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Just Another Subarachnoid Hemorrhage? Or Am I Really Up-to-date on What to Do?

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Stem Case and Key Questions Content

Case:

A 26 year-old woman came into the emergency room shortly after complaining of the worst headache of her life. She had been woken from sleep because of the pain. On arrival her vital signs were: BP 174/83, Pulse 57, RR 16, SpO2 99%, Temp 36.7°C Height: 163cm, Weight: 91kg. She was lethargic but followed commands and was alert and oriented to person, place, and time. She had no focal neurologic deficits and had full strength in all extremities. She had no past medical history. She had been smoking since she was 13 years old but denied any alcohol or drug use.

What are the demographic and life style risk factors for intracranial aneurysms and their rupture (aneurysmal SAH)?

In the emergency room a CT scan revealed subarachnoid blood involving the basal cisterns, bilateral Sylvian fissures and the anterior inter-hemispheric fissure. There was mild hydrocephalus. The patient was assessed as Hunt and Hess SAH grade 2. The patient was given 1gm of Fosphenytoin and 1gm of Tranexamic acid and transferred to a specialized hospital with around the clock interventional neuroradiology and vascular neurosurgical services.

What are the clinical severity scales of SAH? What is the prognostic significance of the classification?

What are the treatment guidelines for seizure prophylaxis in patients with SAH?
What is the evidence to support using antifibrinolytics to prevent early rebleeding of SAH?
She was taken to the neuro-interventional suite for emergency cerebral angiography. A radial arterial line was placed under local anesthesia. After rapid sequence induction with Propofol and Rocuronium, the patient's trachea was intubated at the second attempt. The arterial blood pressure rose to 190/100. Esmolol was then given. General anesthesia with muscle relaxation was continued. A 5mm anterior communicating artery aneurysm with a broad base was identified and deemed not amenable to coiling with 3D reconstruction. It was filling from the left anterior cerebral artery.

What are the treatment modalities for ruptured cerebral aneurysms and the treatment timeline? What are the specific anesthetic management goals during intracranial aneurysm interventions? Do they differ for endovascular versus surgical procedures?

The patient was then taken to the OR for left craniotomy and aneurysm clipping. During dissection of the aneurysm, it ruptured. Temporary clips were placed on the anterior cerebral arteries. After 11 minutes the aneurysm clip was applied and the surgeon released the temporary clips. Brisk bleeding from the aneurysm continued. Temporary clips were reapplied and the surgeon requested hypothermia to 35.1°C. After 16 minutes, the clips were again released and the aneurysm was successfully excluded from the circulation. Doppler signals were present in both anterior cerebral arteries.

What is the anesthesiologist's role during aneurysmal rupture? How can we help minimize blood loss and prevent neurological injury from temporary clipping? What is the role of hemodynamic manipulation and "pharmacological brain protection" during temporary clipping?
After the surgery, wake-up from anesthesia was attempted. The patient was moving only her left extremities. A CT scan showed a small left anterior cerebral artery distribution infarct. Several hours later, the patient self-extubated and was noted to have recovered motor function in the right extremities. Her urine output during the surgery was 2 liters. Her sodium level was 127 mEq/L.

What are the common metabolic complications after SAH? How is the diagnosis made? What are the treatments available?

Model Discussion Content
The worldwide incidence of SAH is 2-22.5 cases per 100,000 population per year (1). In the United States there are 14.5 discharges per 100,000 adults annually, but because death from SAH occurs before hospital admission this number may be artificially low. Over the last four decades the incidence has remained stable. The incidence in women is 1.24 times higher than men. Sex-age differences are also seen, with a higher incidence in men aged 25-45, women between 55-85 and men >85 years old. There are race and ethnic differences as well; Blacks and Hispanics have a higher incidence of SAH than Caucasians.

The risk factors are high blood pressure, smoking, alcohol abuse, and sympathomimetic drug use. Other factors that are not adjustable are female sex, having an unruptured aneurysm (especially if symptomatic, large in size, or located on the posterior communicating, vertebral or basilar arteries), a history of previous SAH, having autosomal dominant polycystic kidney disease or Ehlers-Danlos syndrome type IV and having a 1st degree relative with an intracranial aneurysm (2). Aneurysms located in the anterior circulation are more likely to rupture in patients less than 55 years of age. Patients who smoke or have hypertension experience rupture at smaller aneurysm sizes than patients without these risk factors (3). Aneurysms larger than 7mm

are more likely to rupture. There is no increase in rupture risk during pregnancy or post-partum. Inflammation seems to play a role in the pathogenesis and growth of the aneurysms; NF-κB, tumor necrosis factor, macrophages, and reactive oxygen species have been implicated. There are no studies in humans that show targeting these mediators affects aneurysm presentation or outcome.

Modifiable risk factors for aneurysmal SAH are low BMI, smoking, and alcohol abuse. Public health interventions have lowered their prevalence; however, this has not translated into a decrease in the incidence of aSAH. Dietary factors can increase the risk of aSAH (yogurt), lower the risk of stroke and SAH (vegetables), or have no effect (coffee, tea, or magnesium). Certain characteristics of aneurysm shape and overall aneurysm size (>8mm) have been associated with rupture but there is great variability even within individual patients. Screening may be effective in patients with a history of familial aneurysms or patients who have 1st degree relatives with SAH. For patients who have had an incomplete obliteration of a ruptured aneurysm, recurrence of the bleed is most likely 3 days to 1 year after the event (4). With completely obliterated aneurysms there is a low risk of repeat SAH for the first 5 years.
80% of patients who present with SAH have a headache. This headache is typically described as "the worst headache of my life". Patients who experience a sentinel headache have a 10 times greater risk of early re-bleeding. The inciting factor for rupture may be stress or physical exertion but a retrospective review of 513 patients found most SAH ruptures occurred during normal daily activity (5). SAH may be associated with other clinical signs such as nausea, vomiting, stiff neck, photophobia, brief loss of consciousness, or focal neurologic deficits. Although the symptoms of SAH are often classical, there is enough individual variation that an estimated 12% of cases are misdiagnosed. This delay is associated with a 4 fold increase in the rate of neurologic complications or death after 1 year despite good neurologic condition at presentation (6). The most common diagnostic error is a failure to obtain a non-contrast head CT. A small subset of patients will be diagnosed by vascular imaging after a negative head CT and negative cerebral spinal fluid tests.

A minor hemorrhage, called either a sentinel bleed or warning leak, may occur within 2 to 8 weeks before a SAH. It manifests as a memorable headache, but milder than the one due to SAH. The patient may experience periods of nausea and vomiting but meningeal signs are usually absent. Among 1752 patients with an aneurysm rupture, 340 had not had a history of sudden severe headache before the event (7). It is important to recognize the early symptoms because timely diagnosis and intervention can prevent major rupture of the aneurysm. Seizures can occur in up to 20% of patients with subarachnoid hemorrhage; they occur most commonly within the first 24 hours after the bleed (8).

Patients at risk for seizures after SAH have the following risk factors: surgical repair after 65 years of age, thick subarachnoid clot and possibly intraparenchymal hematoma or infarction (9). A study showed prophylactic treatment of patients with anti-seizure medications may worsen

long-term outcomes but most of the patients were taking phenytoin. 527 patients were followed prospectively and their phenytoin burden was calculated as the average serum phenytoin level multiplied by the time in days from the first and last measurement. At 14 days then again at 3 months patients were given a telephone interview to assess neurologic status. Prophylactic use of phenytoin was shown to worsen outcomes in a dose dependent manner. Routine use of phenytoin as anti-seizure medication is not recommended (10). Patients who experience a seizure should be treated with anticonvulsants and if the seizures do not recur the medication should be discontinued within 3-6 months.

One of the major complications after SAH is early rebleeding. This event has been reduced by early aneurysm coiling and clipping, usually within 24 hours of SAH. There is evidence that another phenomenon, ultra-early rebleeding, can occur after a SAH but before any definitive therapy can be achieved. In a prospective randomized trial tranexamic acid (TXA) decreased rebleeding rates in the first 24 hours from 10.8% to 2.4% (27 patients vs. 6). The protocol for this study gave the patients 1gm of TXA upon diagnosis of a SAH and 1gm two hours later, followed by 1gm every 6 hours until the aneurysm was treated. The study did not find an increase in delayed ischemic neurological deficits or vasospasm (11).

