**Pregnancy with Subarachnoid Hemorrhage**

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**CASE:** A 29-year-old, 26-week pregnant female patient was admitted to the emergency room with history of acute onset of severe headache with vomiting. On examination, she appeared a little drowsy, but was neurologically intact. Emergent non-contrast CT scan revealed blood in the anterior inter-hemispheric fissure suggestive of subarachnoid hemorrhage in the anterior circulation. A digital subtraction angiogram was performed which confirmed an anterior communicating artery aneurysm. The patient was diagnosed with an aneurysmal subarachnoid hemorrhage (aSAH), Hunt and Hess Grade 3; WFNS grade 1 and Fisher grade 3

**PMH:** No medical illness

**Medications:** None

**Physical Examination:** BMI-20.5 cm/m², conscious, oriented but drowsy.

**Cardiovascular Examination:** S1, S2 present, no murmurs.

**Respiratory System:** Air entry equal. Clear to auscultation bilaterally

**Central Nervous System:** GCS 15, mild neck rigidity, No focal neurological deficits

**Vital signs:** Pulse: 98/min; Blood Pressure (BP): 170/90mm Hg, Temperature: 36.8° C,

**Respiratory Rate:** 20/min, SpO2 98% on room air

**Airway:** Mallampati-1, adequate mouth opening of > 3 finger breadths, no loose or missing teeth, normal c-spine range of movement

**Laboratory studies:** Hemoglobin: 11 g/dl, Sodium: 139 mmol/L, K: 3.8 mmol/L, Glucose: 140 mg/dl

**Electrocardiogram:** normal sinus rhythm
1. **Explain the choice of endovascular coiling versus open clipping in a pregnant woman with aSAH. How will you decide the time and method of delivery of a viable fetus?**

In patients with aSAH, aneurysms are technically amenable to both endovascular coiling and surgical clipping; endovascular coiling however should be considered. Microsurgical clipping may be preferred in patients having large (>50 mL) intraparenchymal hematomas and MCA aneurysms. Endovascular coiling may be preferred in elderly patients, patients with basilar apex aneurysms, and those presenting with a poor-grade aSAH. There are no separate dedicated guidelines for pregnant patients with aSAH.

The risk of aSAH was previously believed to be increased during pregnancy, potentially caused by pregnancy-induced increased circulating blood volume, cardiac output, and the hormonally-induced changes in the arterial wall. Recent studies however do not find an increased association between pregnancy or delivery and the risk of rupture of cerebral aneurysms (1.4% and 0.05%, respectively, comparable to the rates of aneurysm rupture in the general population). Parity may confer a moderate long-term protective effect on the risk of aSAH. Once ruptured, prompt aneurysmal obliteration (either surgical clipping or endovascular coiling) should be undertaken to decrease the rate of poor outcomes.

If the gestational ages is < 24 weeks, neurosurgical intervention should proceed, and all care should be taken to optimize maternal hemodynamics to preserve fetal well-being. Fetal management following surgery then proceeds as dictated by obstetric indications. At gestational age > 24 weeks, one of the following three decisions should be made:

a. Caesarean delivery followed by neurosurgery as sequential procedures
b. Caesarean section followed by neurosurgical intervention at a later date

c. Neurosurgical intervention followed by continued support of the pregnancy for as long as possible to ensure fetal maturity.

Caesarean section most certainly should be the priority if the gestational age of the fetus is beyond 32 weeks. Regardless of the timing of delivery, the basic fundamentals of avoiding maternal hypoxemia, hypotension, and acid base changes remain the top priority.

2. **Discuss the radiation hazards in the neurointerventional suite and appropriate preventive measures.**

Radiation exposure is an important concern for the pregnant patient, which can occur during CT scan, digital subtraction angiography (DSA) or during aneurysm coiling in the neurointerventional suite. The radiation risk of a CT scan is quite low and is outweighed by its benefit. The risk of radiation exposure depends on the time of gestation and the amount of absorbed radiation dose. The most sensitive period is the prenatal period and time of fetal organogenesis [6-10 weeks of gestation]. The risks of radiation to the fetus include prenatal death, growth retardation, impaired mental ability, low intelligence quotient and childhood cancer. Various precautions should be employed, including keeping the radiation dose as low as reasonably achievable (ALARA) levels, minimizing the total time of procedure, using decreased magnification and lead shielding of abdomen.

