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Pregnancy-Related Cardiovascular Complications: Case Presentation and Review of Literature

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ABSTRACT

Background: Cardiovascular complications that can cause severe catastrophic outcomes for both the mother and the fetus are rarely seen during pregnancy. Time to diagnosis is often delayed by a low degree of suspicion and atypical presentation. We report surgical strategies in three pregnant women with cardiovascular complications.

Methods: A retrospective search from 2009 to 2016 identified three pregnant women who underwent urgent cardiac surgery. We used extracorporeal circulation (ECC) without cesarean section with careful follow-up of the fetuses during the perioperative and postoperative period. We used levosimendan as a potent inodilator in all patients to increase fetoplacental blood flow and fetal heart rhythm.

Results: Median time to diagnosis was 23.8 h (range 11.7-120 h) and median time from diagnosis to arrival in the operating theater was 9.8 h (range 7.4-19.8 h). One patient with prosthetic heart valve thrombosis underwent concomitant cesarean section prior to cardiac surgery. In a young pregnant woman who had spontaneous dissection of the left anterior descending artery, on-pump beating heart coronary artery bypass grafting was performed without cross clamping. Two and three months after surgery, cesarean sections were performed without any complication in two pregnant women.

Conclusion: Because unusual cardiovascular complications are the main cause of maternal and/or fetus death during pregnancy, prompt and exact diagnosis is very important. Life-saving surgical strategy with the help of appropriate teams are necessary to optimize outcome for both mother and baby.

INTRODUCTION

Pregnancy-related cardiovascular complications are rarely seen and can be the cause of maternal and fetus death. In pregnant women, the volume of body increase in about 30-50%, and a high level of estrogen is the main cause of a hypercoagulability state which significantly increases the risk of arterial dissections, and thromboembolic complications [Larson 1984; Ricci 1997; Mészáros 2000; Clouse 2004]. Spontaneous coronary or aortic dissection requiring urgent surgical approaches can be seen in these particular patients. The cause of spontaneous dissection of the arteries in pregnant patients remains unclear but theories of etiology include a medial eosinophilic angiitis, pregnancy-induced degeneration of collagen in conjunction with the stresses of parturition, and rupture of the vasa vasorum [Tsai 2006; von Kodolitsch 2000]. The cardiovascular complications must be considered when a pregnant woman presents with myocardial ischemia, symptoms of aortic dissection, or a history of prosthetic heart valve replacement. Therefore, full physical examination including cardiac functions and an aortic pathology should be evaluated by the familiar teams including an obstetrician, cardiologist, and anesthetist. In women at high risk, a noninvasive method such as echocardiography or magnetic resonance imaging might be utilized in young females to screen for rare but life-threating cardiovascular conditions.

Herein, we report three pregnant women who underwent urgent cardiovascular surgery using cardiopulmonary bypass due to aortic and coronary artery dissection, and an acute prosthetic heart valve thrombosis.

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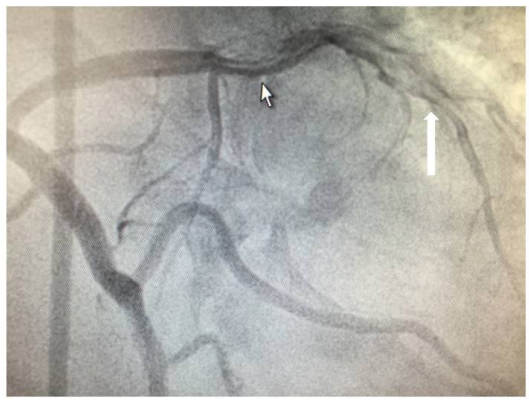

Figure 1. Dissection of the left anterior descending coronary artery. The dissection is starting from the proximal and continuing along the coronary artery (arrowheads).

