epilepsy will need to continue anticonvulsant treatment for years.

23.5 Clinical Pearls

- Nonconvulsive or subclinical seizures should be on the differential for comatose patients, and diagnostic studies including EEG monitoring should be included in the workup.
- Occult seizures may present with unexplained ICP elevation in patients with acute brain injury.
- Subtle exam findings such as nystagmus or an unexplained gaze deviation suggest the presence of subclinical seizures or nonconvulsive status epilepticus.
- Many medications used to treat refractory seizures and status epilepticus can cause hemodynamic instability. Be prepared to manage hypotension with fluids and vasopressors, as necessary.
- When deciding which anticonvulsant medications to use to treat refractory seizures or status epilepticus, look for those that have IV formulations and the fewest drug–drug interactions.
- When deciding which anticonvulsant medications to use in a given patient, consider patient-specific characteristics such the underlying diagnosis, as well as renal and liver function.

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Chapter 24
Encephalopathy and Delirium

Xiaofei Zhou and Alan Hoffer

Clinical Scenario

*A 72-year-old woman with a history of dementia and prior intracerebral hemorrhage presents to the Emergency Department (ED) for evaluation of confusion. Her past medical history is also significant for seizures—for which she is on phenobarbital—and a deep vein thrombosis diagnosed 12 months ago that is being treated with a factor Xa inhibitor. Initially, the patient was slightly confused but close to her reported neurologic baseline—oriented to self and place and following commands on the right but contracted on the left. Computed tomography (CT) of the head reveals an acute right frontal intracerebral hemorrhage (*Fig. 24.1*). After reversal of her anticoagulation, she is admitted to the intensive care unit (ICU). Repeat imaging demonstrates stability of the hemorrhage; however, over the next 2 days, she becomes increasingly more lethargic and confused.*

24.1 History and Physical Exam

Presentation with altered mental status, as in the current scenario, often confounds efforts to obtain information relevant to the patient's current illness and past history and poses challenges to objective neurological exam. As the provider caring for a patient with altered mental status, it is important to understand the definitions of some of the terms used to describe these conditions. It should be noted that historically there have been many definitions for alterations in consciousness. They have been difficult to define because these conditions exist on a spectrum [1].

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_24

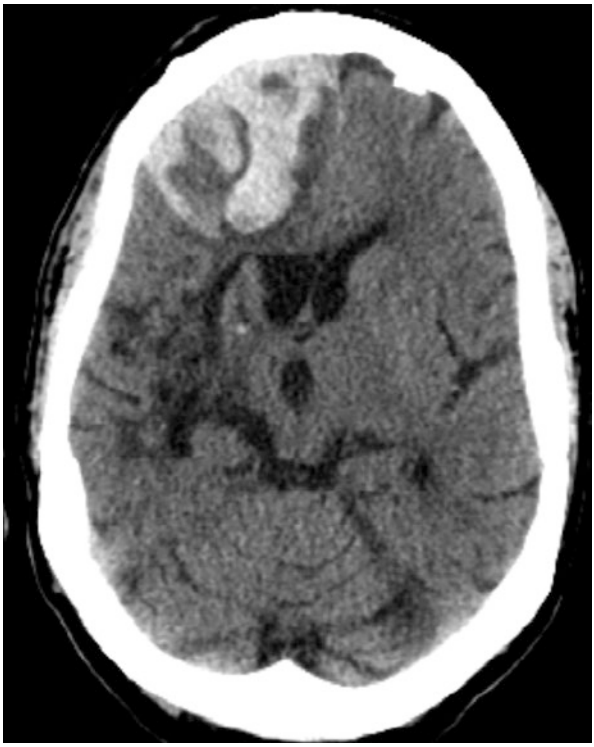

Fig. 24.1 Axial noncontrast CT image demonstrating the patient's right frontal intracerebral hemorrhage

- *Acute encephalopathy*: a rapidly developing (<4 weeks) pathobiological brain process that is expressed as subsyndromal delirium, delirium, or coma.
- *Delirium* (based on criteria from Diagnostic and Statistical Manual of Mental Disorders, 5th edition) [2]:
  - Disturbance in attention that develops over a short period of time (usually hours to days), representing a change from baseline, with fluctuation in severity throughout the day.
  - Disturbance in cognition (e.g., memory, disorientation, language, visuospatial ability, or perception).
  - Disturbance not explained by preexisting neurocognitive disorder and not in the context of a reduced level of arousal (i.e., coma).
  - Evidence that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication/withdrawal, or exposure to a toxin, or secondary to multiple etiologies.
- *Coma*: Coma has had many definitions. Previous ones have included unresponsiveness to external stimuli; however, it is unclear how reflexive movements to noxious stimuli, such as posturing, fit into this definition. Because of these issues, a recent consensus statement could only describe coma as severely depressed responsiveness defined using a Glasgow Coma Scale (GCS) score <8.

There are multiple considerations to take into account when working up a patient with progressive encephalopathy in the ICU. This is particularly true for patients with primary neurologic conditions that predispose them to alterations in mental status. The patient's medical history and physical examination are extremely valuable in identifying factors that may contribute to encephalopathy. The patient's prior medical diagnoses may be exacerbated in a critical care scenario and contribute to neurologic changes. It is important to establish a patient's neurological history and baseline neurologic condition, including a history of dementia or prior neurological injury (e.g., stroke, traumatic brain injury, or seizures), as a new insult may provoke recrudescence of prior neurologic injuries. Lack of compliance with medications such as anti-epileptic or anti-hypertensive drugs should be noted.

The presence of chronic medical conditions plays an important role in the course of encephalopathy in the ICU. In addition, there are several factors that predispose a patient to the development of delirium, including older age, prolonged hospitalization, recent surgery, and medications. Chronic diseases such as obstructive sleep apnea, chronic obstructive pulmonary disease, congestive heart failure, liver disease, and renal insufficiency may contribute to changes in mental status even in the absence of exacerbation.

The prevalence of substance abuse is often under-recognized. Early identification of substance abuse is extremely important as it facilitates the treatment of intoxication and withdrawal. As such, it is necessary to ask about the use of tobacco, alcohol, and other substances, including prescribed medications that may be abused even in patients in whom substance abuse is perceived as unlikely.

Constitutional symptoms such as fever and chills may indicate a developing infection. A small infection, such as a urinary tract infection, can lead to significant changes in cognition. This is particularly true in the elderly, though it should be kept in mind that they may not demonstrate typical constitutional signs and symptoms of infection. Fever can also be a sign of deep vein thrombosis, especially in patients who are immobilized. Only 46% of febrile episodes are associated with an infectious etiology. Central or neurogenic fever is an additional concern specific to patients with neurological insults. However, this is generally a diagnosis of exclusion. Of note, patients whose initial presentation includes fever are more likely to have an active infection. A febrile episode within 72 h of a major surgical procedure more likely represents a postoperative, non-infectious process [3].

The physical exam in the setting of encephalopathy must be comprehensive. Establishing the level of consciousness and orientation is essential. It is important to note the degree of change from baseline in patients with prior neurologic conditions. Similarly, ongoing documentation of the neurological examination must be accurate to ensure that changes can be detected over time. This is particularly important when hand-offs occur between caregivers, as poor communication may result in failure to recognize an important clinical event.

In addition to a neurological exam to look for focal and diffuse neurological dysfunction, other organ systems should be evaluated. Signs of infection, hypoxia, and intravascular depletion may be seen in the patient's vital signs. Direct examination should include evaluation of jugular venous distention and skin turgor to

determine volume status. Lung auscultation and percussion may reveal abnormal airflow, the presence of pulmonary edema, or focal fluid collections. Hepatomegaly may be a sign of liver disease. Substance abuse may result in decreased respiratory rate, bradycardia, and hypotension in some cases. Cutaneous signs of substance abuse, such as needle marks, nicotine stains, or finger clubbing, may be present.

For our patient, her history of dementia, intracerebral hemorrhage, and seizures are important to understanding the findings that are the result of her new hemorrhage. She is noted to be oriented to herself and location and following commands at the time of her presentation to the hospital. This provides some information about the extent of her dementia and baseline function. Because spasticity takes days to weeks to develop, it is a sign of her prior hemorrhagic stroke, not the new one. Further information from her caregivers regarding her baseline physical and cognitive deficits would be helpful to better define her functional status. Another contributing factor to her condition may be the barbiturate she takes for seizure control. A medical comorbidity, such as decrease in hepatic function, could be altering the metabolism of the medication, increasing its circulating levels and contributing to her encephalopathy.

24.2 Differential Diagnosis

Encephalopathy may result from primary neurological states or systemic conditions. It is important to consider both of these possible sources, particularly in critically ill patients with complex medical conditions (Fig. 24.2).