3. **Describe the anesthetic considerations in a pregnant patient undergoing aneurysm coiling.**
GOALS

1. To maintain uteroplacental perfusion and fetal oxygenation by avoiding hypoxia, hypotension, hypocapnia, acidosis, and hypothermia.
2. To prevent a rise in intracranial pressure or the development of brain edema.
3. To maintain cerebral homeostasis with adequate cerebral perfusion pressure.
4. To maintain hemodynamic stability, particularly at the induction and maintenance phases until the aneurysm is secured.

General anesthesia may be preferred for aneurysm coiling, and the basic principles of management remain the same as that for craniotomy. Invasive blood pressure monitoring is indicated for the control of arterial pressure, because of the risk of poor uteroplacental perfusion with hypotension, as well as the risks imposed by hypertension on the integrity of the aneurysm.\(^8\) Fetal hear rate (FHR) monitoring may be useful in the endovascular suite to guide the range of blood pressure to be maintained for an adequate uterine perfusion and oxygen delivery. If fetal distress is detected, heparin should be immediately reversed and the procedure aborted to allow emergent caesarean delivery.\(^9\)

Radiation exposure

As evaluated by the International Commission on Radiation Protection (ICRP), as well as the report by Kuon et al., with optimized lead shielding the coiling-related fetal radiation is negligible\(^10\).\(^11\) According to the recommendation of the ICRP on the Radiological Protection, the radiation threshold above which abortion should be considered is 100 mGy.\(^12\) As per an experiment by Marshman et al. that utilized a standard body phantom conducted in a DSA suite,
in a general endovascular procedure the absorbed fetal dose was measured to be 2.8 mGy (which is magnitude below the risk threshold as mentioned above). Therefore the radiation risk associated with endovascular procedure is minimal. This might be reassuring to the pregnant patient, especially because abdominal shielding is also employed.

*Contrast Agent–Related Hazards*

For endovascular coiling, the most commonly used contrast agent is iohexolomnipaque. The contrast is injected through a proximally-placed catheter, which creates a map of the vascular anatomy. This image is superimposed on a live fluoroscopy image to obtain a “roadmap” that allows visualization of the microcatheter tip the vascular tree. This allows for the placement of the microcatheter in the distal circulation. Reproduction studies have been performed in animals with up to 100 times the recommended human dose. No evidence of impaired fertility or harm to the fetus has been demonstrated due to iohexolomnipaque. For ethical reasons, there are no similar human studies that have been conducted. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the expected benefits outweigh the theoretical risk.

*Anticoagulants*

Heparin, the anticoagulant of choice during pregnancy, does not cross placenta because its polysaccharide structure is highly ionized. Warfarin, on the other hand, is contraindicated in pregnancy, as it readily crosses the placental membrane and has potential teratogenicity in the fetus. If fetal distress is detected by FHR monitoring, the heparin should be immediately reversed and the procedure aborted.
4. Does anesthetic selection impact fetal outcome?

A normal uteroplacental circulation is critical for the development and maintenance of a healthy fetus, the integrity of which depends on an adequate uterine blood flow and a normal placental function. Placental transfer of drugs occurs by simple diffusion, the rate of which primarily depends on the physicochemical characteristics of the drug, such as molecular size, lipid solubility, and degree of ionization. Inhalational agents cross the placenta freely owing to their low molecular weight and high lipid solubility and may cause fetal depression if administered for a long duration.

- Induction agents, thiopental sodium, propofol, etomidate, and ketamine, readily cross placenta (highly lipophilic and low degree of ionization), but their effect on fetus is limited, owing to rapid drug distribution and metabolism.

- Muscle relaxants, both depolarizing and nondepolarizing, are less lipophilic and predominantly ionized at physiologic pH, and their rate of transfer is therefore limited. The reversal agents, neostigmine and edrophonium, exhibit similar characteristics. Regarding Sugammadex, no safety studies had been conducted in humans, and therefore, unless it is a case of vital necessity, it is discouraged to use because of potential harm (for the patient and particularly for the fetus).¹⁴

- Local anesthetics and opioids are weak bases, with a relatively low degree of ionization and considerable lipid solubility. They cross the placenta readily, and because pH is lower in the fetus, will be subject to ion trapping.
• Atropine (tertiary amine), but not glycopyrrolate (quaternary ammonium), crosses the placenta.

• All β-blockers freely cross placenta. Labetalol is the drug of choice for treating maternal hypertension, as it is considered safe for the developing fetus. Esmolol infusions have been implicated as a cause of persistent fetal bradycardia and should be cautioned.15

CASE CONTINUED: The surgeon, who does both interventional endovascular coiling and open clipping, determines that the anatomy of the aneurysm is more amenable to clipping.

