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A Case Series of Anesthetic Management of Pregnant Women with Takayasu Arteritis

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Abstract

Takayasu arteritis or pulseless disease (TD) is a chronic progressive inflammatory disease of the aorta and aortic arch branches. It affects females in reproductive years, accounting for almost 80% of the cases. TD complications may affect pregnancy and labor, thus anesthetic and surgical planning are essential during cesarean delivery. The authors report four cases of patients with TD that have undergone cesarean delivery and discuss their anesthetic management. In all cases anesthesia was carried out with neuraxial anesthesia and hemodynamic parameters were kept stable. Although the anesthetic management of TD is not well defined, it is consensual that one of the main objectives of the management of these patients is the maintenance of maternal and fetal tissue perfusion. It is essential to be cautious about the use of drugs that act on vascular tonus, such as oxytocin and vasoconstrictions drugs, because it can result in reduction of systemic vascular resistance and decrease in cardiac output, increase the risks of angiotensin or vasculitis of the central nervous system. In relation to the other transoperative anesthetic care, these are similar to those required for cesarean sections in non-compliant parturients. A regional anesthetic technique allows the monitoring of cerebral function and can be slowly titrated to prevent hemodynamic instability. It is crucial that the anesthesiologist understands the pathophysiology of TD and the pregnancy-induced physiological changes for the safe management of these patients.

Keywords

Anesthetic Management, Takayasu Arteritis, Cesarean Delivery

1. Introduction

Takayasu arteritis or pulseless disease (TD) is a chronic progressive inflammatory idiopathic disease of the aorta and aortic arch branches, commonly involving the subclavian, carotid, and renal arteries, that causes narrowing, occlusion, and aneurysms of the affected vessels [1, 2, 3]. It is a relatively rare condition that affects females in reproductive years, accounting for almost 80% of the cases [4]. The cause of the disease remains unknown, although infectious and autoimmune etiologies have already been suggested [5]. The management of pregnant patients with TD is challenging because some patients may develop severe complications such as hypertension, multiorgan involvement/dysfunction, and vascular stenosis that impairs uterine blood flow and can result in restricted intrauterine growth and fetal complications [6]. Blood pressure control is a main goal during the anesthetic management of these patients because they frequently have arterial aneurysms and cerebral hypoperfusion due to carotid occlusion. The anesthetic technique for patients with TD is not standardized and regional and/or general anesthesia has been used. General anesthesia could avoid the sympathectomy and hypotension induced by regional anesthesia, which is advantageous in such patients. However, regional anesthesia, in an awake patient, promotes the easiest way to monitor cerebral function and usually is the preferred technique for the

parturient.

The objective of the current case series was to report cases of patients with TD that have undergone cesarean delivery, discussing their anesthetic management, and review the implications of TD during pregnancies that are important for the safe anesthetic management of these patients.

2. Cases Series

Case 1

A 42-year-old-woman, 50 kg, gravida 1, para 0, asthmatic and hypertensive, at 37 weeks of gestation was admitted for cesarean delivery due to acute fetal distress. TD was diagnosed when she was 13-years-old, affecting the cephalic arch, right internal carotid artery, right subclavian artery, infrarenal abdominal aorta, and left renal artery. She had a clinical history of aortorenal graft and abdominal aortic surgery, cerebrovascular accident, and myocardial infarction and was in use of acetylsalicylic acid, methyldopa, azathioprine, prednisone, propranolol, and folic acid. Her electrocardiogram (ECG) showed a left anterior hemiblock and left ventricular hypertrophy. A transthoracic echocardiogram showed diastolic dysfunction.

Into the operating room she was monitored with five-lead ECG, noninvasive blood pressure (cuff on left arm), and pulse oximetry. On admission blood pressure was 142/76 mmHg and heart rate was 100 beats/min. Spinal anesthesia was administered with the patient in left lateral tilt at L3-L4 with 12 mg of 0.5% hyperbaric bupivacaine and 60 mcg of morphine, which produced a T4 block. At the same time, she was infused with 1000 ml of Ringer lactate solution. Before the incision, 100 mg of hydrocortisone and antibiotic prophylaxis with 2 g of cefazolin were administered. After neuraxial anesthesia, her systolic blood pressure decreased from 140 to 95 mmHg, leading to the administration of 40 mg of ephedrine (4 bolus of 10 mg each). A 2375-g infant was delivered with Apgar scores of 8 at 1 and 9 at 5 min. During the remainder of cesarean delivery, the patient was infused with 500 mL of Ringer's lactate and 100 ml of sodium chloride 0.9% solution containing 10 units of oxytocin and 8 mg of ondansetron. She was transferred to the intensive care unit (ICU) and monitored for 24 hours postoperatively. During this period, the patient had one episode of hypotension that was treated with 10 mg of ephedrine. After ICU discharge, she showed no intercurrences and was discharged home 6 days later.