24.2.1 Common Neurological Conditions

Alterations in level of consciousness can be the result of primary or structural neurological injuries. Stroke, hemorrhage, edema, or hydrocephalus can result in decreased arousal and depressed mental status secondary to local injury, brain compression, or intracranial hypertension. Epileptiform activity, including general

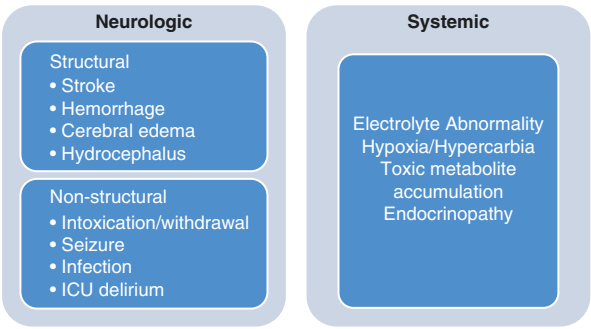

Fig. 24.2 Differential diagnosis of delirium in the ICU

convulsive seizures, focal seizures, subclinical seizures, and other abnormal electrical discharges may result in changes in mental status. Because of the episodic nature of some of these events, a waxing and waning pattern may emerge. Continuous seizure activity, also called status epilepticus, may depress level of consciousness in an ongoing fashion. Encephalopathy may be due to the epileptiform activity itself or a post-ictal state in which normal electrical activity has not yet recovered. In the 24-h period after a generalized seizure, 48% of patients may have non-convulsive seizures or 16% may be in non-convulsive status epilepticus [4]. As such, there should be a low threshold for initiating continuous electroencephalography (EEG) monitoring. The prevalence of seizures that are detected by continuous EEG is significantly higher than with routine EEG. In high-risk populations, such as patients who are admitted for convulsive status (15%), infection of the central nervous system (CNS) (15%), or post-cardiac arrest (18%), it is especially important to have a low threshold for initiating EEG to detect non-convulsive status epilepticus [5, 6]. The recognition and management of seizures are discussed separately in Chap. 23.

Substance abuse and withdrawal are common causes of encephalopathy and delirium. These syndromes may include legal substances, such as alcohol and nicotine, and illegal drugs of abuse. Sixteen to thirty percent of ICU patients are at risk of developing acute alcohol withdrawal. Patients who are suffering from alcohol withdrawal syndrome have a higher mortality, longer length of stay, and higher hospitalization costs compared to other ICU patients [7]. This type of delirium presents with more agitation (i.e., hyperactive) as opposed to the depressed mental status (i.e., hypoactive) seen in other patients. Alcohol abuse may also be associated with vitamin B1 (thiamine) deficiency. This can result in Wernicke's encephalopathy and worsening mental status.

Recently, the phenomenon of ICU delirium has been recognized as an important cause of encephalopathy. A systematic literature review of delirium in ICUs has shown a pooled prevalence of 31%, with the majority of cases (17%) being hypoactive delirium [8]. This is common in critically ill patients with neurological conditions, particularly the elderly. ICU length of stay, altered sleep/wake cycles, sedating medications, and removal from the home environment can all contribute to ICU delirium [9]. Sleep intervention has been studied with some benefit with respect to length of stay and duration of delirium [10], but studies are often limited by confounding factors. The presence of delirium is an independent predictor of ICU and in-hospital mortality [11]. The two most commonly accepted delirium assessment tools are the Intensive Care Delirium Screening Checklist (ICDSC) and ICU-Confusion Assessment Method (ICU-CAM). The CAM-ICU test is more sensitive (80%) and specific (95.9%) than the ICDSC checklist (74% sensitivity and 81.9% specificity) [12].

24.2.2 Systemic Conditions

A range of electrolyte abnormalities can contribute to changes in mental status. Altered sodium homeostasis is particularly common among patients with neurological injury. Hyponatremia can result from either cerebral salt wasting (CSW) or

syndrome of inappropriate antidiuretic hormone secretion (SIADH), both commonly seen after traumatic brain injury, aneurysmal subarachnoid hemorrhage (SAH), and other brain insults. In a study of SAH patients, 59.2% patients had hyponatremia; patients having this electrolyte abnormality had an increased length of stay [13, 14]. It can also be seen with other organ dysfunction such as cirrhosis, congestive heart failure, and nephrotic syndrome, which may cause encephalopathy directly or by lowering the seizure threshold. Pseudohyponatremia may be seen in the setting of hyperglycemia. Injury to the hypothalamic–pituitary axis can cause loss of antidiuretic hormone function, resulting in hypernatremia from diabetes insipidus. Mild hypernatremia itself may be well tolerated; however, it may be associated with hypovolemia, which can be life-threatening [15]. Hypernatremia is an independent predictor of inpatient mortality and poor outcome [16].

Abnormalities in blood glucose are frequently encountered in critically ill patients and may be from chronic disease, acute conditions, or iatrogenic in origin. Diabetes is highly prevalent in the ICU population, with critical illness as a source of exacerbation even in non-diabetic patients. Hyperglycemia and hypoglycemia are both associated with altered mental status. Because of the recognition of the negative effects of hyperglycemia on patient outcomes, iatrogenic hypoglycemia from aggressive insulin therapy for strict blood glucose control is common. The lack of control in either direction is associated with a higher mortality. Tighter control of hyperglycemia episodes has been shown to result in cerebral hypoglycemia, contributing to cerebral energy crisis [17]. This correlates with a worse outcome in some stroke patients [18, 19].

Hypothyroidism is another endocrine abnormality that can cause encephalopathy. Hypothyroidism is a common medical disorder. Failure to recognize it in the patient's history and continue thyroid replacement can lead to low levels of circulating thyroid hormone. Acute illness can alter the production of thyroid stimulating hormone, also resulting in hypothyroidism. If left untreated, progressive encephalopathy and myxedema coma may occur.

An excess of metabolic by-products can be the result of organ malfunction and failure. The accumulation of these molecules can affect brain function. Chronic obstructive pulmonary disease or restrictive lung disease may cause chronic elevations in carbon dioxide. More acute elevations may lead to decreased mental status. Concomitant hypoxia may also contribute. Hyperammonemia can arise secondary to liver disease or as a side effect of medications such as valproic acid, a commonly used anti-seizure medication. Patients with diminished renal function from chronic renal disease or acute kidney injury may have uremia.

Infections, whether systemic or confined to the CNS, can contribute to encephalopathy. The prevalence of any form of infection in ICU patients is as high as 50%, as seen in the EPIC II study with more than 14,000 globally enrolled patients. The majority of infections in the ICU are attributable to a pulmonary source; however, cerebrospinal fluid should be considered as the source of the infection in neurologic patients who have had placement of an external ventricular or lumbar drain [20].

For our patient, there are many possibilities for her worsening encephalopathy. The most concerning cerebral etiologies would include expansion of her

hemorrhage or recurrence of her seizures. From a systemic standpoint, common conditions in the elderly include infection or electrolyte abnormality. Iatrogenic causes, such as analgesia or sedatives, are important to remember. Finally, the combination of her dementia, sleep deprivation from frequent neurological evaluations, and being in an unfamiliar setting could also be contributing to her decline.

24.3 Diagnostic Evaluation

The diagnostic evaluation of encephalopathy and delirium requires a broad approach to address the many possibilities. CT is the mainstay for initial evaluation of structural pathology. While not as sensitive as magnetic resonance imaging (MRI) for some pathologies such as hyper-acute ischemic stroke, CT is useful and effective for many other pathologies and can be rapidly obtained, minimizing the amount of time necessary for the patient to be outside the monitored setting of the ICU.

A thorough laboratory investigation is often required and should include evaluation of serum electrolytes and arterial blood gas levels. Measuring urine osmolyte levels may also be necessary to differentiate some pathophysiologies such as CSW and SIADH. Any patient with signs of infection such as fever, pulmonary infiltrate or consolidation, leukocytosis, or nuchal rigidity, should undergo further workup that might include urinalysis, chest X-ray, and cultures of blood, sputum, and urine. In patients with a history of intradural surgery who show signs of infection, sampling of cerebrospinal fluid should be considered. A low threshold for obtaining serum and urine toxicology screens should be set if there is any question about substance intoxication. At many institutions, these screens are routinely performed on admission.

A thorough encephalopathy evaluation was performed in our patient. This included repeating her CT scan to look for new hemorrhage and obtaining an EEG, a chest X-ray, and urinalysis. Blood tests included a complete metabolic panel, complete blood count, and ammonia level. It was felt that because the patient did not have a history of hypothyroidism, a thyroid stimulating hormone level was not necessary in the initial evaluation but could be considered if no other etiology was identified.

