Emergency Cesarean Section in a Quadriplegic Patient
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Stem Case and Key Questions Content
Your patient is a 23-year-old, gravida 5 para 1 female, at 38 weeks gestation with delivery planned via elective cesarean section. She has a complex medical history, including quadriplegia due to cervical (C6–7) spinal cord injury (resulting from a motor-vehicle accident 7 years ago), and past deep venous thrombosis/ pulmonary embolism and pyelonephritis.

The patient woke up 2 hours ago with a severe headache described as throbbing. She has had similar episodes of headache triggered by urinary retention that were treated at home with urinary catheterization. This time, however, catheterization did not provide any relief so her husband took her immediately to the emergency room. On arrival, she had a gush of clear fluid and was transferred to the Labor and Delivery Unit. While in the Unit, the patient reemphasized her severe headache was occurring with each contraction, as well as flushing and shaking.

Q1: What is the differential diagnosis for severe headache in pregnancy?
Your patient has not experienced any recent vision changes, upper abdominal pain, nausea/ vomiting, or shortness of breath. However, she claims that she has never felt any fetal movements. She has been noncompliant with her medication, and took her last dose of Lovenox 10 days ago.

Q2: Why was the patient prescribed Lovenox and are there any alternatives?
Additional complications of your patient’s pregnancy include: Gestational diabetes, neurogenic bladder, a previous elective cesarean section, and congenital anomalies with the last pregnancy. A neurological exam is consistent with quadriplegia secondary to a C6-C7 spinal cord partial transection, with lack of sensation below C5 and strength 2/5 in both upper extremities with distal contractures. Patient has not shown any signs of respiratory distress and never required ventilator support.

In triage, the patient’s initial blood pressure was 180s/110s and her obstetrician raised concerns about
acutely dropping her blood pressure given a baseline in the 90s/60s. A repeat check was undertaken a short time later and blood pressure improved to 130s/105s, so no medication was given. The obstetric resident then prescribed 10 mg Hydralazine I.V. PRN for blood pressure above 180/110.

**Q3:** What is the optimal systolic blood pressure associated with adequate placental blood flow?

**Q4:** What anti-hypertensive medications are safely used in pregnancy? At what point in the pregnancy should medication be started?

While waiting for laboratory results to rule out pre-eclampsia, the obstetrician was called to your patient’s bedside as she was seizing. A further blood pressure check revealed a blood pressure of 180/110 mmHg. Since the patient’s airway was maintained, she was administered 5 mg IV hydralazine and an IV loading dose of 6 g magnesium. Following administration, your patient became responsive and the seizures resolved. Fetal heart monitoring showed a reactive tracing with fetal heart rate of 140 bpm and no decelerations.

A diagnosis of eclampsia was ruled out by routine laboratory studies. The working diagnosis of acute onset autonomic hyperreflexia was established and a decision was made to proceed with labor analgesia.

**Q5:** What are the clinical manifestations of autonomic hyperreflexia?

On further consultation, the obstetrician raised concerns about hemodynamic instability and associated morbidity risks to the mother and fetus, so a decision was made to undertake an emergent repeat cesarean section. Your patient last ate approximately 4 hours previously.

**Q6:** What are the anesthetic options? Is regional analgesia safer than general anesthesia in this patient population?

**Q7:** What are the implications of Lovenox administration in this patient?

In the operating room, after placement of routine monitors, direct arterial blood pressure monitoring was instituted by the means of the right radial artery placed under local anesthetic. An additional 16G peripheral IV was placed. Your patient’s initial arterial blood pressure is 160/93, heart rate 76 beats a minute, and respiratory rate 16 per minute. The patient has been using Lovenox for prophylaxis of deep venous thrombosis and a history of pulmonary embolism. However, the last dose of Lovenox was taken over one week ago. A routine blood test showed a clotting profile within normal limits, so you decide to proceed with epidural anesthesia. Patient was placed in a left lateral decubitus and an epidural catheter inserted at the L2-L3 vertebral interspace using a sterile technique. No procedural
difficulties were encountered. Aspiration from the epidural catheter was negative for both blood and CSF. After the first epidural dose of 5 ml, consisting of lidocaine 2% with epi 1:200,000 and 8.4% sodium bicarbonate, the patient’s blood pressure dropped acutely to 70/50 mmHg. Her sensory block level was difficult to assess because of the quadriplegia. The level of the block was demonstrated by absent patellar reflexes and loss of muscle tone in the legs.

