5 Management of Patient with Aneurysmal Subarachnoid Hemorrhage

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Stem Case Terminology

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

5.1 Preoperative

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The commonly used scales are as follows:

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

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

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

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

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

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

Fisher Scale (1980) [5]

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Question 13:
Will you premedicate this patient?

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

5.2 Intraoperative

Question 14:
What are your anesthetic goals?

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

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

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

Question 16:
How does anesthetic technique affect the aneurysm?

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

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

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

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

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

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

Question 18:
How will you manage?

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

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

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

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

Question 20:
How is it performed?

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

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

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

5.3 Postoperative

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

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

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

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

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

Question 23:
How will you diagnose cerebral vasospasm?

Answer:
Various modalities for diagnosis of cerebral vasospasm are:

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

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

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

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

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

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

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

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

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

Question 24:
Discuss the management of DCI.

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

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

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

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

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

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

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

Multiple Choice Questions

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

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