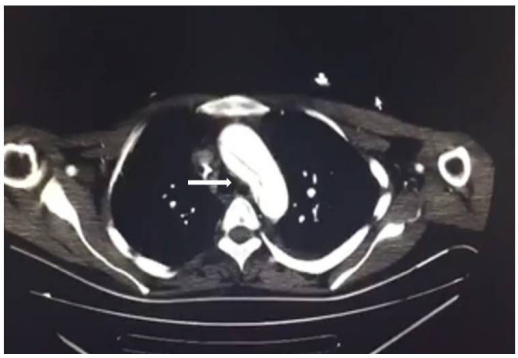

Figure 2. Transverse section of computed tomography demonstrates the dissection of the ascending aorta (white arrow).

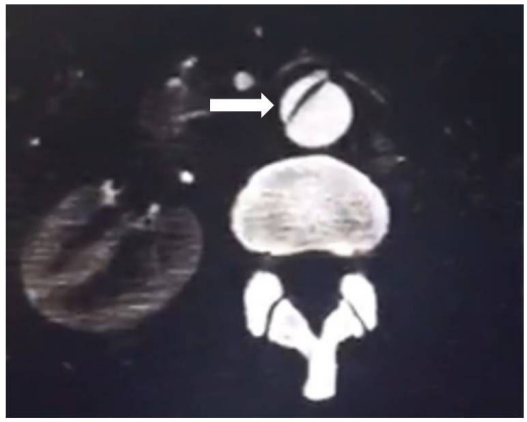

Figure 3. Tomographic image of the abdominal aorta. Computed tomography demonstrates the dissection of the abdominal aorta (white arrow).

CASE REPORT

Case 1

A previously healthy 32-year-old twenty-three week pregnant woman with unstable angina pectoris and an episode of vomiting was referred to our hospital. The electrocardiogram showed ST-segment elevation in D2, D3 and AVF segment. The levels of cardiac enzymes were significantly high. The transthoracic echocardiogram demonstrated the left ventricular impairment (ejection fraction was 35%). Angiography revealed that there was a spontaneous dissection of the left anterior descending artery (LAD) (Figure 1). Coronary stenting was not successful. To relieve symptoms we started beta-blocker, nitrate, and a low molecular weight heparin. The patient received levosimendan infusion at a dose of 0.05 microgram/kg/min followed by a intravenous bolus administration. Because the ischemic symptoms were resistant to medical therapy, the patient was transported into the operating theater for surgical revascularization. In the operating room, fetal monitorization was performed. In the operation, midline sternotomy was performed and a left internal thoracic artery was harvested. We tried to perform off-pump coronary artery bypass grafting (CABG). However, severe hypotension and ventricular arrhythmia were seen. Because hypotension was resistant to inotropics, surgery was performed under on-pump beating heart. A left anterior descending artery was anastomosed to the LAD artery. In the postoperative period, the patient received noradrenaline as an additional inotropic. Cardiac function was improved after surgery. Levosimendan and noradrenaline infusion continued during 24 hours in the ICU. Postoperative period showed no complications, except for mild hypotension easily corrected with noradrenaline. During CPB, the fetus's heart rate dropped with natural recovery after surgery. Fetal heart rate remained normal throughout the whole course of CPB. After surgery, abdominal ultrasonography was performed every 4 hours in the ICU. US showed that fetal status including heart rhythm was normal in the ICU. Fetal US was performed again every day. Physical and hemodynamic examinations were normal reported by the gynecologist. The patient was discharged to home at postoperative day 21. During the follow-up period the conditions of the patient and fetus were normal. At the term of gestation, the cesarean section was performed using epidural anesthesia without any complication. The Apgar score for the newborn was 7/10.

The patients' age, the type of cardiovascular complications, and treatment strategies including ECC time are summarized in the Table.