24.4 Clinical Decision-Making

Triage and treatment of encephalopathy begin with the ABCs: airway, breathing, and circulation. While cardiopulmonary dysfunction may diminish mental status, encephalopathy can result in airway compromise and aspiration, which, in turn, can worsen hypoxia and hypotension. To minimize the risk for these complications, a secure airway may be necessary to ensure adequate oxygen delivery and ventilation; most often this is accomplished by endotracheal intubation and mechanical

ventilation. Non-invasive positive pressure ventilation may have the undesired effect of increasing the risk of aspiration in some patients.

Treatment depends largely on identifying the aggravating factors in encephalopathy. It should be kept in mind that changes in mental status are often multifactorial. There may be several contributing conditions that all deserve attention. While many considerations go into elucidating the nature of each patient's encephalopathy, a useful strategy is to rule out the most harmful etiologies first. These include conditions that may be fatal or irreversible such as worsening brain compression, intracranial hypertension, status epilepticus, meningitis, and sepsis. Structural brain conditions and intracranial hypertension may require emergent surgical intervention. Fever or hypothermia with associated hypotension may be indicative of sepsis or septic shock. Because of the high mortality associated with this condition, cultures should be obtained and empiric antibiotics and intravascular volume resuscitation initiated immediately unless a non-infectious etiology is identified [21]. Central fever should be considered a diagnosis of exclusion when no other cause of fever can be found. When available, EEG may be used to diagnose and treat seizures and epileptiform activity. It should be kept in mind that because of the episodic nature of seizures, a brief EEG exam can be insufficient to document epileptiform activity. Patients with a history of epilepsy, reported seizure-like activity, or no other clear cause of encephalopathy may benefit from continuous EEG monitoring. Continuous EEG monitoring is also useful in patients with known seizures to follow the frequency and duration of seizure activity. If EEG is not available, patients should be treated empirically for seizures if there is high clinical suspicion, as in the setting of patients with convulsions or episodic clinical changes.

Further management of encephalopathy should be done in a timely fashion. This includes correction of electrolyte abnormalities, glucose control, and reversal of toxic metabolite accumulation. Therapies may include alterations in ventilator parameters or initiation of hemodialysis. For some forms of substance abuse, such as opioid or benzodiazepine use, a specific antagonist may be administered. However, most treatment for intoxication is supportive. Mild receptor stimulation may be useful in preventing withdrawal syndromes. Examples include nicotine patches for tobacco addiction, benzodiazepines for alcohol abuse, and mild opioid agonists for opioid abuse. Thiamine should be administered empirically in patients with alcohol abuse to minimize the risk of Wernicke's encephalopathy.

In the ICU setting, the need for sedation must be balanced with the function of other organ systems and the clinician's need to obtain an accurate neurological exam. Sedation should be minimized as much possible. If sedation is necessary, short-acting agents are preferred to allow frequent pauses for clinical neurological evaluation. Unless medically indicated, benzodiazepines, in particular, should be avoided as these have been shown to aggravate delirium and have long-term effects on cognition [22]. Agents with a shorter duration of activity, such as dexmedetomidine, propofol, or fentanyl, are often preferred because they allow frequent sedation holidays to obtain an accurate neurological exam and have fewer neurological side effects.

Sleep deprivation is a known cause of acute delirium and contributes to ICU delirium in the hospital setting. To counteract this, patients may benefit from attempts to normalize sleep. Strategies to achieve this may include highlighting the cycles of day and night with lighting and other environmental cues, administrating agents that facilitate sleep cycles such as melatonin, and decreasing sleep disruptions. Unfortunately, the benefits of rest must be balanced with the need for regular neurological evaluation in the ICU. As patients become more stable and close monitoring is less necessary, increasing periods of rest may facilitate recovery from encephalopathy.

After a thorough workup for our patient, it was found that she had received several doses of lorazepam that had been given to her for agitation. Her repeat CT did not show any new hemorrhage, but there was some worsening of the perihematomal edema. There was not significantly worsening brain compression, however. It was felt that the edema, sedatives, and sleep deprivation were all contributing to her encephalopathy. The sedation was held, the frequency of neurological evaluations was decreased, and care was taken to highlight day/night cycle awareness. These measures helped somewhat, but she did not completely return to her baseline. The patient was able to feed herself with some assistance. She was discharged to a skilled nursing facility for further therapy and recovery.

24.5 Clinical Pearls

- Encephalopathy and delirium can result from a variety of causes in the ICU patient. A systematic approach to diagnosis and treatment that accounts for both neurological and systemic conditions should be used. This may include brain imaging, laboratory investigation, and functional studies (such as EEG).
- A basic workup might include brain imaging, serum electrolytes and blood cell counts, and arterial blood gas measurement. Infection (central or systemic) and seizure (including non-convulsive status epilepticus) should always be considered in cases where initial investigation does not reveal a clear cause.
- Preventative measures may be undertaken to reduce ICU delirium, including treatment of withdrawal syndromes, avoidance of sedating medications, and optimizing rest periods.

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Chapter 25
Thrombosis and Coagulopathy

P. B. Raksin

Clinical Scenario

A 66-year-old female presents to the Emergency Department for evaluation of headache. The patient states that her headache began upon waking that day. She denies discrete antecedent trauma. Her presentation is complicated by end-stage renal disease (ESRD) for which she undergoes hemodialysis, as well as by hypertension and atrial fibrillation for which she takes clopidogrel and aspirin. She also reports a history of bilateral, untreated middle cerebral artery aneurysms. She is afebrile. Her blood pressure is recorded as 196/80 at presentation.

On neurologic exam, the patient speaks with her eyes closed. She will briefly open them to command. She states her name but is otherwise uncooperative with assessment of orientation. Pupils are equally round and reactive to light. There is flattening of the left nasolabial fold. There are no cutaneous signs of trauma about the head or face. She is not cooperative with full, objective motor assessment. She seems to be less spontaneous with the right upper and lower extremities. There is a left forearm AV fistula present.

Initial imaging reveals a large, mixed density left extra-axial collection with focally increased thickness over the area of the left Sylvian fissure. After appropriate correction, the patient is taken to the operating room for evacuation of hematoma.

She is transferred, still intubated, to the NICU. She is extubated on postoperative day (POD) # 2. She remains lethargic but arousable. She follows

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P. B. Raksin (ed.), *Acute Care Neurosurgery by Case Management*,
https://doi.org/10.1007/978-3-030-99512-6_25

simple commands. The Nephrology service is consulted and elects to initiate continuous renal replacement therapy (CRRT).

On POD # 7, she is noted to be increasing tachycardic and tachypneic. Her oxygen saturation is marginal (90–92% on room air). Additional diagnostic evaluation is performed.

25.1 History and Neurologic Exam

This patient presents with the nonspecific complaint of headache. While she reports no history of blunt head trauma, multiple comorbid factors make intracranial hemorrhage a primary consideration. The elicited history should unfold across a broad range of possible diagnoses. Is hypertensive crisis the triggering factor or a reaction to the underlying event? Is this a spontaneous hemorrhage? Did she experience aneurysmal rupture? What, if any, role does platelet dysfunction—secondary to ESRD and/or dual antiplatelet therapy—play in her presentation?

Areas to query might include:

- *Constitutional symptoms*. Has the patient experienced recent fever, sweats, chills, or cough? Has the patient experienced generalized lethargy or malaise? Anorexia and/or weight loss?
- *Neurologic symptoms*. The quality, frequency, and duration of the headache should be elicited. Did onset occur suddenly—suggesting an acute bleed—or more gradually, suggesting the possibility of a subacute or chronic hemorrhage. Determine whether there are ameliorating or exacerbating conditions. Is the headache accompanied by other symptoms such as nausea/emesis, dizziness, or vision changes? Are there symptoms that are suggestive of a subarachnoid hemorrhage, such as nuchal rigidity or photophobia. Ask about events suspicious for seizure activity. Inquire about weakness and/or numbness of the extremities.
- *Recent or prior head trauma*. Headache alone is a nonspecific symptom, providing little information to assist anatomic localization. A report of discrete antecedent trauma (and an accounting of the time elapsed since that event) may focus further diagnostic evaluation and provide clues regarding the anticipated age of blood, if present. Determine if the patient has had prior episodes of blunt head trauma and/or prior intracranial bleeding.
- *Recent illnesses or sick contacts*. Establish if the patient has been in her usual state of health. Have there been any recent hospitalizations? Has she been exposed to sick contacts?
- *Use of antiplatelet or anticoagulant agents*. Document current and recent use of antiplatelet or anticoagulant agents. It is important to establish the indications for the use of these agents as withholding them may have systemic implications for the patient. Inquire about the use of herbal supplements that might contain substances with blood-thinning properties. Hemodialysis may suggest platelet dysfunction.

- *Personal history of cancer*. Document any history of a neoplastic process. Cancer may be accompanied by hypercoagulability, predisposing the patient to stroke, deep venous thrombosis (DVT), and/or venous thromboembolic (VTE) events.
- *Personal or family history of thrombophilia or bleeding disorders***.** Has the patient or a family member experienced a DVT or VTE event in the past? If so, what were the clinical circumstances surrounding that event (i.e., provoked or unprovoked)? Does the patient experience bleeding with brushing or flossing the teeth? Does the patient have unexplained ecchymoses? A patient presenting with abnormal clotting or bleeding may harbor an undiagnosed familial disorder.

A targeted neurologic exam may assist in localization of the pathologic process before diagnostic imaging is available. The objective exam should include standard mental status, cranial nerve, motor, sensory, and cerebellar elements. The presence of lateralizing signs should prompt concern for a space-occupying lesion and trigger expeditious imaging. Given the use of antiplatelet therapy, as well as presumed platelet dysfunction, the general systemic evaluation should include assessment for systemic signs of bleeding, including multiple ecchymoses, bleeding from the nares, and bleeding gums. Examination of any peripheral dialysis access site should include inspection (to exclude infection, edema, aneurysm, or pseudoaneurysm), palpation (for pulse and thrill), and auscultation (for bruit) [1].

On neurologic exam, the patient was observed to speak with her eyes closed but would open her eyes briefly to command. She stated her name but was otherwise uncooperative with assessment of orientation. Her pupils were equally round and reactive to light. Horizontal nystagmus was present on bilateral lateral gaze. The left nasolabial fold was flattened. The patient was not fully cooperative with objective motor assessment. Grossly, no pronator drift was present, though the patient could not maintain her upper extremities in a raised position for long. Motor power was at least 4+/5 in the bilateral upper extremities and full in the bilateral lower extremities. There were no cutaneous signs of trauma about the head or neck. No nasal or intraoral bleeding was observed; multiple bruises were present on the extremities. A left forearm AV fistula was present, without signs of infection of malfunction.

25.2 Differential Diagnosis

While hemorrhage is a primary concern in this setting, localizing the compartment of the bleed—particularly in the absence of lateralizing findings—may prove a more challenging exercise. Altered mental status might also reflect electrolyte derangement, uremia, or infection. Given the available data, the differential diagnosis remains broad.

25.2.1 Toxic-Metabolic or Infectious Insult

Alteration in mental status or level of consciousness, without lateralizing findings, may reflect a more global, systemic process. A patient receiving hemodialysis is vulnerable to electrolyte derangement and may become symptomatic from uremia. Impaired clearance of certain medications due to renal failure may result in toxicity, with associated altered mental status. Finally, active infection may present with altered mental status in an elderly, medically frail individual. (It was later revealed, for example, that the patient had been recently admitted to an outside hospital for treatment of pneumonia.)

25.2.2 Subarachnoid Hemorrhage

Review of the electronic medical record revealed that the patient previously underwent vascular imaging revealing small, bilateral middle cerebral artery (MCA) bifurcation aneurysms. These findings were stable across subsequent imaging studies, most recently 3 years prior. The aneurysms were untreated. Given this history and presentation with hypertension, it is plausible that the patient experienced an aneurysmal rupture with bleeding into the left extra-axial space. It was also noted that the blood was focally thicker at the level of the Sylvian fissure. A ruptured MCA aneurysm could certainly present as a subdural hematoma.

25.2.3 Extra-Axial Hemorrhage

Epidural hematoma is unlikely in the absence of a reported history of trauma. However, subdural hematoma—whether acute, chronic, or of mixed chronicity—is a strong possibility in this hypertensive patient with ongoing dual platelet therapy and presumed platelet dysfunction. Patients with non-traumatic subdural hematoma typically present with a more insidious course and with a constellation of complaints ranging from headache alone to confusion, lethargy, and/or hemiparesis.

25.2.4 Intraparenchymal hemorrhage

Hypertension-associated intraparenchymal hemorrhage is a possibility in this patient. A bleed localizing to the left basal ganglia might result in presentation with right hemiparesis, as observed. A brain stem bleed might present with ipsilateral facial and contralateral extremity deficits.

25.2.5 Hemorrhage into an Existing Lesion

In the setting of antiplatelet or anticoagulant therapy, hemorrhage into a previously undiagnosed neoplasm or occult vascular malformation is a possibility.

Of course, in the setting of coagulopathy, any combination of the above findings would be possible.

25.3 Diagnostic Evaluation

25.3.1 Coagulopathy

After attending to the ABCs of resuscitation, CT head without contrast is the next most appropriate step in the evaluation of this patient. CT will provide basic, yet critical information regarding pathology and its impact on normal intracranial structures. Acute blood will appear "bright," or hyperdense, with respect to brain. An evolving ischemic stroke may manifest as subtle fullness of the cortical mantle, with blunting of the sulcal-gyral pattern, or as frank hypodensity within a known vascular territory. This stands in contrast to a mass lesion, where the hypodensity will appear to follow white matter structures rather than a defined vascular territory. Prominence of ventricular spaces—whether generalized or asymmetric—should be noted. The status of cisterns and the shifting of normal anatomic structures will give an indication of the degree of mass effect, if present. The pattern of bleeding may provide clues regarding the likely etiology and will direct further diagnostic evaluation.

In the current clinical scenario, the initial CT head demonstrated a large left mixed density extra-axial collection with focal increased thickness over the area of the left Sylvian fissure, as well as effacement of the local sulcal-gyral pattern. There was midline shift of ~4 mm. No subarachnoid blood was observed (Fig. 25.1a–c). Sudden onset headache upon waking, coupled with the observed bleeding pattern, a known vascular neurologic history, and an absence of defined antecedent trauma, raised concern for middle cerebral artery aneurysmal rupture. Therefore, CT angiography (CTA) brain was requested. This study revealed no significant change from prior studies and no direct communication between the previously observed small left MCA aneurysm and the current hemorrhage.

Coincident with imaging, baseline laboratories—including a complete metabolic panel (CMP), complete blood count (CBC), coagulation parameters (prothrombin—PT/partial thromboplastin—PTT), and a toxicology screen—should be obtained.

While thrombocytopenia is easy to document, it should be recognized that an absolute platelet count within the normal reference range does not exclude impaired

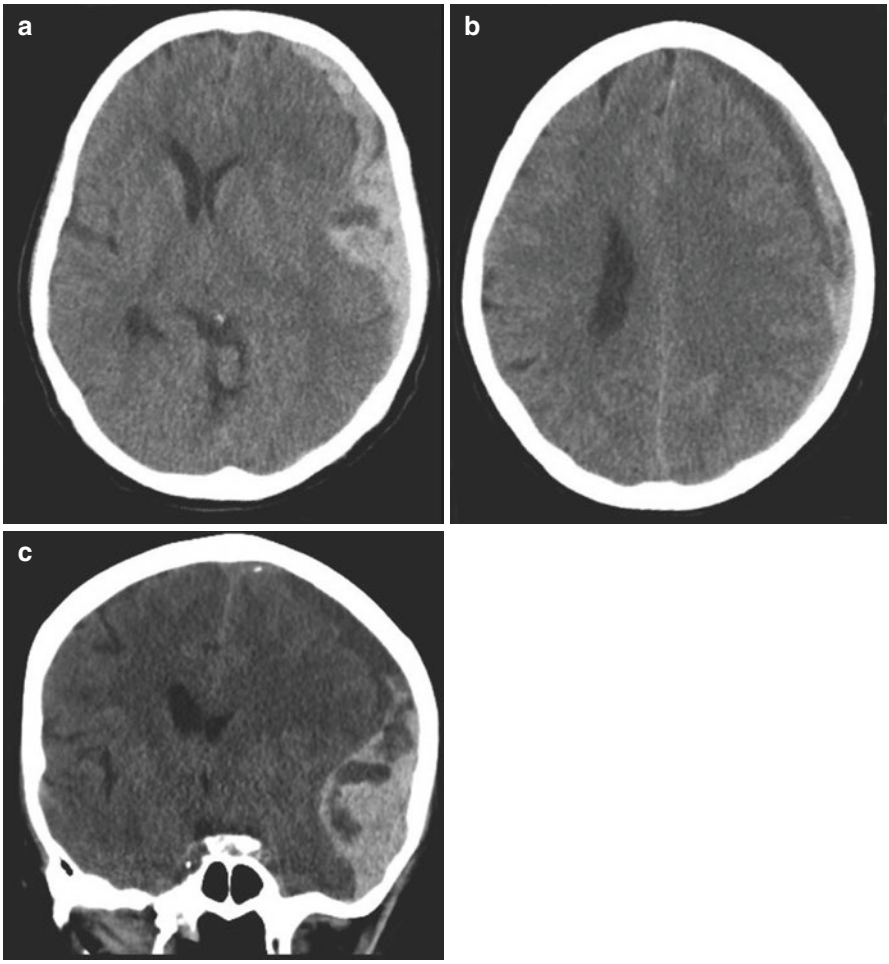

Fig. 25.1 A noncontrast CT head was obtained at presentation. (**a**, **b**) Select axial images demonstrating a large, predominantly hyperdense left extra-axial collection; small areas of hypodensity within this collection may signify a so-called hyperacute hemorrhage. (**c**) Coronal image demonstrating the degree of mass effect, with effacement of the sulcal-gyral pattern, compression of the ipsilateral lateral ventricle, and midline shift

platelet function in the appropriate clinical setting; therefore, reliance on platelet number alone is not sufficient to guide therapy [2]. Platelet function may be impaired secondary to ongoing antithrombotic therapy and/or an underlying disease process (such as ESRD), or as a response to trauma itself [3].

For a patient receiving antithrombotic therapy, the Neurocritical Care Society (NCS) recommends assessment of platelet function, when possible, to inform decision-making about the necessity of platelet transfusion (see Sect. 25.5) [4].

However, this is not always feasible or practical. Light transmission aggregometry is perhaps the most reliable but generally available only in a central laboratory setting. Multiple point-of-care (POC) assays offer a means to survey platelet function [5]. Commercially available POC assays include TEG® Platelet Mapping™ (Haemonetics, Braintree, MA, USA), Platelet Function Analyzer (PFA)-100 (Siemens Diagnostics, Deerfield, IL, USA), VerifyNow (Accumetrics, SanDiego, CA, ISA), and Multiplate® analyzer (Roche Diagnostics, Mannheim, Germany). These assays will detect the impact of aspirin, thienopyridines, and glycoprotein IIb/IIIa antagonist agents on an individualized basis. The latter two POC modalities have been demonstrated to correlate well with light transmission aggregometry results [6, 7].

Similarly, a prolonged PT or PTT may reflect ongoing anticoagulant use or the presence of underlying disease. PT evaluates coagulation factors X, VII, V, II (prothrombin), and I (fibrinogen), while PTT evaluates factors XII, XI, X, IX, VIII, V, II, and I, as well as prekallikrein (PK) and high molecular weight kininogen (HK). A prolonged PT may be observed in the setting of liver disease, vitamin K deficiency, decreased or defective factor VII, chronic disseminated intravascular coagulation (DIC), or warfarin or other vitamin K antagonist therapy. PTT is often normal in these conditions. A normal PT and prolonged PTT, on the other hand, may signify the presence of Hemophilia A or B (decreased or defective factor VIII or IX), factor XI deficiency, severe von Willebrand disease, factor XII deficiency, or a nonspecific inhibitor (such as lupus anticoagulant). Heparin therapy and direct oral anticoagulants (DOACs) can also prolong PTT (though heparin therapy is now monitored with an anti-factor Xa test in some clinical settings). Low molecular weight heparins (and danaparoid) typically will not prolong PTT and, therefore, will only be detected by the anti-factor Xa assay. Prolongation of both PT and PTT may be seen in the setting of decreased or defective factor I, II, V, or X; severe liver disease; and acute DIC.

For a patient receiving DOAC therapy, it may be reasonable to consider laboratory evaluation to determine if there is a "clinically relevant" level of drug present at the time of presentation to medical care. Clinically relevant, in this context, refers to a level that might contribute to bleeding or surgical bleeding risk. The International Society on Thrombosis and Hemostasis (ISTH) recommends reversal for patients requiring an invasive procedure with high bleeding risk and DOAC level $\geq$30 ng/mL or with serious bleeding and a DOAC level >50 ng/mL [8]. When specialized assays are available, a normal result for a dilute thrombin time (TT), an ecarin chromogenic assay (ECA), or an ecarin clotting time (ECT) likely excludes a clinically relevant level in a patient taking dabigatran, while absent chromogenic anti-Xa activity probably excludes clinically relevant levels in a patient receiving a factor Xa inhibitor [9].

Where specialized assays are not available, it is helpful to know that a normal PT or PTT does not exclude a clinically relevant level in a patient receiving a factor Xa inhibitor; for a patient taking dabigatran, a normal thrombin time (TT) *does* exclude

a clinically relevant level, though a prolonged TT will not discriminate between relevant and insignificant levels. In this setting, a normal PTT usually excludes a clinically relevant level.

25.3.2 Thrombosis

When, later in her postoperative clinical course, the patient develops acute onset tachycardia and tachypnea, accompanied by desaturation, concern shifts to diagnostic evaluation for possible thrombotic complications.

D-dimer—one of the final fibrin degradation products involved in the dissolution of clot—may be used to gauge the likelihood that thrombosis is present when the pre-test probability is deemed to be low (≤5%) or intermediate (~20%). In such cases, a negative D-dimer can be helpful to exclude excessive clotting as the underlying cause. However, an elevated value does not mean that thrombus is necessarily present. Rather, it suggests that additional testing (such as CTA or a ventilation-perfusion (VQ) scan) is appropriate. Note that D-dimer has limited utility in the assessment of hospitalized patients and, specifically, in the post-surgical setting, where nonspecific elevation of D-dimer is often observed [10–12].

For a patient with a high pretest probability, it is recommended to start the evaluation with a CTA chest PE protocol if there is clinical suspicion for a venous thromboembolic (VTE) event. If it is not possible to perform a CTA (due to renal failure or dye allergy, etc.), a VQ scan may be substituted. VQ scan and/or ultrasound may also be considered when the initial CTA is nondiagnostic and there remains strong clinical suspicion for a VTE event [13]. A high-probability VQ scan suggests a pulmonary embolism (PE) is present, while a normal VQ scan indicates no clot. A nondiagnostic VQ scan, coupled with a positive D-dimer, may prompt a proximal duplex ultrasound to search for a potential source of clot.

In the current clinical scenario, after ensuring hemodynamic stability as well as providing supplemental oxygen, this post-surgical, sedentary patient with chronic kidney disease would be treated as having high pretest probability. A VQ scan would be the most appropriate choice of diagnostic modality in the setting of renal failure; however, because the patient in question was anuric, CTA of the chest was obtained in coordination with her dialysis. CTA chest PE protocol demonstrated thrombus within the bilateral main pulmonary arteries (Fig. 25.2).

If the patient was not stable to permit transport to the Radiology department, a bedside echocardiogram (ECHO) may provide sufficient data to “rule in” a PE; studies have shown high specificity and low sensitivity for echocardiography employed for this purpose [14]. “Right heart strain” is the most commonly cited finding suggestive of PE. Doppler ultrasound of the lower extremities can be performed at bedside to exclude the presence of lower extremity DVT. Asymmetric upper extremity swelling may provide an indication to obtain an ultrasound of the affected extremity as well.

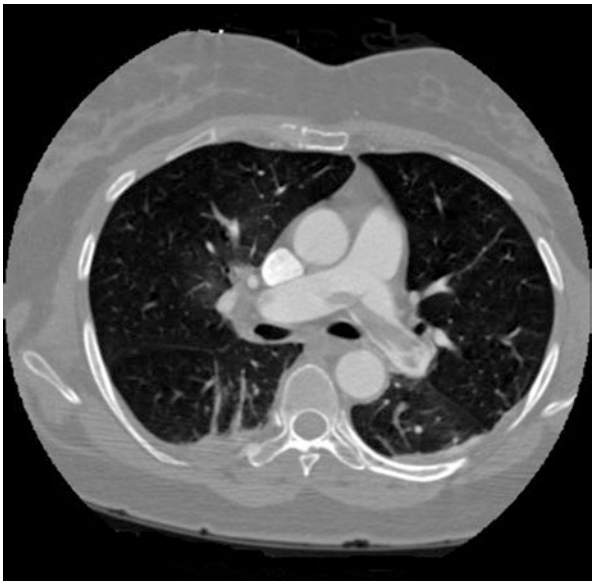

Fig. 25.2 CTA chest PE protocol demonstrating thrombus (hypodensity) within in the main pulmonary arteries bilaterally

25.4 Clinical Decision-Making and Next Steps

25.4.1 Coagulopathy

The patient in the current clinical scenario presents a challenge to neurosurgical care. The combination of dual antiplatelet therapy and presumed impaired platelet function in the setting of ESRD increases the likelihood that a severe headache—independent of defined blunt head trauma—heralds an intracranial bleed. Multiple studies suggest that patients presenting with intracranial hemorrhage in the setting of antithrombotic therapy carry an increased risk for hematoma expansion, with a concomitant increased risk for poor functional outcome or death [15–17]. And, indeed, the initial CT head in this case demonstrated a large, acute subdural hematoma with associated mass effect and midline shift. Uncontrolled hypertension at presentation may encourage progression of any hemorrhage present.

There is little question about the indication for emergent operative intervention in this setting. However, the patient's advanced age and significant medical comorbidities raise at least subjective concern for potential perioperative morbidity or mortality. Though her absolute platelet count is sufficient ($329 \times 10^3/\mu L$), platelet dysfunction is presumed due to the use of antiplatelet therapy and ESRD. While it is intuitive to withhold further antithrombotic therapy, one must also assess the gravity of the bleed, address the systemic consequences of withholding therapy, and develop an action plan to permit expedient, yet reasonably safe invasive intervention.

The 2017 American College of Cardiology (ACC) consensus statement on reversal of anticoagulation provides a useful framework to guide the approach in this setting [9]. The first step is to establish if the bleed in question is "major" or

"non-major." "Major," in this context, denotes hemorrhage at a critical site, accompanied by hemodynamic instability, a hemoglobin drop of at least 2 g and/or a need to transfuse two or more units of packed RBCs. Bleeding at a critical site may compromise function of the organ involved, contribute to severe disability, and require operative intervention to achieve control. Because the intracranial (or any central nervous system) compartment is a critical site, any intracranial hemorrhage is considered "major."

Next, it is imperative to consider the consequence(s) of withholding the antiplatelet or anticoagulant therapy. Table 25.1 provides a listing of commonly used

Table 25.1 Overview of antiplatelet and anticoagulant agents [55]

Agent	Route of administration	Mechanism of action	Recommended time from last dose to elective procedure
Anticoagulant agents			
Warfarin	Oral	Inhibition of vitamin K-dependent factors II, VII, IX, X, and proteins C and S	1–8 days depending on INR and patient factors[a]
Unfractionated heparin	Intravenous or subcutaneous	Antithrombin activation (inhibition of factors IIa, IXa, Xa, XIa, XIIa)	Intravenous, 2–6 h, depending on dose; subcutaneous, 12–24 h, depending on dose
Low molecular weight heparins	Subcutaneous	Antithrombin activation (inhibition of factors Xa, IIa)	24 h
Fondaparinux	Subcutaneous	Antithrombin activation (inhibition of factor Xa)	36–48 h
Dabigatran	Oral	Direct thrombin inhibitor	1–2 days, CrCl ≥50 mL/min 3–5 days, CrCl <50 mL/min
Rivaroxaban	Oral	Direct factor Xa inhibitor	≥1 day with normal renal function; up to 4 days with CrCl 15–29 mL/min
Apixaban	Oral	Direct factor Xa inhibitor	1–2 days with CrCl >60 mL/min; up to 5 days with CrCl <30–49 mL/min
Antiplatelet agents			
Aspirin	Oral	Cyclooxygenase inhibitor (irreversible)	7–10 days
Thienopyridine agents (clopidogrel, ticlopidine, prasugrel, ticagrelor)	Oral	ADP receptor antagonist	5 days (clopidogrel, ticagrelor), 7 days (prasugrel), or 10–14 days (ticlopidine)

[a] INR decreases to ≤1.5 in approximately 93% patients within 5 days [56]

antithrombotic agents, with their route(s) of administration, mechanism of action, and recommended time interval for holding therapy prior to a *non-emergent* procedure. In the current scenario, where the patient is receiving dual antiplatelet therapy for non-valvular atrial fibrillation, the CHA_2DS_2-VASc score can be used to estimate the 1-year risk of a thromboembolic event while withholding therapy [18]. The calculated score may range from 0 to 9, with higher scores signifying increased risk. A patient with a score of 2 or greater is considered "moderate-high" risk and should be considered a candidate for anticoagulation. This patient's score is calculated as 3 (age 65–74, +1; sex female, +1; HTN history, +1), translating into an approximately 4.6% risk of stroke, TIA, or systemic embolism per year [19]. Finally, the risk of perioperative bleeding can be estimated. Intracranial procedures—for which any associated bleeding is considered "major"—are high risk by definition [20].

For a major bleed that is life threatening or at a critical site, ACC guidelines recommend to stop the antithrombotic agent, take appropriate measures to control bleeding, and administer a reversal agent, if available [9]. Antiplatelet therapy can be reversed with desmopressin. If invasive intervention is planned, a single unit of platelets may be given. NCS guidelines recommend platelet function testing in this setting, if available. The NCS, however, cautions against administration of platelets in the absence of planned intervention—regardless of the agent involved, platelet function testing, volume of hemorrhage, or neurologic status. This is a conditional recommendation, based on a low level of evidence [4]. The recommendation stems, in part, from mixed data regarding the impact of platelet transfusion on mortality of patients with intracranial hemorrhage [21]. The author modifies that recommendation to consider platelet transfusion when—in select cases—there is evidence of clinical and/or radiographic progression (that might trigger invasive intervention). The NCS also recommends against platelet transfusion for intracranial hemorrhage in the setting of nonsteroidal anti-inflammatory agent or glycoprotein IIb/IIIa inhibitor use.

In the current clinical scenario, antiplatelet agents were held at presentation. The patient received desmopressin and a single unit of platelets upon entry to the operating room. Figure 25.3a, b demonstrates immediate postoperative CT head findings. Note evacuation of the large left extra-axial hematoma, with improvement of both midline shift and effacement of the sulcal-gyral pattern. There has been interval development of diffuse subarachnoid hemorrhage. A subsequent cerebral angiogram revealed known small, bilateral aneurysms without evidence of recent hemorrhage.

Though not directly relevant to the patient in the current scenario, it is instructive to consider strategies for reversal of anticoagulant agents under the similar clinical circumstance of an intracranial hemorrhage requiring emergent invasive intervention. The first step, of course, would be to discontinue the agent in question. The same principles apply in terms of classifying the severity of the bleeding, considering the systemic implications of discontinuation, and developing a correction plan to allow for safe intervention. Table 25.2 details available strategies for reversal of common antiplatelet and anticoagulant agents.

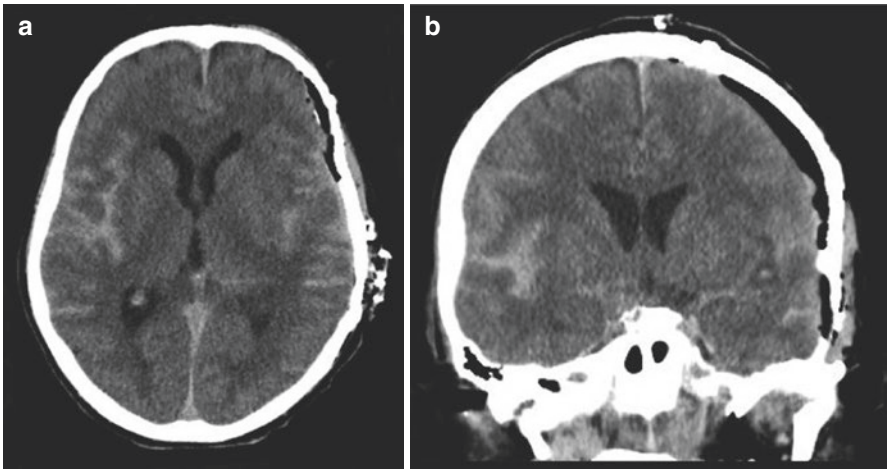

Fig. 25.3 Postoperative CT head. (**a**, **b**) Select axial and coronal images demonstrating evacuation of the previously noted large left extra-axial collection, with improvement of both midline shift and effacement of the sulcal-gyral pattern. Interval development of diffuse subarachnoid hemorrhage. A cerebral angiogram revealed known small, bilateral aneurysms without evidence of recent hemorrhage

NCS guidelines recommend discontinuation and reversal of vitamin K antagonists (VKAs) when intracranial hemorrhage is present [4]. The effect of VKAs can be reversed within 24–48 h with intravenous vitamin K. Obviously, this is not optimal in the emergency setting. Therefore, a combination of vitamin K and fresh frozen plasma (FFP) may bring about reversal within a few hours [22, 23]. However, infusion of FFP may contribute to volume overload—particularly in a patient such as the one in this clinical scenario with underlying renal and/or cardiac disease [24]. For this reason, prothrombin complex concentrates (PCCs) have come into favor [25]. Preferential use of 3- or 4-factor (the former containing factors II, IX, and X in unactivated form and the latter containing factors II, VII, IX, and X, as well as proteins C and S) PCC is recommended, in conjunction with vitamin K. The dosing regimen is based on weight, INR at presentation, and the specific PCC type. If PCC is not available, FFP can be used instead.

If necessary, protamine can be used to reverse the effects of unfractionated heparin (UFH). The reversal of LMWHs, on the other hand, is dependent upon the specific agent and time since most recent administration. Enoxaparin can be reversed with protamine, in a ratio that depends upon the time elapsed since anticoagulant dosing. There is minimal utility to reversal greater than 12 h from administration. For other LMWHs within 3–5 half-lives of dosing, protamine may be given as 1 mg IV per 100 anti-Xa units of LMWH (up to 50 mg in a single dose). Recombinant factor VII (rFVIIa) can be given if protamine is contraindicated. Pentasaccharides (fondaparinux) can be reversed with activated PCC or rFVIIa. Thrombolytic agents can be reversed with cryoprecipitate (10 units IV) or antifibrinolytics (tranexamic

Table 25.2 Options for reversal of antiplatelet and anticoagulant agents [4, 55]

Agent	Laboratory monitoring	Reversal agents	Comments
Anticoagulant agents			
Warfarin	INR	Vitamin K (10 mg IV) plus 4-factor PCC favored over 3-factor [57, 58] (dosing based on weight, INR, PCC type) *OR* FFP (10–15 mL/kg), if PCC not available	Reversal with PCC offers requires less volume than FFP
Unfractionated heparin	PTT	Protamine sulfate (1 mg IV for every 100 units of heparin administered in the previous 2–3 h, up to 50 mg in a single dose)	
Low molecular weight heparins	None, anti-factor Xa antibody levels in select patients	*Enoxaparin*: Within 8 h, protamine 1 mg IV per 1 mg enoxaparin (up to 50 mg); Within 8–12 h, protamine 0.5 mg IV per 1 mg enoxaparin; > 12 h, minimal utility *Dalteparin, nadroparin, tinzaparin*: Within 3–5 half-lives of LMWH, protamine 1 mg IV per 100 anti-Xa units of LMWH (up to 50 mg) *OR* rFVIIa 90 μg/kg IV, if protamine contraindicated	
Fondaparinux	None; may consider fondaparinux-specific anti-Xa assays	Consider rFVIIa 90 μg/kg IV in high-risk patient with major bleeding [59] *OR* 3-factor PCC (20 units/kg IV)	Elimination is impaired in stage IV or V CKD
Dabigatran	PTT or thrombin time may be used to rule out substantial residual effect	*Direct reversal*: idarucizumab (5 g IV, in two 2.5 g/50 mL vials) *AND* consider activated charcoal if within 2–4 h of ingestion *Other direct thrombin inhibitors*: Activated PCC (50 U/kg IV) *OR* 4-factor PCC (50 U/kg IV)	Consider holding for longer period before high-risk bleeding procedures Consider hemodialysis or idarucizumab redosing for refractory bleeding after initial administration

(continued)

Table 25.2 (continued)

Agent	Laboratory monitoring	Reversal agents	Comments
Rivaroxaban	Prothrombin time or anti-factor Xa antibody; if normal, may rule out clinically relevant residual anticoagulant effect	*Direct reversal*: andexanet alfa, regimen based on the timing and dose of last Xa inhibitor given: *Low-dose* (if last dose ≤10 mg AND timing <8 h or unknown; any dose ≥8 h): 400 mg IV bolus at 30 mg/min, followed within 2 min by an IV infusion of 4 mg/min for up to 120 min *High-dose* (if last dose >10 mg or unknown AND timing <8 h or unknown): 800 mg IV bolus at 30 mg/min, followed within 2 min by an IV infusion of 8 mg/min for up to 120 min *When specific antidote not available*: Activated charcoal (50 g) within 2 h of ingestion, *OR* Activated PCC (50 U/kg IV), *OR* 4-factor PCC (50 U/kg IV)	Consider withholding for longer period before high-risk bleeding procedures
Apixaban	Anti-Xa antibody; normal level may rule out clinically relevant residual anticoagulant effect	*Direct reversal*: andexanet alfa, regimen based on the timing and dose of last Xa inhibitor given: *Low-dose*: if last dose ≤5 mg AND timing <8 h or unknown; any dose ≥8 h (see above regimen) *High-dose*: if last dose >5 mg or unknown AND timing <8 h or unknown (see above regimen) *When specific antidote not available*: Activated charcoal (50 g) within 2 h of ingestion, *OR* Activated PCC (50 U/kg IV), *OR* 4-factor PCC (50 U/kg IV)	

Table 25.2 (continued)

Agent	Laboratory monitoring	Reversal agents	Comments
Antiplatelet agents			
Aspirin	None, but consider platelet function testing	Desmopressin 0.4 μg/kg IV × 1 Platelet transfusion × 1 unit	Platelet transfusion for invasive intervention
Thienopyridine agents (clopidogrel, ticlopidine, prasugrel, ticagrelor)	None, but consider platelet function testing	Desmopressin 0.4 μg/kg IV × 1 Platelet transfusion × 1 unit	Indications vary by drug Platelet transfusion for invasive intervention

acid 10–15 mg/kg IV over 20 min or ε-aminocaproic acid 4–5 g IV) if cryoprecipitate is contraindicated.

DOACs deserve special attention, in so far as their increasing popularity—for any number of medical indications—has provided a unique challenge to the management of intracranial hemorrhage. Prescribing providers point to the ease of administration, lack of need to monitor levels or to adjust dosing, fewer dietary restrictions, and lower rates of major bleeding as favorable factors driving practice. For populations with a high risk of bleeding, preferential use of DOACs over VKAs may produce a reduction of 8 fewer bleeding events per 1000 patients [26, 27]. A ~50% reduction in intracerebral hemorrhage and fatal hemorrhage has been described for DOACs as compared with VKAs [28, 29]. However, the development of direct reversal agents initially lagged widespread adoption of these drugs, creating a perilous situation when a patient receiving DOAC therapy required an unplanned, invasive intervention.

Of course, the agent in question should be held at first identification of hemorrhage. Information should be solicited regarding the time interval since the most recent dose was given, as well as possible drug interactions. This will help estimate anticoagulant exposure. The NCS suggests that reversal should be guided by clinical evidence of bleeding (major or intracranial) rather than by laboratory values. In one study, factor Xa (rivaroxaban, apixaban) but not factor IIa (dabigatran) inhibitors were reversed after administration of a 4-factor PCC [30]. Factor Xa inhibitors can be treated with activated charcoal within 2 h of ingestion, activated PCC (containing factors II, IX, X, and activated factor VII), or 4-factor PCC. Factor Xa inhibitors are not dialyzable. Dabigatran—specifically—can be treated with activated charcoal within 2 h of ingestion. Hemodialysis or charcoal hemoperfusion may be considered for patients receiving dabigatran who experience life-threatening bleeding, bearing in mind that placement of a dialysis catheter may not be feasible due to said bleeding and that dialysis may not increase drug elimination in the absence of renal failure [31]. Other factor IIa inhibitors can be treated with activated or 4-factor PCC.

Fortunately, two direct reversal agents for DOACs have recently achieved FDA approval. The RE-VERSE AD study was designed to demonstrate the safety and efficacy of idarucizumab, a monoclonal antibody fragment, to reverse the effects of dabigatran in a prospective trial comparing cohorts requiring reversal for life-threatening bleeding and those requiring reversal for an elective procedure [32]. Idarucizumab was shown to fully reverse the anticoagulant effect of dabigatran at 4 h in 88–98% of patients with prolonged clotting times at baseline. Thrombotic events were observed in 6.3% of patients with life-threatening bleeding and 7.4% of those reversed to permit an invasive intervention. Idarucizumab received full FDA approval in April, 2018 as a reversal agent for dabigatran.

Andexanet alfa was approved by the FDA in May, 2018 for reversal of factor Xa inhibitors. The ANNEXA-4 study reported significant reduction in anti-factor Xa activity, with 82% of patients achieving "excellent" or "good" hemostatic efficacy at 12 h [33]. Thrombotic events were rare among patients for whom parenteral or oral anticoagulant therapy was eventually restarted. For comparison, a prior study reported 72% hemostatic efficacy in a cohort of patients treated with prothrombin complex concentrates for major bleeding related to the use of VKAs [34]. A major limitation in the use of these antidotes relates to cost. The estimated cost (to the hospital) for idarucizumab is $5135 for a single treatment (5 g administered as two consecutive 2.5 g infusions at 2.5 g/50 mL, $51.35 per mL); in one study, 20% of patients required a second dose—doubling that cost [35]. Pricing for andexanet alfa is estimated at $58,000 per high-dose reversal (800 mg bolus + 960 mg infusion at $6600 per 200 mg vial) [36]. For this reason, hospital systems may elect not to stock these agents, necessitating the use of alternative modalities for clotting correction prior to invasive intervention.

25.4.2 Thrombosis

When, early in her postoperative course, the patient develops signs and symptoms concerning for VTE—and bilateral PE is confirmed by CTA—considerations turn toward the advisability and feasibility of anticoagulation. The risk of venous thromboembolic (VTE) events is increased 25–30% in chronic kidney disease (CKD) [37]. Yet, the management of VTE in this population is complex in so far as CKD itself is a risk factor for bleeding [38].

The 2020 American society of Hematology (ASH) guidelines for VTE management recommend the use of DOACs over VKAs—with moderate certainty in evidence of effects and with the caveat that this advice may not apply to the subgroup of patients with renal insufficiency (creatinine clearance (CrCl) <30 mL/min), moderate to severe liver disease, and antiphospholipid syndrome [39, 40]. No preference for one DOAC over another is provided.

Indeed, patients with renal insufficiency or significant liver disease pose a distinct challenge. Renal dose adjustment may be indicated when the CrCl falls below 30 mL/min. Unfractionated heparin, VKAs, and argatroban generally do not require

dose adjustment; however, most DOACs do. Traditionally, warfarin has been used for anticoagulation when necessary in ESRD patients due to its extensive hepatic metabolism into inactive compounds. Rivaroxaban and dabigatran (the latter for which 85% is renally excreted as active metabolites and up to 60% is dialyzable) specifically are not used in ERSRD and dialysis patients. However, apixaban has now been approved for stroke prevention in atrial fibrillation for ESRD patients as well as for treatment of venous thromboembolism.

The pathway for initiation of therapy differs with the choice of agent. If a VKA will be used, overlapping use of UFH or LMWH is necessary for a minimum of 5 days, with transition occurring once a therapeutic INR is achieved for 24 h. If a factor IIa agent is selected, the patient must be pretreated with UFH or LMWH for 5–10 days prior to initiation of the DOAC. Pretreatment is not necessary if a factor Xa agent is used; however, a higher dose of the agent is necessary for the first 3 weeks (rivaroxaban) or the first week (apixaban) of treatment.

Primary treatment for a provoked (by a transient or persistent risk factor) or unprovoked VTE event is recommended for 3–6 months [39, 40]. Once the primary course of treatment is satisfied, the provider must decide if there exists an indication for secondary prevention; an unprovoked VTE or recurrent events provide indications for indefinite therapy. ASH also recommends suspension of chronic antiplatelet therapy (taken for cardiac risk factor modification) for the duration of anticoagulation due to an increased risk of bleeding relative to likely benefit.

The patient in the current clinical scenario presents with two major transient risk factors for provoked VTE—surgery with general anesthesia ≥30 min and bedrest in hospital for ≥3 days [41, 42]. Of course, the use of anticoagulation is complicated in this setting. This patient has multiple major contraindications to thrombolysis—structural intracranial disease, recent brain surgery, recent head trauma with brain injury—and the relative one of female gender [42]. She presents with multiple risk factors for bleeding with anticoagulant therapy, including age greater than 65 [43, 44], renal failure [45–49], recent surgery [48], and frequent falls [50].

The optimal timing for introduction of anticoagulation and safest, most effective regimen is unknown for postoperative neurosurgical patients because they largely have been excluded from randomized trials of anticoagulant therapy. There is a presumption that neurosurgical patients are at significant risk for re-bleeding. The perceived risk of a catastrophic outcome encourages a healthy measure of trepidation among providers and yet, neurosurgical patients often harbor multiple risk factors for VTE events. In one small cohort of neurosurgical patients, there was a statistically significant delay (more than 2 days) in starting therapeutic anticoagulation for patients presenting with VTE within 0–4 days of the invasive intervention [51]. There, likewise, was a statistically significant increased rate of bleeding among patients receiving warfarin as compared with DOACs (13.8% versus 0%). The timing of anticoagulation, however, was not associated with the risk of bleeding. Other studies in neurosurgical patients have demonstrated a statistically significant decrease in VTE events with pharmacologic prophylaxis and a non-significant overall increase in ICH but a statistically significant doubling of “minor” bleeding [52, 53]. Another registry study concluded that neurosurgical patients experiencing a

VTE event were more likely to die from embolism than bleeding in the first week, despite anticoagulation [54].

Other considerations potentially relevant to the neurosurgical population when selecting an anticoagulant agent may include the use of cytochrome P450-inducing or inhibiting agents. For these patients, treatment with LMWH or VKA agent should be considered to avoid drug interaction with DOACs. Patients with antiphospholipid antibody syndrome, conditions that affect medication absorption at the gut, or with extremes of weight may also be suboptimal candidates.

This patient harbors multiple indications for anticoagulation with high thrombotic risk. VTE within 3 months provides the immediate cause, while her history of atrial fibrillation with a CHA_2DS_2-VASc score of 3 provides a longer-term indication. A noncontrast CT head was obtained at the time of PE diagnosis in order to assist clinical decision-making and to provide a baseline point of reference in the event of acute neurologic change after introduction of anticoagulant therapy (Fig. 25.4). Given an identified ongoing indication for anticoagulation, the provider ultimately must weigh the net clinical benefit of anticoagulation in the context of the recent hemorrhage to determine whether the risk of bleeding temporarily or permanently outweighs the benefit of treatment with the anticoagulant agent. Factors to consider include (but are not limited to): the specific indication for treatment; reversible conditions that contributed to the bleed; characteristics of the bleed including location, mechanism, whether it was treated definitively, and whether additional invasive interventions may be necessary; the appropriateness of the drug

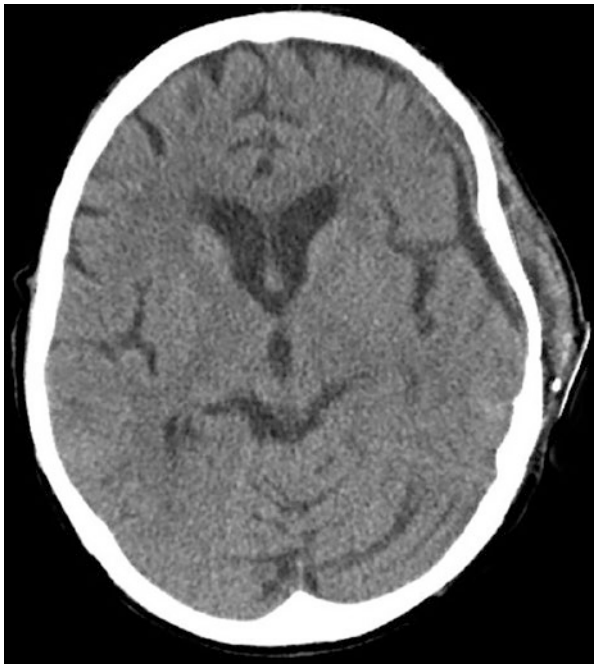

Fig. 25.4 A noncontrast CT head was obtained at the time of PE diagnosis, approximately 7 days postoperatively. Note the overall improvement with respect to mass effect and brain edema, with a small residual hypodense left extra-axial collection

and dosing regimen on the basis of age, weight, and renal function; risk for falls; and whether dual antiplatelet therapy is necessary. Multi-disciplinary input may be necessary to support this decision-making process. The patient should be engaged, where feasible, in discussion of the potential risks and benefits of medical therapy.

25.5 Clinical Pearls

- A focused history in the setting of intracranial hemorrhage should include an accounting of abnormal bleeding and clotting—including personal and family history, medications, use of herbal supplements, and other medical comorbidities that may contribute to risk.
- An absolute platelet count in the normal reference range does not exclude impaired platelet function in the appropriate clinical setting.
- Reversal of antiplatelet therapy is indicated for planned invasive intervention but not simply due to the radiographic presence of intracranial hemorrhage.
- While the rate of bleeding with VKA or UFH use may exceed that associated with DOACs, the neurologic impact of DOAC-associated hemorrhage may be greater, particularly if a direct reversal agent is not accessible.
- The decision to initiate full anticoagulation for an early postoperative neurosurgical patient is individualized, nuanced, and dependent upon an analysis of the potential risks and benefits of the specific clinical scenario.

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