5. What anesthetic agents will you use for maintenance of anesthesia?

As in any non-pregnant patient, anesthesia can be maintained with a propofol and remifentanil infusion and a 1:1 O2–air mixture. The MAC of most volatile anesthetics is reduced by approximately 25% during pregnancy, and initial end-tidal isoflurane or sevoflurane concentrations of 1.0% and 1.5%, respectively, are therefore appropriate.16 These maintain a suitable depth of anesthesia and a degree of uterine relaxation because of their tocolytic effect and preservation of cerebral autoregulation.

6. What monitors would you use in the intraoperative period?

Apart from standard ASA monitors like electrocardiography (ECG), pulse oximeter [SpO2], non-invasive blood pressure (NIBP), end tidal carbon dioxide concentration (ETCO2), temperature and urine output, invasive blood pressure should be used in the intraoperative setting. A central venous catheter should be considered if intravenous access is poor or 3%
hypertonic saline is administered. Combined electrophysiological monitoring like electroencephalography (EEG) along with somatosensory evoked potentials (SSEP) reduce complications due to excessive retraction of cerebral tissue, which facilitates the safety of temporary clipping and improves the results of middle cerebral artery aneurysm surgery. The SSEP and motor evoked potentials (MEP) have also found utility during the surgery of intracranial aneurysms, where outcomes have correlated with monitoring changes.

7. **We know that hyperventilation reduces intracranial pressure. What would your target PaCO₂ be?**

Hyperventilation to maintain maternal PaCO₂ between 28 and 30 mmHg should be employed in the intraoperative period to decrease ICP. The compensated maternal respiratory alkalosis that preexists in pregnant women should be taken into consideration, and a pre-induction baseline arterial blood gas analysis might be helpful in guiding an appropriate target PaCO₂. The leftward shift of the autoregulatory curve provides little scope for further reduction in cerebral blood flow by institution of hypocapnia. A PaCO₂ < 28-30 mmHg provide little additional benefit and might be associated with cerebral ischemia and impaired oxygen dissociation from hemoglobin, along with uterine artery vasoconstriction leading to fetal distress. Therefore, once ICP is reduced, normocapnia should be maintained in pregnant patients (e.g. ~32 mmHg).

8. **What would be your hemodynamic goals in this patient?**

Maintenance of a normal blood pressure close to baseline values is mandatory during the operative course, for the maintenance of cerebral perfusion pressure in the mother on one hand,
and avoidance of intrauterine fetal asphyxia on the other. Invasive blood pressure monitoring is therefore recommended prior to induction to rapidly recognize and treat excessive swings in blood pressure. Large-bore intravenous access should be taken for appropriate administration of intravenous fluids. Central venous access should be considered for the administration of concentrated vasoactive drugs, central venous pressure monitoring, or aspiration of air emboli (in the context of craniotomy in the sitting position). Effective maternal positioning also aids in preventing hypotension.

9. The surgeon finds the brain is edematous and requests brain relaxation. How would you achieve that?

Optimal brain relaxation helps the surgeon achieve a good surgical exposure and facilitate clipping of the aneurysm. Maneuvers and pharmacological agents used in combination to achieve brain relaxation are following:

- Positioning: 15-30° head-up position is the optimal position to decrease ICP. Excessive neck flexion or rotation should be avoided. The endotracheal tube should be taped instead of tying it around the neck.

- Hyperventilation: Regulating CO₂ levels can be used therapeutically to lower ICP. However, excessive hyperventilation carries the risk of inducing ischemia, especially in poor-grade patients. Thus, the use of hyperventilation should be individualized according to the operating conditions. A reasonable approach is to institute mild hypocapnia (30-35 mm Hg) before the dura is open, moderate
hypocapnia (25-30 mm Hg) after the dura is open, and relative normocapnia during induced hypotension and after the aneurysm is clipped.\textsuperscript{20}

- **Mannitol**: Mannitol is usually the drug of choice to decrease the brain water content. A 20\% mannitol infusion at 0.5-2 g/kg is typically administered over 30 minutes.

- **Frusemide**: Frusemide reduces CSF formation and water and ion movement across the blood–brain barrier. The prolonged diuresis after the administration of frusemide can potentiate the effect of mannitol. It is typically administered at a dose of 0.25-1 g/kg.