Case 2

A 33-year-old-woman, 74 kg, gravida 1, para 0, at 36 weeks of gestation was admitted for cesarean delivery because of severe preeclampsia. At the age of 22 she was diagnosed with TD after a cerebrovascular accident. Her treatment included azathioprine, hydralazine, acetylsalicylic acid, prednisone, and magnesium sulfate. Her laboratory tests showed anemia.

Into the operating room she was monitored with five-lead ECG, noninvasive blood pressure (cuff on right leg), and pulse oximetry. On admission blood pressure was 115/98

mmHg. Spinal anesthesia was administered with the patient in left lateral tilt at L3-L4. A dose of 12 mg of 0.5% hyperbaric bupivacaine and 20 mcg of fentanyl produced a T4 block. At the same time, she was infused with 1000 ml of Ringer´s lactate solution. Before the incision, 100 mg of hydrocortisone and antibiotic prophylaxis with 2 g of cefazolin were administered. After neuraxial anesthesia, her systolic blood pressure decreased from 120 to 91 mmHg, leading to the administration of 10 mg of ephedrine. A 2890-g infant was delivered with Apgar scores of 7 at 1 and 8 at 5 min. During the remainder of cesarean delivery, the patient was infused with 500 mL of Ringer lactate containing 5 units of oxytocin and 8 mg of ondansetron. She was transferred to the ICU, where she was monitored for 24 hours postoperatively. After ICU discharge, she showed no intercurrences and was discharged home 3 days later.

Case 3

A 33-year-old-woman, 63 kg, gravida 1, para 0, at 38 weeks of gestation was admitted for elective cesarean delivery. She was diagnosed with TD at 14-years-old and reported episodes of headache, claudication and paresthesia of the upper limbs, chest pain, dyspnea on medium exertion, and orthopnea. At physical examination, the patient had bilateral carotid murmur (3+/6) and arterial hypertension with reversed coarctation (blood pressure of 118/67 in the right arm, 122/69 in the left arm, 160/72 in the right leg, and 159/72 mmHg in the left leg). Her computed tomography aortic angiography, carotid ecodoppler, and transthoracic echocardiogram revealed ascending aortic dilatation, parietal thickening in the ascending aorta, aortic arch, descending aorta, and adrenal portion of the abdominal aorta and parietal thickening with bilateral carotid caliber reduction. Her treatment included prednisone, acetylsalicylic acid and azathioprine.

Into the operating room she was monitored with five-lead ECG, noninvasive blood pressure (cuff on left leg), and pulse oximetry. On admission blood pressure was 145/85 mmHg. An epidural catheter was inserted at (L3 L4) with the patient in left lateral tilt. Spinal anesthesia was administered at (L4 L5) with 10 mg of 0, 5% hyperbaric bupivacaine, 60 mcg of morphine, and 20 mcg of fentanyl, producing a T4 block. After neuraxial anesthesia, her blood pressure decreased to 70/40 mmHg and she had nausea and vomiting, leading to the administration of 40 mcg of phenylephrine. Before the incision, 100 mg of hydrocortisone and antibiotic prophylaxis with 2 g of cefazolin were administered. A 2855-g infant was delivered with Apgar score of 8 and 9 at 1 and 5 min, respectively. After delivery, 2 consecutive bolus of 3 units of oxytocin were administered. During the remainder of cesarean delivery, the patient was infused with 500 mL of Ringer's lactate containing 10 units of oxytocin. She was monitored in the ICU for 24 hours postoperatively. After ICU discharge, she showed no intercurrences and was discharged home 3 days later.

Case 4

A 36-year-old woman, 67 kg, gravida 3, para 0, abortus 2 at 38 weeks of gestation was admitted for cesarean delivery

due to non-progressing labour. She had a clinical history of a previous cesarean delivery under spinal anesthesia, angioplasty of right renal artery and right subclavian artery and was in use of methyldopamine and prednisone. Her angiogram showed significant stenosis of the left subclavian artery (her left arm was pulseless) and occlusion of the right internal carotid artery.

Into the operating room she was monitored with five-lead ECG, noninvasive blood pressure (cuff on right arm), and pulse oximetry. On admission blood pressure was 120/80 mmHg and heart rate was 80 beats/min. Spinal anesthesia was administered with the patient in left lateral tilt at L3-L4 with 10 mg of 0.5% hyperbaric bupivacaine and 60 mcg of morphine leading to a T6 block. At the same time, she was infused with 1000 ml of Ringer´s lactate solution. During the procedure her blood pressure ranged from 120/80 to 90/50 mmHg with the heart rate varying between 60 and 80 beats/min. A 3010–g infant was delivered with Apgar score of 9 and 9 at 1 and 5 min, respectively. During the remainder of cesarean delivery, the patient was infused with 1000 mL of Ringer's lactate containing 10 units of oxytocin. She was monitored in the ICU for 24 hours postoperatively. After ICU discharge, she showed no intercurrences and was discharged home 3 days later.