Q8: Why did the patient’s blood pressure drop acutely?

To increase blood pressure, a few IV boluses of 100 mcg phenylephrine were given and your patient’s blood pressure increased to 75s/60s mmHg. Additional IV boluses of 5 mg ephedrine were given, and her blood pressure further improved to 110s/60s mmHg.

Q9: What are the effects of phenylephrine and ephedrine on placental and uterine blood flow? What other vasopressors can be used given this patient’s comorbidities?

A healthy 2,100 gm male with Apgar scores of 8 and 9 (after 1 and 5 minutes respectively), was delivered by cesarean delivery. A large broad ligament hematoma 8 cm x 8 cm x 12 cm was tracked down the broad ligament to the cervix and a 100 ml blood clot evacuated. The cesarean section was successfully completed without any further complications. Total estimated total blood loss was 1,500 ml. Post-operative analysis of the patient’s arterial blood gas sample showed a hemoglobin level of 11.5 g/L (down from 13.5 g/l preoperatively).

Following Cesarean section, your patient was admitted to the ICU. During the first 6 hours in the unit, patient’s mean arterial blood pressure was in the 40s and she remained asymptomatic with preserved mentation. She continued to receive magnesium up to 24 hours post-delivery. Her hemoglobin dropped from 13.5 g/L to 7.8 g/L over a period of 12 hours so 3 units of packed red blood cells were transfused. Hemoglobin increased to 9.8 g/l after the second unit. During this period, no signs of active bleeding were noted. Further blood tests also showed no evidence of disseminated intravascular coagulopathy.

Towards the end of postoperative day 1, your patient’s temperature spiked to 38.6 Celsius. Blood culture results were negative. Urine analysis, chest X-Ray and bilateral extremities Doppler were also normal. No prophylactic antibiotics were given. On postoperative day 2, her fever was resolved without the need for treatment, so she was transferred out of the unit and remained stable. On postoperative day 3, the patient was restarted on prophylactic Lovenox and instructed to continue treatment for a further 6 weeks postpartum. Her blood pressure remained relatively low (80/90s/40-50s) but in the range of baseline. Having attained all of her postoperative milestones, the patient was discharged the same day.
Model Discussion Content

The Effects of Quadriplegia on Pregnancy

According to the American College of Obstetricians and Gynecologists (Committee Opinion No. 275, 2002) about 11,000 new cases of spinal cord injuries are reported each year in the US, with younger patients between the ages of 16-30 years representing more than 50% of cases. Around 18% of such cases occur in women. A spinal cord injury does not impact fertility, so cases of pregnancy in quadriplegic women are on a rise as well. Premature labor is of particular concern in a patient with traumatic spinal cord injury, and especially so if the lesion is above T10. In these patients, it may be difficult to determine the onset of labor, since uterine contractions are often painless [1].

The risk of pregnancy-induced hypertension in women with spinal cord injuries is 38% versus only 13% in patients without this type of injury [2]. As the clinical presentation is quite similar, it is difficult to differentiate between pregnancy induced hypertension and autonomic hyperreflexia.

Definition, Mechanism and Symptoms of Autonomic Hyperreflexia

Autonomic hyperreflexia is a life-threatening condition characterized by an abnormal autonomic response below the level of spinal cord injury. Clinical observations have shown that the higher the level of injury, the greater the significance of cardiovascular symptoms [3]. In patients with a spinal injury at T6 or above, the incidence for autonomic hyperreflexia increases to 85% [4].

Traditionally, a dysreflexic episode is defined as an increase in systolic blood pressure more than 20-30 mmHg from baseline [5]. However, patients with spinal cord injury above T6 present with lower resting arterial blood pressure. In these patients, a systolic blood pressure of 90-110 mmHg is considered normal because their systolic blood pressure is approximately 15-20 mmHg lower than in individuals without spine injury. Accordingly, an acute rise of blood pressure to either normal or slightly elevated levels could represent a significant risk of autonomic dysreflexia in this population [6].

Labor is a well-known stimulus for autonomic hyperreflexia. In patients with spinal cord injury, stimulation originating below the level of injury (e.g. genital areas and organs such as the uterus, bladder, or bowel) send nerve impulses that ascend in the posterior columns of the spinal cord and spinothalamic tracts until they are blocked at the level of spine injury. This causes a reflex activation of sympathetic component of autonomic nervous system without central modification [7]. [See Diagram below].

High catecholamine release and vasoconstriction may produce a hypertensive crisis. The brain detects the hypertension through intact aortic arch and carotid sinus baroreceptors. The brain then attempts to mitigate the hypertensive episode through a vagal (parasympathetic) discharge to the sinoatrial node causing bradycardia and vasodilation above the level of injury - resulting in sweating.
and flushing [8]. However, the descending inhibitory parasympathetic response stops at the level of spine injury and leaves imbalanced sympathetic tone that leads to piloerection and cool, pale skin below the level of injury. Severe hypertension may lead to seizures, retinal detachment, or fatal cerebral hemorrhage [9]. Utero-placental vasoconstriction may result in fetal hypoxemia.

**Treatment of Autonomic Hyperreflexia and Anesthetic Implications**

Despite a number of case reports [10, 11, 12, 13], treatment of autonomic hyperreflexia in pregnancy remains controversial. During an episode of autonomic dysreflexia, blood pressure fluctuates rapidly because of impaired autonomic regulation. In 2015, the American College of Obstetricians and Gynecologists issued guidelines for emergent therapy in pregnant women with severe, acute-onset hypertension that appears during pregnancy and postpartum period (Committee Opinion No 623). The Committee suggested that if systolic blood pressure is equal to or greater than 160 mmHg or if diastolic blood pressure measurement is equal to or greater than 110 mmHg, a physician should be consulted. If severe blood pressure elevations persist for 15 minutes or more, treatment should be initiated.

Target blood pressure is controversial. Placental blood flow is not autoregulated, so there is linear relationship between mean arterial blood pressure and placental blood flow. However, a recent study on moderate (100 mmHg target diastolic blood pressure) versus tight (85 mmHg target diastolic blood pressure) blood pressure control in pregnancy has found no major differences between the two groups regarding risk of maternal complications, pregnancy loss, or neonate’s intensive care admission [14].

In 2000, a meta-analysis of clinical trials on anti-hypertensive medication, reported a 145-gram decrease in birth-weight associated with a 10 mmHg decrease in mean arterial pressure from baseline [15].

Traditionally, pregnant patients with spinal cord injury and hypertension of autonomic hyperreflexia were managed with intravenous antihypertensive agents. However, during labor, it may be difficult to titrate these agents to coincide with the hypertension or “hyperreflexia” that occurs with uterine contractions. In 2002, the American College of Obstetricians and Gynecologists suggested that, if autonomic hyperreflexia occurs despite regional anesthesia, or before a regional block is in place, then severe episodes of hypertension may be managed with antihypertensive agents like hydralazine, sodium nitroprusside, nitroglycerine, trimethaphan or guanethidine. This suggestion was reaffirmed again in 2014. Currently, the most reliable measure of either preventing or treating autonomic hyperreflexia is regional anesthesia, particularly epidural anesthesia. Epidural anesthesia is preferred over spinal anesthesia due to a slower and more controlled onset of sympathetic block - thereby allowing greater control of blood pressure, especially in the presence of autonomic hyperreflexia. It
must be noted that patients with spinal cord trauma lack sensory and motor functions below the level of injury, so it is difficult to evaluate the level of the epidural blockade.

General anesthesia is less effective in controlling autonomic hyperreflexia. However, if it is indicated (e.g. bony deformities, inability to flex the back due to spasms), deep anesthesia should be used to control autonomic hyperreflexia. A high dose-opioid technique and short-acting antihypertensive could be used to suppress the hypertensive response to intubation, though there is a higher risk of aspiration and rebound hypotension with associated risk of cord ischemia.

In the past, intravenous hydralazine and labetalol have been considered first-line medications for managing acute-onset severe hypertension in the peripartum period. Animal and clinical studies have shown that labetalol has a safer profile in comparison with hydralazine. Labetalol is an alpha and beta adrenergic antagonist. Studies on fetal lamb showed that labetalol does not compromise uterine blood flow and uterine contractions are not inhibited. Although animal studies have not revealed any teratogenicity [16], Michigan Medicaid Birth Defects study documented 4 cases of 29 infants with major birth defects who were exposed to labetalol during the first trimester [17]. Labetalol crosses into the placenta as well as breast milk and neonates may demonstrate bradycardia, hypotension, or hypoglycemia if the mother takes labetalol on a chronic basis.

Hydralazine may cause a significant decrease in systolic blood pressure with values of 90 mmHg or less [18]. This increases the risk for placental hypoperfusion. Clinical trials have associated IV hydralazine with placental abruptions, higher rates of cesarean sections, and Apgar score less than 7 at 5 minutes [19], whereas the uterine blood flow can decrease by as much as 25% [20]. Cases of neonatal thrombocytopenia have also been reported [21].

Sodium nitroprusside is a direct vasodilating agent whose rapid onset and short duration of action makes it a favorable option for treatment of autonomic hyperreflexia. One study done on animal models showed that more than half of the animals developed tachyphylaxis to the drug and their fetuses died because of lethal levels of cyanide. Studies on pregnant ewes indicate that nitroprusside crosses the placenta but there are no major changes in uterine blood flow[22]. However, more recent observational studies on pregnant women treated with sodium nitroprusside failed to show any direct association between use of nitroglycerine and fetal death [23]. The American College of Obstetricians and Gynecologists recommends sodium nitroprusside to be used in extreme emergencies and for the shortest time possible.

Nitroglycerine is a venodilator and, at higher doses, an arterial vasodilator. It decreases the blood pressure by reducing preload and cardiac output. The net effect is hypotension and reflex tachycardia. Its use is reserved for an episode of severe hypertension especially associated with pulmonary edema [23]. The FDA defines nitroglycerine as a drug class C (animal studies didn’t show any
negative effects on the fetus and in humans there are not well-controlled, adequate studies, but the
drug can be used in pregnancy if benefits warrant agent use).

Trimethaphan is a ganglionic blocking agent that crosses the placenta. It can cause severe
hypotension and placental hypoperfusion with risk of fetal grow retardation and even death, so close
fetal monitoring is required. Trimethaphan can also decrease motility of the gastro-intestinal tract in
fetus, with risk of meconium ileus or paralytic ileus in a neonate [24, 25].

Guanethidine is a postganglionic adrenergic blocking agent, which reduces catecholamine’s release,
such as norepinephrine. It is in the FDA pregnancy class C. Guanethidine reduces the uterine blood
flow. It is not known if it crosses the placenta, but it is secreted in the breast milk [26].

**Systolic Blood Pressure requirements for adequate Placental Blood Flow**

During normal pregnancy, systemic vascular resistance decreases significantly, while conversely the
cardiac output increases. Beginning in the third trimester, blood pressure rises by about 10 mmHg,
and returns to the individual’s baseline value by the end of pregnancy. Low systemic vascular
resistance is attributed to the systemic vasodilation caused by hormones such as progesterone,
estrogen, prolactin and relaxin, together with a reduced response to hormones such as angiotensin II
or vasopressin [27]. In addition, the low resistance of the utero-placental circuit combined with
systemic vasodilation causes the marked decrease in systemic vascular resistance.

To compensate for reduced systemic vascular resistance, plasma volume increases gradually through
an increase in plasma renin, and a reduction in atrial natriuretic peptide level [28]. Systemic
vasodilation also causes a reflex increase in the heart rate. As the result, cardiac output increases
[29].

Animal studies have demonstrated that the uteroplacental circulation is a low-resistance system,
widely dilated, and in which perfusion is largely pressure-dependent [30, 31]. Limited autoregulation
present in placental circulation means that the placental blood flow may decrease with reduction in
maternal blood pressure. Using an aortic occluder, Laird et al found that a 22% reduction in arterial
pressure produced a reduction in placental blood flow and total uteroplacental flow in pregnant rabbits
[31].

Wilkening et al have demonstrated on animal models that, in normal physiologic conditions, there is
more uterine blood flow than is required to support fetal oxygen demand [32]. This feature protects the
fetus from variations in uterine blood flow [33]. A 50% reduction in the uteroplacental flow for short
periods of time can be without damaging effects on the fetus.

Studies in sheep found that fetal oxygen uptake remains almost constant despite large variations in
uterine blood flow. As uterine blood flow decreased, uterine venous oxygen content dropped and arteriovenous oxygen content difference increased. This suggests a greater oxygen extraction when perfusion decreases [34].

**Effects of Vasopressors on Uterine and Placental Blood Flow**

The choice of vasopressor to treat regional-anesthesia induced hypotension in obstetric patients is controversial [35], particularly regarding adverse effects on utero-placental blood flow and fetal acid-base status.

Ephedrine’s action is considered to be mainly indirect, via stimulating release of norepinephrine from sympathetic nerve terminals. Animal and in vitro studies have showed that ephedrine increases blood pressure with minimal effect on utero-placental blood flow because of predominately beta agonist effect [36]. In vitro studies in pregnant sheep have also shown more vasoconstrictive effects on femoral vessels than on uterine vessels and less uterine vasoconstriction because of nitric oxide release [37]. Ephedrine crosses the placenta to a greater extent than phenylephrine, and is associated with higher levels of lactate, norepinephrine and epinephrine in the fetus [38]. An important concern about ephedrine in obstetrics has been the association between its use and worsening of fetal acid-base status [39]. This effect seems to be related more to direct beta-adrenergic effect on fetal metabolism.

Traditionally, phenylephrine was contraindicated in obstetrics because of concern about utero-placental constriction and it was reserved as a second-line drug for use after ephedrine. However, clinical studies have failed to show any evidence of adverse fetal or neonatal effects with the use of alpha agonists [40]. On a sheep model, Erkinaro et al compared phenylephrine and ephedrine for treating epidural-induced hypotension after an experimental period of fetal hypoxia and showed that although ephedrine had more favorable effects on uterine and placental circulation, there was no difference in fetal acid-base status and lactate concentration [41]. Often, phenylephrine is associated with a reflex bradycardia and a subsequent drop in cardiac output. However, concerns should rise only in large doses, when cardiac output can drop below the baseline [42]. As a result, phenylephrine is currently the initial vasopressor of choice in obstetrics to treat regional anesthesia-induced hypotension.

In summary, the choice of vasopressor should be based on maternal considerations which might affect fetal oxygen demand and supply, and not primarily on maintaining the uteroplacental perfusion.

**Anticoagulation Treatment and Pregnancy**

If a parturient has been on anticoagulation before pregnancy, most likely she will need to continue the treatment during pregnancy and after delivery. Unfractionated heparin (UH), low molecular weight
heparin (LMWH), and warfarin are commonly used. The first two are the safest anticoagulants to use in pregnancy [43] because they do not cross the placenta [44, 45].

Pregnancy-induced changes such as increased blood volume, increase in protein binding of heparin [46], and an increase in glomerular filtration causing increased renal excretion of heparin should be considered when addressing anticoagulation therapy. During pregnancy, the heparin compounds have lower peak plasma concentration and half-lives. These changes require higher doses and more frequent administration to maintain effective plasma levels [47, 48].

Warfarin is reserved in parturients with mechanical heart valves with high risk of thrombus formation [49]. Because of its low molecular weight, warfarin easily crosses the placenta. During the first trimester it is teratogenic, with the risk of fetal defects between 5-10% [50]. The risk may be lower for doses less than 5 mg daily [51]. Fetal warfarin syndrome includes hypoplasia of nasal bridge, laryngomalacia, pectus carinatum, congenital heart defects (atrial septal defect and patent ductus arteriosus), ventriculomegaly, stippled epiphyses, telebrachydactyly, and growth retardation. As an alternative to warfarin, either LMWH or unfractionated heparin can be used as anticoagulants. Lovenox (enoxaparin sodium) is a LMWH which affects coagulation factors IIa and Xa. The advantages of LMWH over UH include: less bleeding events, lower risk of heparin-induced thrombocytopenia, more predictable response, and less bone demineralization. A relative disadvantage of Lovenox is its longer half-life. Reports of congenital anomalies and even fetal death were reported in infants born to women who received enoxaparin during pregnancy. Notably, Lovenox does not cross into the breast milk.

In 2010, The American Society of Regional Anesthesia published the evidence-based guidelines on antithrombotic therapy in pregnancy [52], highlighting that:

1. Patients on antithrombotic therapy before pregnancy should be switched from oral treatment to LMWH or UH no later than 36 weeks, using the same dose and monitoring as throughout pregnancy. LMWH should be discontinued at least 36 hours before induction of labor or cesarean section, and intravenous or subcutaneous UH given if needed. If UH is given intravenously, it should be stopped 4-6 hours before estimated time of delivery.

2. Patients who take LMWH and think they are in labor, should stop the agent, and be assessed by an obstetrician. If the labor is confirmed, the next doses should be withheld until after delivery.

3. LMWH or UH prophylaxis (40 mg enoxaparin once daily or 5000 U UH twice daily) should be re-started at least 12 hour following either vaginal delivery or epidural catheter removal, whichever is later. This period should be increased to 24 hours following a cesarean section. If higher doses of LMWH or UH are needed (1mg/kg enoxaparin twice daily), then a period of 24 hours is recommended.
before thromboprophylaxis is restarted, regardless of type of delivery.

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