- **Hypertonic saline**: Hypertonic saline (3\%) is an equally effective to 20\% mannitol in the extent of brain relaxation.\textsuperscript{21} However, mannitol remains the agent of choice for intraoperative brain relaxation.

- **CSF drainage**: Decreasing the volume of CSF using a lumbar subarachnoid or ventriculostomy catheter is an effective means of reducing brain bulk and may become necessary to achieve satisfactory brain relaxation. Extreme caution should however be exercised during insertion of the drain to minimize CSF loss and a sudden decrease in ICP, as to avoid an abrupt increase in transmural pressure and a re-bleed of the aneurysm. Theoretically, free drainage should be allowed only after the dura is open to minimize the risk of re-bleeding; in practice; however, 20-30 ml of CSF is usually drained just before dural opening to facilitate dural incision. The drain is usually left open during the procedure, until the aneurysm is
clipped or until the beginning of dural closure.

10. **After exposure of the aneurysm, the surgeons decide to do temporary clipping and requests burst suppression. How would you achieve this?**

    Metabolic suppression can be achieved using propofol at bolus dose of 1 mg/kg followed by infusion until burst suppression is achieved. The theoretical basis for its use is that cerebral metabolic suppression reduces the energy consumed by the brain cells, thus ischemia is better tolerated. Ideally, EEG should be employed while achieving burst suppression using these agents.

11. **What will be your concerns during emergence? How will you blunt the hemodynamic response during tracheal extubation?**

    The pregnant patient is at a high risk of aspiration following extubation and therefore should be extubated only after the patient is fully awake and the airway reflexes are intact. Airway stimulation and bucking on the endotracheal tube can be prevented by administering lidocaine, fentanyl, or sedative doses of propofol. Early extubation is favored to facilitate early neurological evaluation. However, the patient may be ventilated postoperatively if the preoperative neurologic status was poor, or the intraoperative course has been significant in terms of bleeding, cerebral edema, or ischemia.
CASE CONTINUED: After a successful surgery, the patient has been transferred to the ICU.

12. What postoperative concerns do you have for this patient?

Pain

As with most neurosurgical procedures, the neurological status of pregnant patients undergoing neurosurgery should be monitored closely in the intensive care unit in the immediate postoperative period. Adequate postoperative analgesia should be provided for maternal comfort and mobility, and to reduce undesirable hemodynamic disturbances. Multimodal analgesia using local infiltration of the incision site/scalp blocks, intravenous paracetamol or acetaminophen, and opioids such as fentanyl and morphine in controlled doses should be administered. Tramadol is discouraged in neurosurgical patients because it lowers the seizure threshold. The nonsteroidal anti-inflammatory drugs should also be avoided because of their antiplatelet effect and the potential to cause bleeding after intracranial surgery, and because of their potential fetal complications (renal failure, necrotizing enterocolitis, and persistent fetal circulation after birth) when used in the last trimester. 23

Deep Vein Thrombosis Prophylaxis

Pregnant women have a 4- to 5-fold increased risk of thromboembolism compared to the non-pregnant population, which is due to a hypercoagulable state. Intermittent pneumatic leg compression devices or elastic stockings should be used in the perioperative period in all patients. Initiating pharmacological prophylaxis with heparin as early as feasible in the postoperative period should be discussed with the neurosurgeon.
Cerebral Vasospasm

Animal studies have demonstrated that nimodipine might increase the risk of intrauterine growth retardation and congenital abnormalities; however in a given situation risk and benefit should be weighed against the overall maternal and fetal outcome. The usual practice is still to administer nimodipine in all cases having aSAH.

13. What is the cause of vasospasm following aSAH and its treatment in this case?

Although parturients are somewhat protected from cerebral artery vasospasm in their relatively hemodiluted and hypervolemic state, in our case the patient had a Fischer grade 3, which is associated with a higher incidence of vasospasm compared to grade 4. Magnesium sulfate, the drug of choice for preventing and treating eclampsia, has been shown to reduce the severity of vasospasm after aSAH. However, according to the recent Magnesium for aSAH (MASH-2): a randomised placebo-controlled trial, magnesium is not superior to placebo for the reduction of poor outcomes after aSAH. The evidence for the use of nimodipine in pregnancy is limited. Animal studies have demonstrated that nimodipine might increase the risk of intrauterine growth retardation and congenital abnormalities, but no comparative studies in humans are available. However, the known benefits of nimodipine in preventing spasm likely outweigh any potential risk to the fetus, and should be administered as clinically indicated.
References:


