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Session: L040
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Ah! I Can't Bear It! This Is the Worst Headache of My Life!

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Stem Case and Key Questions Content

A 47 year old woman presents to ER with a history of severe headache for the past 24 hours. She is confused and disoriented. Her husband says that she described the headache as "The worst headache of my life."

Past medical history significant for hypertension and migraine. She smoked one pack of cigarettes per day since she was a teenager. She never had any hospitalizations or surgeries. She is allergic to penicillin. Her vital signs: pulse 94/min, blood pressure 186/90(right arm) and 180/92 (left arm), respiratory rate 20/min. oxygen saturation 98% with 2L/min nasal cannula. Her EKG shows sinus rhythm, rate 98/min with T wave inversions in multiple leads and multiple premature ventricular contractions.

1. What is your likely diagnosis? What is the differential diagnosis?
How do you assess the neurological status?
2. CT scan shows subarachnoid hemorrhage (SAH) and cerebral CT angiogram shows right middle cerebral artery aneurysm. How would you grade the severity of SAH? What is the likely reason for the EKG changes? Chest X-ray shows pulmonary edema. What is the reason for this finding? What is the prognostic significance of systemic manifestations?
3. What are the risk factors for intracranial aneurysms? What are the risk factors for rupture of aneurysms?
4. What are the advantages and disadvantages of endovascular coiling over surgical clipping of intracranial aneurysm? Which aneurysms are suitable for coiling? In what clinical situations is coiling preferred over clipping? What is the endovascular flow diversion technique for intracranial aneurysm management? What is the role of flow diversion technique in the management of intracranial aneurysms? What are the potential complications of this technique? What are the pros and cons of early intervention compared to delayed intervention?
5. The patient is scheduled for surgical clipping of the intracranial aneurysm under general anesthesia. The patient's blood pressure is 180/98. How would you address this patient's blood pressure preoperatively?
The patient has a lumbar drain in situ which is clamped. What is the optimal time to unclamp this lumbar drain?
6. What monitors would you like to use? What neuromonitors would you like to use during the

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procedure? What is the role of SSEP (somatosensory evoked potential) monitoring during the surgery? What is the role of EEG monitoring during the surgical clipping?

7. How would you induce and maintain anesthesia? Would you prefer intravenous (IV) anesthetic or inhalational agent based technique? What are the advantages of IV anesthetics over inhalational agents? What are your anesthetic goals in relation to cerebral aneurysm surgery? What are your strategies for neuroprotection? What is the role of hypothermia?

8. Upon opening the cranium, dura is bulging. How do you manage patient's ICP? What is the role of hyperventilation to reduce ICP?

9. Now the surgeon wants to apply a temporary clip. What would you do? What is the purpose of a temporary clip? What is the optimal duration of a temporary clip?
The temporary clip is removed. The surgeon asks you to bring down the mean arterial pressure to 50 mm of Hg. so that a permanent surgical clip can be applied to the base of the aneurysm. What would you do? How would you bring down the blood pressure to facilitate the application of a permanent clip? What is the role of intravenous adenosine?
Aneurysm ruptures. What would you do?
The surgeon is successful in applying the permanent clip. Surgery is completed. Would you extubate this patient?

10. The patient is in neurosurgical ICU. What postoperative problems would you anticipate? A repeat CT shows cerebral ischemia. What is the most likely cause? What are the mechanisms of delayed cerebral ischemia (DCI)? Why is the term DCI preferred over vasospasm? What are the mechanisms and pathophysiology of DCI? How would you manage? What is HHH therapy? What is the role of this therapy to manage DCI? What is the role of nimodipine and how would you administer it? What other therapies are available to manage DCI?

11. What neuroendocrine problems are you likely to encounter in the postoperative period? How do you differentiate between Cerebral Salt Wasting Syndrome (CSWS) and Syndrome of Inappropriate secretion of Anti-diuretic Hormone (SIADH)? What is the prognostic significance of sodium abnormalities in the perioperative period?

Model Discussion Content

Ruptured cerebral aneurysms account for 75-85 % of non-traumatic subarachnoid hemorrhage (SAH).^{1,2} The important risk factors for the development of cerebral aneurysms are hypertension, smoking, chronic alcohol use, family history of intracranial aneurysms in first degree relatives, and female gender.^{2,3} Amongst the hereditary conditions polycystic kidney disease is strongly associated with intracranial aneurysms with a prevalence rate 2-4 times higher than the general population.² Other conditions such as Marfan's syndrome, Ehlers-Danlos syndrome type IV, Neurofibromatosis type 1 and fibromuscular dysplasia are weakly associated with intracranial aneurysms.^{2,3} Most of the aneurysms occur in the anterior circulation of Circle of Willis. Aneurysms of posterior circulation of vertebral and basilar systems account for only 15% of intracranial aneurysms and up to 20% of all aneurysmal SAH have more than one aneurysm.⁴ Saccular berry aneurysms account for 90% of the total aneurysm morphology, their rupture is the most common cause of SAH. Fusiform aneurysms account for the remaining 10%; their most common location is posterior circulation. The risk factors for

rupture of aneurysms are posterior circulation aneurysms, size greater than 1 cm, female gender, Japanese or Finnish descent, hypertension, smoking, older patients, and cocaine abuse.^{2,3,4,5}

Clinical presentation and assessment of severity: Most aneurysms remain undetected during one's lifetime unless they rupture. Sometimes aneurysm may be an incidental finding during investigations for other causes of intracranial pathology. Aneurysms may present with headache, bilateral temporal hemianopsia (anterior communicating artery aneurysm), unilateral third nerve palsy (posterior communicating artery aneurysm), facial and orbital pain, epistaxis, progressive vision loss or ophthalmoplegia (intercavernous internal carotid artery), and symptoms of brain stem dysfunction (posterior circulation aneurysms).⁶ The most common presenting feature of an aneurysm is SAH. SAH most commonly presents as a severe headache, most often described by the patient as "This is the worst headache of my life." As many as 30-40% of the patients may present with a sentinel headache; a warning headache occurring a few weeks prior to the major bleed possibly due to a warning leak.⁶ Depending upon the severity of SAH, the patient may present with drowsiness, confusion, focal neurological deficits, hemiparesis, and even coma. Based on clinical features, SAH has been graded using the Hunt and Hess classification. The severity can also be graded using the World Federation of Neurosurgeons Scale (WFNS) which is based on the Glasgow Coma Scale (GCS) and motor deficits. The prognostic advantage of one scale over the other is uncertain and both scales have limitations due to intra- and inter-observer variability.⁷ The WFNS scale is widely used as it is composed of focal neurological deficits and the GCS. Higher grades on both scales are associated with the worst outcomes.⁷ Mortality is commonly caused by neurological injury resulting from the initial bleeding, rebleeding and from delayed cerebral ischemia (DCI). Mortality is a function of the volume of initial hemorrhage and initial neurological status following SAH. Elderly patients and patients with coexisting medical conditions are at a higher risk of mortality. The clinical goal is to prevent rebleeding and DCI. Noncontrast head computed tomography (CT) is the initial imaging modality of choice. The presence of SAH requires further evaluation with CT angiography (CTA) or cerebral angiography. In the presence of a normal non-contrast CT scan, lumbar puncture remains necessary to avoid potential misdiagnosis.⁸ The Fisher scale is used to classify the appearance of SAH on CT scan. This scale is based on the amount of blood in the subarachnoid space on cranial CT scan and is a predictor of cerebral vasospasm and possibly the overall patient outcome.⁹

Cardiac and neurological manifestations: SAH is a systemic condition associated with systemic inflammatory response syndrome (SIRS). Patients following SAH are likely to show a wide variety of EKG abnormalities including ST and T wave changes suggestive of myocardial ischemia, QT prolongation and U waves. Supraventricular and ventricular arrhythmias may be present as well as elevated troponin levels with myocardial dysfunction without coronary vasospasm. These cardiac changes primarily reflect the severity of neurological injury, but are reversible in the majority of cases and are likely to resolve.¹⁰ Neurogenic pulmonary edema (NPE) is associated reduced global and segmental LV systolic function. NPE reflects the severity of the subarachnoid bleed and is associated with poor outcome.^{11,12} Cardiac manifestations and NPE are possibly due to massive sympathetic discharge following SAH.

Preoperative hypertension: Elevated blood pressure (BP) following SAH is associated with higher mortality. However aggressive management of hypertension following SAH is a matter of concern, given that a higher BP is required to maintain cerebral perfusion pressure(CPP) in the

presence of elevated intracranial pressure (ICP).² Sustained elevation of systolic BP above 160 mm/Hg carries the risk of aneurysmal rupture and rebleeding.^{3,8} Labetolol, esmolol or nicardipine should be used to manage sustained hypertension, but vasodilators such as nitroglycerine or sodium nitroprusside should be avoided, as resulting vasodilatation may increase the cerebral blood flow and likely to worsen ICP.^{3,8}

Perioperative hyperglycemia: Hyperglycemia is common in the perioperative period due to sympathetic overactivity and is associated with adverse neurological outcome.¹³ Hyperglycemia should be treated, but there is not enough evidence to recommend a target blood sugar level.