3. Discussion

Takayasu arteritis was first described by Takayasu and Onishi, two Japanese ophthalmologists, who observed retinopathy in the absence of peripheral pulses [7, 8]. There is a predominance of the disease in women, with a ratio of 8: 1 in relation to men, and in populations of Asia and South America. The cause is unknown, but it seems to be related to multiple causative factors. The HLA A24-B52-DR2 haplotype, MICA genes and genes between the HLA B locus and the MIC gene locus in chromosome 6 might be involved with the disease [9, 10].

The clinical manifestations are divided into early and late stages. The early stage is marked by low fever, weight loss and fatigue. After that, there is a vascular inflammatory phase and a quiescente and occlusive late stage [11]. In the late stage decreases or absent pulsations associated with limping of the limbs and blood pressure discrepancies, vasculopathies, hypertension due to renal artery stenosis, mesenteric angina, retinopathy, and aortic regurgitations can be observed. Cardiomyopathy, myocardial ischemia, myocarditis, pericarditis, congestive heart failure, neurological symptoms secondary to hypertension or ischemia, such as postural dizziness, seizures, and amaurosis, renal glomerular lesions, interstitial lung disease, ulcerative colitis and erythema nodosum may also be observed [12, 13].

Six types of TD can be identified: Type I (involving the branches of the aortic arch), Type IIa (involving ascending aorta, aortic arch, and its branches), Type IIb (involving Type IIa region plus thoracic descending aorta), Type III (involving thoracic descending aorta, abdominal aorta, renal arteries, or a combination), Type IV (involving abdominal aorta, renal arteries, or both), and type V (involving entire aorta and its branches) [14, 15].

The presence of a major complication such as hypertension, retinopathy, aneurysms, and aortic insufficiency can classify the disease in stages. Stage I, no complications are observed; stage IIa, patients have only one of these complications; stage IIb, patients have only one of these complications, but a severe form; and stage III, when more than one complication is present. Therefore, patients in cases 1, 3 and 4 are staged as stage III, because they have important arterial disease, while the patient in case 2 can be staged as stage IIb due to the presence of severe preeclampsia.

Diagnosis is based on signs and symptoms, laboratory markers of inflammation, and angiographic demonstration of aortic stenosis and/or of its major branches. Histopathology is the gold standard test for disease activity. Imaging studies (magnetic resonance angiography, doppler ultrasound, and computer tomography) can evaluate TD and avoid the risk of arterial puncture [16].

Corticosteroids and immunosuppressive agents, such as methotrexate and azathioprine, are usually used for the treatment of active inflammation. Chronic corticosteroid use may lead to hypophysis-adrenal suppression with inadequate release of endogenous corticosteroids during stress. Patients on chronic glucocorticoid use, undergoing medium-sized abdominal surgeries (cesarean delivery and cholecystectomies), should receive 50 to 75 mg of hydrocortisone for 1 to 2 days. The first dose (25 mg) should be administered before the incision and the subsequent doses (12.5-25 mg) at 6 hour intervals. High doses are indicated for large procedures (abdominoperineal resection, pancreatoduodenectomy) [17, 18]. Established arterial stenosis or occlusive lesions may require revascularization, such as bypass grafting or percutaneous transluminal angioplasty [19].

Pregnancy does not affect TD progression, but hypertensive complications, such as preeclampsia and exacerbation of chronic hypertension, and fetal complications, such as intrauterine growth restriction (IUGR), abortion, and fetal death, have been reported in up to 90% of the cases [20]. IUGR has been associated to uterine hypoperfusion due to uncontrolled hypertension and/or extensive aortic involvement, with reduced iliac artery blood flow [21]. Rare and potentially fatal maternal complications include TD-related aortic aneurysm rupture during pregnancy [22] or cerebral hemorrhage.

The frequent presence of sustained and severe hypertension leads to a very high rate of cesarean delivery in TD patients [23]. Nevertheless, the choice of delivery route may be guided by the stage of TD during pregnancy. In stages I and IIa, vaginal delivery may be chosen. In such cases, epidural analgesia is suggested for pain relief and the use obstetrical forceps may be considered for abbreviation of delivery in hypertensive patients [24]. Cesarean delivery should be indicated for stages IIb and III, as increased blood volume and blood pressure observed during uterine contractions as well as increase cardiac output observed

during labor may lead to cardiac decompensation [25].

The anesthetic management of TD is not well defined. It is crucial that the anesthesiologist understands the pathophysiology of TD and the pregnancy-induced physiological changes for the safe management of these patients. Because TD frequently evolves with compromised regional circulation due to arterial stenosis, it is consensual that one of the main objectives of the management of these patients is the maintenance of hemodynamic stability, avoiding maternal and fetal tissue hypoperfusion.

In the preoperative period, clinical characteristics suggestive of carotid involvement, such as dizziness, syncope, and carotid murmur, should be evaluated. During anesthesia, placements or procedures that decrease carotid blood flow should be avoided.

Monitoring of patients with TD does not differ from that routinely used in cesarean delivery: pulse oximetry, cardioscope, noninvasive blood pressure, and urine output. During general anesthesia, capnography and cerebral monitoring should also be used. Noninvasive blood pressure has been successfully employed to monitor arterial pressure in TD patients, but if there is significant preoperative discrepancies between upper and lower extremity measures, monitoring should be performed in both limbs. Arterial cannulation may be necessary in TD patient in whom blood pressure cannot be noninvasively measured in any extremity, but it has the potential risk of pseudo-aneurysm formation. Cardioscopy with two or more electrocardiographic leads is necessary in all patients, especially those with ascending aorta disease, which present greater risk of myocardial infarction. Monitoring should always continue after surgery to ensure that adequate blood pressure and peripheral perfusion are maintained. Hemodynamic monitoring in an ICU should be continued for 24 hours postoperatively to detect and treat instability due to pain and fluid redistribution.

Regional anesthesia allows monitoring of brain perfusion through the monitoring of patient's level of consciousness, which is extremely interesting in patients with arterial disease that can cause low cerebral perfusion. Despite this potential benefit, spinal anesthesia may be associated with extensive sympathetic blockade and decreased blood pressure, which can be dangerous in patients with compromised regional circulation. However, in the current case series, a low-dose spinal anaesthesia has proven to be safe and hypotension was easily managed with ephedrine or phenylephrine and crystalloid [26]. Epidural anesthesia is another interesting neuraxial technique for patients with TD as it is associated with gradual onset of sympathetic blockade, better control of blood pressure, and lower hypotension rates [27]. In continuous epidural anesthesia, fractionated doses of local anesthetic are administered, allowing slow titration of the level of the blockade, maintaining hemodynamic stability and reducing the need of vasopressors. Therefore, this anesthetic technique may be preferred for TD patients as a single technique or even associated with spinal anesthesia. Neuroaxial opioids are particularly useful during cesarean delivery to alleviate pain, which may be accompanied by hypertension and tachycardia.

Ephedrine and phenylephrine are usually used to treat anesthesia-related hypotension during cesarean delivery [28]. However, as TD is associated with fetal complications, such as IUGR, ephedrine should be used with caution. This drug may increase the risk of fetal acidosis compared with phenylephrine, worsening the prognosis of the fetus. In addition, ephedrine may trigger the development of vasculitis of the central nervous system. Such syndrome is characterized by encephalitis and recurrent strokes which may lead to important physical limitations, especially in patients with TD who often already have reduced cerebral perfusion [29, 30].

Induction of general anesthesia could avoid the sympathectomy and consequent hemodynamic instability induced by regional anesthesia, which is advantageous in such patients. However, this effect should be weighed against the lesser possibility of monitoring brain function over that which is possible in an awake patient. Besides that, general anesthesia and endotracheal intubation may cause an exaggerated sympathetic response with hypertension, increasing the risks of cerebral hemorrhage, aneurysm rupture and infarction or cardiac dysfunction in patients with TD.

The management of antibiotic prophylaxis, prevention of nausea and vomiting, and administration of intravenous analgesics does not differ from that routinely used during pregnancy. Anti-inflammatory drugs should be used with caution, due to the risk of renal injury and the presence of advanced atherosclerotic disease in these patients [31]. Oxytocin administration after fetal extraction should be carried out with caution, as this may result in systemic effects, such as relaxation of vascular smooth muscle, leading to vasodilation and reduction of systolic and diastolic blood pressures, with reflex tachycardia. This vasodilatation, usually temporary, may be clinically significant after rapidly administration of a bolus dose of oxytocin, and may result in decreased coronary perfusion and cardiac collapse. Such effects tend to be more prominent during general anesthesia.

Despite the difficulties encountered during anesthesia of parturient patients with TD, a serious disease for which anesthetic management is not yet fully established, all patients in the current case series had favorable outcomes. In the reported cases, a low-dose spinal anesthesia has proven to be safe, with minimal adverse hemodynamic effects. Besides that, a thorough preoperative evaluation, careful monitoring, and extra care during administration of drugs with vascular tonus effects (vasoconstrictors, oxytocin) contributed to the desired hemodynamic stability and positive outcomes.

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