The two main treatment options for a ruptured cerebral aneurysm are surgical clipping and endovascular coiling. The landmark trial comparing clipping and endovascular coiling of ruptured aneurysms was the 2005 ISAT (International Subarachnoid Aneurysm Trial) (12). This trial randomized 2143 out of 9559 screened patients across 42 different centers. The patients eligible for the trial had an aneurysm that was suitable for either treatment modality. The primary outcome of this trial was death or dependent living and the secondary outcome included risk of seizures and rate of re-bleeding. At one year, there was a reduction in the primary outcome from 31% in the surgical arm to 24% in the endovascular arm. This represents a relative risk reduction of 24%. The main difference between the two treatment options was the greater incidence of technical complications in the surgical clipping of 19% versus 8% complication rate in the coiling arm. The rate of disability was 16% in the endovascular treatment arm and 22% in patients who had a craniotomy. The risk of epilepsy and significant cognitive decline was also reduced in the endovascular group; however the incidence of re-bleeding was higher: 2.9% versus 0.9%. Also, only 58% of aneurysms that were coiled were completely obliterated versus 81% of aneurysms treated with surgical clipping. The rate of recurrence because of incomplete occlusion depended on the neck diameter and dome size of the aneurysm. Endovascular treatments of very small aneurysms, less than 3 mm, showed no coil deployment in 5% of cases and residual dome filling or a neck remnant in 30%. The small aneurysms also had a higher coiling complication rate than larger aneurysms.

Endovascular treatment of ruptured aneurysms using stents is associated with a higher risk of complications, primarily intracranial bleeding. This is largely due to the dual antiplatelet medications required to prevent stent thrombosis. For this reason, stenting is not a treatment

option in ruptured aneurysms. Biologically active coils, rather than plain platinum coils, constitute another endovascular treatment modality. A few uncontrolled studies show a potential reduction in the rate of aneurysm re-growth and recurrence.

There have been multiple efforts to identify the best treatment modality for different subgroups of patients. There is some evidence that middle cerebral artery aneurysms, located more distally, can be difficult to treat with coils and that surgical treatment yields more favorable results. Older patient are best treated with coiling because of increased perioperative morbidity but there is sparse data on the subject. Patients with large intraparenchymal hemorrhages (greater than 50ml) have worse outcomes overall but evacuation of the hematoma in less than 3.5 hours improves these outcomes. These patients will probably benefit from open surgery. In contrast, patients who have vasospasm may be better treated with endovascular techniques. Poor clinical grade aneurysm patients seem to benefit more from endovascular coiling especially when elderly, but aneurysms in general should only be treated in centers that can perform both interventions.

Posterior circulation aneurysms seem to be best treated with endovascular coils. A meta-analysis has shown that mortality from coiling of basilar bifurcation aneurysms is 0.9% and results in permanent complications in 5.4% of cases. In a 2002 study looking at 112 ruptured aneurysms in the posterior circulation, mortality was 3.7% and morbidity was 9.4% (13). This study comparing clipping and coiling of basilar apex aneurysms found a lower rate of poor neurological outcomes in the endovascular treatment than in the open, microsurgical treatment group (11% versus 30%).

Incomplete occlusion and recurrent aneurysm filling of basilar artery aneurysms was looked at in 2001 (14). 41 posterior circulation aneurysms were followed for 17 months. 85% had complete or near complete occlusion. At the end of the study, 29 patients were followed. Those with complete occlusion had no complications. Of those patients with near complete occlusion 47% had recanalization and 1% had re-hemorrhage of the aneurysm. With this in mind, follow-up digital subtraction angiography is recommended for patients who have posterior circulation aneurysms, especially if they have not been completely occluded. Regardless of the treatment choice, earlier treatment with the goal of complete obliteration of the aneurysm helps lower the rate of re-bleeding.

The main goal during aneurysm treatment is the maintenance of hemodynamic control. A retrospective look at 164 patients who had a decrease in mean arterial pressure found those who had a decrease of greater than 50% had worse outcomes. However, after adjusting for age and World Federation of Neurosurgeons grade of SAH the results were no longer statistically significant (15). If the patient is hypertensive, maintaining the systolic blood pressure <160mmHg is recommended (16). Blood pressure management for delayed cerebral ischemia

(DCI) was initially described as triple-H therapy (hypertension, hemodilution, hypervolemia). Neither hemodilution nor hypervolemia offer any benefit for DCI treatment. Hypervolemia caused an increase in cerebral blood flow but also caused a decrease in arterial oxygen content thus lowering the total delivery of oxygen to the brain (17). Hypertension has been shown to improve neurologic outcomes in patients and thus a trial of hypertension is recommended if DCI is suspected (18).