Early vs. late intervention?: Early therapy with surgical clipping or neuroradiological intervention with endovascular coiling will prevent rebleeding and will enable safe and effective management of vasospasm.¹⁴ On the other hand, early surgery on an edematous brain makes the surgeon's task difficult. In the past, early intervention was advocated for better neurological grades, now surgical intervention is done for higher grades as well. The results of a meta-analysis showed that early intervention on day 0-3 is associated with improved clinical outcome. The outcome is also dependent on the clinical condition on admission.¹⁴ An analysis of data from a Nationwide Inpatient Sample (NIS) from the United States (US) from 2005-2008 comprising 32,048 patients with aneurysmal SAH revealed that patients, who had early treatment within 48 hours of hospital admission with coiling or surgery are more likely to be discharged from the hospital with none to minimal disability.¹⁵

Clip Vs Coil?: The International Subarachnoid Aneurysm Trial (ISAT), a prospective international multicenter randomized controlled trial in 2002 involving 2143 patients, revealed that the primary outcome measure (death or dependency rate) was better with the endovascular coiling group (23.5%) compared to the surgical clipping group (30.9%).¹⁶ However the rate of rebleeding at the end of one year was higher with the coiling group (2.6%) compared to the surgical group (1%). A five year follow up of results from the ISAT trial in 2009 showed a reduced death rate in the coiling group vs. clipping group (11 vs. 14%) and confirmed an increased risk of recurrent bleeding in the coiling group compared to the surgical clipping group.¹⁷ The difference in outcome in the ISAT trial is less for patients younger than 40 years of age; in these patients surgical clipping provides better protection from recurrent SAH. Another recent prospective randomized controlled trial, the Barrow Ruptured Aneurysm Trial (BRAT) involving 471 patients showed improved clinical outcome with endovascular coiling compared to surgical clipping only in posterior circulation aneurysms at the end of a three year follow up.¹⁸ Endovascular technique is increasingly used in the U.S. since the publication of ISA results according to the NIS data base review on cerebral aneurysms.¹⁹ Even though the current data favors endovascular coiling, certain aneurysms are not suitable for endovascular coiling, such as giant aneurysms, wide neck aneurysms (a neck to dome ratio greater than 0.5), fusiform aneurysms and aneurysms at certain anatomical locations; such as arterial bifurcation. On the other hand aneurysms located in vertebrobasilar distribution can be easily accessed by endovascular approach compared to surgical clipping.²⁰ In particular basilar tip aneurysms are not amenable to surgery due to their deep location and difficulty in proximal control. These aneurysms can be safely treated with an endovascular approach, with or without stent use. Cavernous sinus internal carotid artery (ICA) aneurysms are the most difficult aneurysms to treat, due to their close relationship to venous structures, cranial nerves, and the intercavernous ICA.²¹ Surgical access is difficult for aneurysms at this location. Aneurysms located at the intercavernous ICA can be managed with balloon occlusion of the parent vessel and coiling.²¹

On the other hand, middle cerebral artery(MCA) aneurysms are difficult to treat by coil embolization and are better suited for surgical clipping, however recent evidence suggests these aneurysms can be safely treated with coiling embolization.^{8,22} Ruptured aneurysms with mass effect are better suited for surgical therapy as it enables the surgeon to evacuate a hematoma and thereby decreases the incidence of vasospasm.³ In younger patients, surgical clipping is preferred because it provides better protection from future SAH. Coiling is suitable for older patients and patients with comorbid conditions.³