Case 2

A 45-year-old asymptomatic pregnant woman in her 21st gestation week presented to the gynecology department in another hospital. She had no cardiovascular complaints. She had eight pregnancies and six full-term births. On admission, she had a blood pressure reading of 145/90 mmHg, a pulse rate of 90 beats/min, and a respiratory rate of 24 breaths/min. She was oriented to person, place, and time. Her physical and ultrasonographic examination showed no abnormalities. Due to sudden respiratory distress, she was intubated in this hospital. Invasive monitorization demonstrated normal systolic and diastolic blood pressure and a normal heart rhythm. Chest X-ray showed a bilateral pulmonary plethora due to acute pulmonary edema. The systolic murmur was noted on her physical examination after intubation. She was referred to a cardiologist for cardiovascular evaluation. The echocardiogram showed a dilated aortic root, mildly aortic valve regurgitation, and concentric left ventricular hypertrophy. The left ventricular ejection fraction was 30%, and there was a diastolic dysfunction. A dilated aortic root with a suspected mobile flap was noted in the ascending aorta. A contrast CT scan of the chest showed an aortic dissection extending from the aortic root along the right lateral wall of the aortic arch (Figure 2). The ascending aorta measured 4.7 cm transversely (Figure 3). The descending aorta appeared normal, measuring 2.5 cm at

Patients' Age, Type of Cardiovascular Complications, and Treatment Strategies

Patient No	Age	Diagnosis	Gestation age, weeks	Time to diagnosis, h	Operation, min	ECC, min
1	32	CAD	23	19.6	154	34
2	45	AAD	21	134	194	96
3	27	PHVT	34	96	152	98

CAD indicates coronary artery dissection; AAD, ascending aortic dissection; PVT, prosthetic heart valve thrombosis.

its widest diameter. There was no pericardial effusion. However, there was a dissection of distal descending aorta (Figure 4). After extubation, she was referred to our cardiac surgeon for surgical therapy. Cesarean section and surgery under circulatory arrest for aortic dissection was proposed to her, but she did not accept. She accepted only the surgery for aortic dissection. Because the patient had an impaired left ventricle, levosimendan infusion was started preoperatively.

Fetal and invasive pregnancy monitoring were performed in the operating room prior to sternotomy incision. The right femoral and axillary artery were cannulated, and midline sternotomy incision was performed. There was an aortic root dilatation (Figure 4). Normothermic extracorporeal circulation (ECC) was initiated by the use of the right axillary artery and a right atrial cannulation. Myocardial temperature was kept below 20°C by cardioplegic perfusion via the coronary sinus. Ventricular distention was avoided by decompressing the left ventricle by venting through the right superior pulmonary vein. The ascending aorta was inspected for the site and extent of the tear, the involvement of the transverse arch, and for an assessment of intimal disruption that requires repair. Through a longitudinal approach, the ascending aorta was opened and transected just proximal to the innominate artery. The aortic valve was suspended with 4-0 polypropylene pledgeted sutures because aortic valve failure was present. Cerebral perfusion via axillary artery cannulation was started.

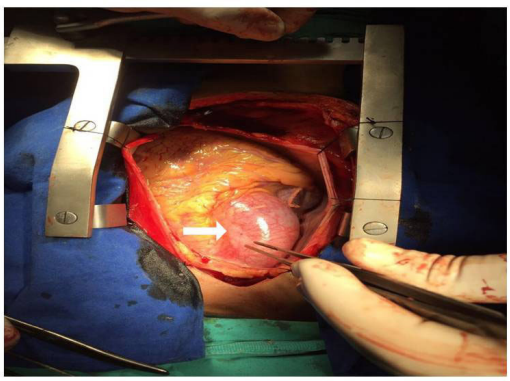

Figure 4. Intraoperative view of the ascending aorta in patient with aortic dissection. This picture exhibits an aneurysmatic dilatation of the aortic root and the ascending aorta (white arrow).

We examined the ascending aorta. The dissection flap was not involved in the transverse aortic arch. The intima was not fragmented and there was no evidence of rupture. All air and debris from the brachiocephalic vessels were evacuated. Therefore, systemic circulation started again via axillary cannulation side. The ascending aorta was resected, and interposition of a 30 mm collagen woven Dacron graft was carried out with the use of double-felt sandwich technique on both anastomoses with fine 4-0 polypropylene suture. At the time of completion of the distal anastomosis, systemic circulation was started via the dacron graft. Flow to cerebral and systemic circulation was restored after clamping the graft proximal to the origin of the innominate artery (Figure 5). The time of total circulatory arrest was 7 minutes. No complication was detected in the postoperative period. Postoperative vital signs of the baby including fetal heart rate, were normal. The patient was discharged from the hospital 21 days after her initial admission. At the 33rd week of gestation age, the patient delivered a healthy baby by cesarean section.