Hyperglycemia during aneurysm surgery is associated with a decline in long-term cognition and gross neurologic function. A glucose level of 129 mg/dl or greater was shown to increase the risk of alterations of consciousness. A glucose level of 152 mg/dl or greater was shown to increase neurologic deficits (19). A glucose level should be maintained under 200 mg/dl.
Many different agents have been used to promote cerebral protection but none of these agents have shown any efficacy. Only oral nimodipine has been shown to improve neurologic outcome, but it does not affect the rate of symptomatic cerebral vasospasm (delayed cerebral ischemia). Other calcium channel blockers have been tested and the evidence for their use is uncertain (20).

Systemic mild hypothermia was investigated in the IHAST (Intraoperative Hypothermia for Aneurysm Surgery) trial to test its efficacy during aneurysm clipping. Hypothermia has been shown to be protective and preserve function in organ systems such as the heart, but it did not prove to have any protective effect on the brain in the setting of open surgery for ruptured aneurysms. The study concluded that even though mild hypothermia has very little negative effect, mainly an increase in infection rates. At follow-up after 1 year mild hypothermia did not show any benefit (21).

Temporary clipping of an aneurysm during surgery is used to improve surgical conditions and prevent rupture of the aneurysm. A retrospective trial looked at the outcomes after pre-emptive temporary clipping but found no change in clinical outcomes (22). A protective strategy used during temporary clipping is induced hypertension. It is thought to increase collateral perfusion but this has not been well studied. In giant aneurysms, deep hypothermic circulatory arrest has been used in certain patient subtypes (23). It has proven to be a feasible technique but outcome data is lacking. Transient cardiac pause using adenosine has been used to help clip large aneurysms or to control bleeding in ruptured aneurysms but there are no controlled studies to validate this intervention (24). After the IHAST trial the investigators looked at hypothermia and aneurysm clipping with and without supplemental neuroprotective drugs. No benefit was found in any of the arms of this study (25).

Neurophysiologic monitoring can be used intra-operatively to assess the integrity of the motor and sensory pathways that are vulnerable during surgery. Motor evoked potentials and somatosensory evoked potentials have both been shown to be able to predict post-operative

deficits, however, they only changed management in a minority of cases. Their use is center and surgeon specific.

There is very sparse literature comparing anesthetic techniques for endovascular surgery. The anesthetic principles applied to open surgery are also applied to endovascular surgery. It is important to have the patient remain still during the procedure and thus intubation and general anesthesia is usually preferred.

Rupture of the aneurysm during an endovascular procedure is a complication that will usually result in a sudden increase in blood pressure with or without bradycardia due to the increased intracranial pressure. Hyperventilation and osmotic diuretics may be required to control the intracranial hypertension. Over aggressive treatment of the blood pressure can cause brain ischemia, so antihypertensive treatment should be reserved for hypertensive crises.
Another difference between endovascular and open procedures is the use of anti-coagulation with heparin during endovascular interventions, especially for unruptured aneurysms. Protamine should be available to reverse the effects of heparin. There is an increasing use of intracranial stents in elective circumstances and these patients may be on anti-platelet therapy. There are no randomized control trials evaluating the use of platelets to reverse antiplatelet medication in patients who have intracranial bleeding. One retrospective study of patients who had spontaneous intracranial bleeding while on anti-platelet medication found an increased risk of death. Treatment with platelets did not improve outcome or prevent death (26). Another systematic review also found no evidence to recommend the routine use of platelets in adult ED patients with traumatic intracranial bleeding on anti-platelet therapy (27). Nevertheless platelets should still be used to reverse the effects of anti-platelet medications until more information is available.

Hyponatremia is the most common electrolyte disturbance found after SAH, occurring in 14-30% of patients. Two main causes exist that may cause hyponatremia, cerebral salt wasting syndrome (CSW) and syndrome of inappropriate antidiuretic hormone (SIADH). To differentiate between the two syndromes one can assess the patient's fluid status. CSW requires hypovolemia whereas SIADH requires euvolemia or modest hypovolemia (28). Treatment with corticosteroids can limit the hyponatremia and excessive natriuresis when started early. Side effects include hyperglycemia and hypokalemia but these can be treated (29). 3% saline can also be used. A retrospective study evaluated the side effects of treatment but the sample size was small and they could not conclude if the therapy is safe (30).

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