Endovascular flow diversion-a new technique: This is a relatively new endovascular technique whereby an endovascular device with a porous, tubular tight mesh with a high metal ratio is deployed across the neck of the aneurysm which redirects the flow from the aneurysm to the parent vessel. This flow diversion eventually leads to intra-aneurysmal thrombosis and angiographic obliteration of the aneurysm.²³ The larger aneurysms may require a combined technique of flow diversion and coiling. The advantage of this technique is that it does not require coiling and thereby aneurysmal perforation secondary to coiling can be avoided. After the deployment of endovascular flow diverter devices, patients require dual antiplatelet therapy; the duration of such therapy is currently debated. The Pipeline embolization device (PED) and silk flow diverter (SFD) are the two commercially available flow diverting devices worldwide; PED is approved by the US Food and Drug Administration (FDA). The recognized problems with this technique are delayed aneurysm rupture due to inadequate occlusion, ischemic stroke, early and delayed distal intraparenchymal hemorrhages (IPH) and perforator infarction.^{23, 24} A meta-analysis involving 29 studies with 1654 aneurysms treated with flow diverters reported the total occlusion rate as 76%.²⁴ The peri-procedural mortality and morbidity rate was 4% and 5% respectively in this study. The overall incidence of ischemic stroke was 6% and rate of IPH was 3% as per this meta-analysis.²⁴ The perforator infarction is more common in posterior circulation compared to anterior circulation. The ischemic stroke is thought to be due to stent occlusion from thrombus formation and thromboembolism. The exact mechanism of IPH is not known. The proposed mechanisms are hemorrhagic transformation of ischemic stroke, hemodynamic alteration from flow-diverter placement and dual antiplatelet therapy.²⁴ Currently Flow diversion in Intracranial Aneurysm Treatment (FIAT) trial, a large multicenter trial is underway comparing flow diversion technique to conservative treatment, endovascular coiling and surgical clipping.

Anesthetic management of surgical clipping: Depending on severity of SAH, cerebrovascular reactivity and cerebral autoregulation are likely to be impaired in these patients. Patients with impaired cerebral autoregulation are at risk of delayed cerebral infarction following SAH.²⁵ In these patients, cerebral perfusion depends directly on the mean arterial pressure (MAP). The anesthetic goal is to maintain transmural pressure gradient (TMPG) across the wall of the aneurysm and to maintain CPP. A sudden increase in MAP coupled with a sudden decrease ICP can cause sudden changes in TMPG across the wall of the aneurysm increasing the risk of rupture. If the patient has a lumbar drain, the optimal time for release of the drain is after opening the dura which will prevent a sudden drop in ICP, and a sudden change of TMPG across the wall of the aneurysm. Smooth induction and maintenance of anesthesia is desired. Hypotension or hypertension at the time of induction, intubation, surgical pinning, incision, and opening the dura should be avoided. An arterial line should be placed prior to induction for close hemodynamic monitoring during induction and surgical pinning.

Choice of Anesthetic technique: Inhalational versus intravenous anesthesia?: Anesthesia can be maintained with inhalational agents less than or equal to 1 MAC, using narcotics such as

fentanyl, sufentanil or remifentanyl with adequate neuromuscular blockade using nondepolarizing agents. The difference in the cerebral vasodilator effect of modern inhalational agents such as desflurane, isoflurane and sevoflurane is not clinically relevant when used at 1 MAC or lower.^{26,27} A propofol based total intravenous anesthesia (TIVA) technique is likely to reduce the cerebral blood flow and ICP. . However its superiority over inhalational agents in brain relaxation and neurological outcome is not proven, when used at 1 MAC or lower.²⁸ Alternatively, a combination of intravenous and inhalational techniques can be used. Patients with raised ICP, at the upper portion of the intracranial volume-ICP curve are likely to benefit from a TIVA technique. If patients are monitored using evoked potentials, TIVA is preferred, because volatile agents have a significant effect on evoked potentials.

ICP Management: Elevated ICP should be managed along with simple measures such as head end elevation, prevention of jugular venous compression, maintenance of a low normal arterial carbon dioxide (PaCO₂ of 35 mm of Hg.), ensuring adequate anesthetic depth, utilizing intravenous mannitol and CSF drainage. Hyperventilation produces brain relaxation and improves surgical conditions, but results in cerebral vasoconstriction with reduction in cerebral perfusion and cerebral tissue oxygen content. The potential benefits and risks of hyperventilation in terms of patient outcome is not known and should only be used when all other measures have failed to control the ICP and should be terminated when indication for its use ceases. Mannitol is a commonly used agent to reduce the ICP in a dose range of 0.25-1gm/kg body weight, with 0.5 gm/kg being the most common.

Neuroprotection : A large international multicenter study the “Intraoperative Hypothermia for Aneurysm Surgery Trial” (IHAST II) determined that mild induced hypothermia (33⁰ C) is not associated with improved neurological outcome.²⁹ This finding is limited only to patients with good neurological grades. The role of hypothermia has not been studied in patients with poor neurological grades.³⁰ The role of SSEP, BAEP and EEG monitoring in terms of improved neurological outcome is not proven, but may assist in identifying an improperly placed permanent clip. These techniques should be considered when a temporary clip or induced hypotension is planned. SSEP monitoring is useful for aneurysm surgery involving anterior circulation and a combination of SSEP and BAEP monitoring is useful for aneurysms of posterior circulation.³¹ Surgeons may apply a temporary clip to the feeding vessel to produce local induced hypotension in order to reduce the vascularity of the aneurysm. This facilitates dissection around the neck of the aneurysm enabling the surgeon to place a permanent clip in difficult cases. The application of a temporary clip also reduces the incidence of intraoperative aneurysm rupture. After the temporary clip is placed, MAP should be maintained or elevated to improve perfusion through collateral circulation while avoiding hypotensive episodes. The safe duration of temporary clipping is not entirely known.³² However clipping for MCA aneurysm should be limited to less than 10 minutes.³³ Patients with poor neurological grades, elderly patients, delayed surgery 4-10 days after SAH or episodes of multiple clipping are at risk of ischemia and stroke.³⁴ During temporary clipping, burst suppression on EEG using propofol is commonly practiced, though its benefit in terms of clinical outcome is not proven; according to the subset analysis of IHAST II where patients received supplemental drug for neuroprotection when a temporary clip was applied. Intraoperative hypothermia did not affect the outcome in patients who had temporary occlusion.³⁵ A surgeon may request a brief period of induced hypotension to gain surgical access to the base of the aneurysm. A retrospective analysis of data from two centers in the US showed that adenosine can be safely used to produce transient flow arrest.^{36, 37} A mean duration of 45 second circulatory arrest can be achieved with 0.3-0.4

mg/kg of adenosine.

Delayed Cerebral Ischemia (DCI): The term DCI is preferred over vasospasm because cerebral ischemia can occur without angiographically detected vasospasm. The mechanism of DCI is not known and likely to be multifactorial with severity a function of initial hemorrhage. The suggested mechanisms are loss of blood brain integrity, initial cerebral edema, loss of autoregulation, cortical spreading depression and microthrombosis.³⁸ Cortical spreading depression is a slow depolarization wave in the grey matter which suppresses spontaneous and evoked EEG activity. The spreading clusters of such waves results in severe vasoconstriction, impairment of brain ion homeostasis and recurrent tissue ischemia.³⁸ Microthrombosis is a result of activation of coagulation cascade following initial hemorrhage. There are currently no established biomarkers to predict the development of vasospasm or to monitor its progression. At present oral nimodipine has an established role in the management of DCI along with maintenance of euvolemia and induced hypertension. The role of HHH (hypertension, hypervolemia, hemodilution) is not proven in randomized controlled trials. Hypertension is the more important component of HHH therapy and increases cerebral blood flow, brain tissue oxygen levels and reverses neurological symptoms.^{39, 40} There is currently insufficient data to prove usefulness of hypervolemic therapy.⁴⁰ Isovolumic and hypervolemic hemodilution increases global cerebral blood flow, but it is associated with decreased oxygen delivery.⁴⁰ Transluminal ballon angioplasty and intra-arterial vasodilatation therapy with nimodipine and milrinone have shown promising results in some small casestudies and additional large studies are required.⁴¹ The effectiveness of magnesium, simvastatin, clazosentan and tirilazid has not been demonstrated for DCI management. Cerebral angiography is a technique of choice for diagnosing intracranial arterial vasospasm, but is invasive and carries the risk of stroke due to arterial dissection, embolism and rupture. Transcranial Doppler (TCD) has the advantage of being noninvasive and portable, but has a limited role in the diagnosis and monitoring of vasospasm progression and overall neurological outcome.⁴² TCD is more useful for monitoring vasospasm in ICA and MCA distribution than other circulations and detecting proximal than distal vasospasm.

Neuroendocrine abnormalities: Neuroendocrine and sodium abnormalities are common following SAH. Hyponatremia is more frequently seen than hypernatremia. Hyponatremia is due to either **Cerebral Salt Wasting Syndrome (CSWS)** or **Syndrome of Inappropriate Secretion of Anti-Diuretic Hormone (SIADH)**. Both conditions may co-exist. Patients with CSWS typically show a triad of hyponatremia, hypovolemia and high random urinary sodium concentration (>50 mmol/l). Patients with SIADH are likely to show normovolemia or mild hypervolemia. Hypernatremia may also be found in patients with SAH. It is most likely to be iatrogenic secondary to mannitol or hypertonic saline infusion. Rarely hypernatremia is due to Diabetes Insipidus (DI). DI is most likely due to hypothalamic ischemia. Hyponatremia is associated with longer hospital stay, but is not associated with increased mortality. On the other hand hypernatremia after SAH is independently associated with other organ dysfunction with adverse outcome and death.⁴³

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