Case 3

A 27-year-old pregnant woman (in her 34th gestation week) was referred with complaints of dyspnea and palpitations. Her history revealed that she underwent mitral prosthetic valve replacement in 2008. We were informed that warfarin treatment was stopped. She received low molecular weight heparin twice daily. Her heart rate was 106 beats/min, and her blood pressure was 85/50 mmHg. Her transthoracic echocardiography demonstrated an echogenicity consistent with thrombus formation on the left ventricular side and on the mechanical mitral valve (Figure 5). In her Doppler evaluation a pressure difference of maximum 15 mmHg, and an average of 10 mmHg, was identified as caused by thrombus on the valve, which inhibited the valve to open. The patient's activated partial thromboplastin time (aPTT) was measured as 35.6 sec, whereas the prothrombin time (PTT)-INR valve was measured as 1.32 sec. Fetal and maternal ultrasonography showed normal development of the fetus. The ultrasonographic examination showed that the development of the fetus was normal. Thus, we planned urgent cesarean and mitral valve replacement. We offered the choice of heart valve, mechanical and bioprosthesis to our patient, preoperatively. Because the patient do not foresee pregnancy in the future, she chose the mechanical mitral valve replacement. Spinal anesthesia was performed for the delivery. The fetus was healthy and Apgar score was normal. Fifteen minutes after, general anesthesia was induced followed by rapid cesarean

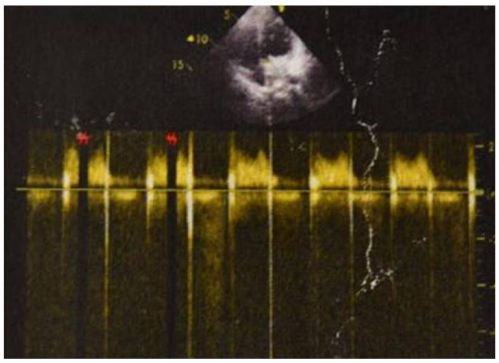

Figure 5. Transthoracic echocardiography demonstrating the echogenicity with thrombus formation on the left ventricular side and on the mechanical mitral valve.

section delivery of the baby by the obstetric team. A median sternotomy incision was performed and mediastinal adhesion was released carefully. Aortic and bicaval cannulation was performed, and cardiopulmonary bypass (CPB) was instituted. The left atriotomy was done. There was a large thrombus formation on the left ventricular side and on the mechanical mitral prosthesis. The Bjork-Shiley mitral mechanical valve was nearly stuck. An organized and fresh thrombus was carefully cleared from the prosthetic valve. The Bjork-Shiley mechanical valve was excised and a no. 25 St. Jude mechanical mitral prosthesis was replaced using 2/0 teflon pledgetted suture. The patient was weaned from CPB without any inotropic support. During the postoperative period, LMWH was started twice daily followed by the initiation of warfarin treatment. The patient was discharged with instructions after the regulation of the INR values above 2.5.

DISCUSSION

As we know, 0.2-4% of all pregnancies are complicated by cardiovascular diseases, and the number of patients who develop cardiac problems during pregnancy is increasing. Knowledge of the risks associated with cardiovascular disease during pregnancy and their management are of pivotal importance for advising patients before pregnancy [Tsai 2006]. Because prospective or randomized studies are lacking, recommendations in the guidelines mostly correspond to the evidence level C. In young pregnant women, the most severe complications are aortic [Larson 1984; Mészáros 2000; Clouse 2004; Tsai 2006; von Kodolitsch 2000; American College of Cardiology/American Heart Association Task Force 2006; Mehta 2002; Erbel 2001] and spontaneous coronary artery dissection [Krishnamurthy 2004; Bac 1995; Badmanaban 2002; Thistlethwaite 1998; Aliyary 2007; Kearney 1993; Almeda 2004; Arnold 2008; Ardehali 2007; Shirakawa 2002; Cini 2008; Koul 2001]. These complications cause 3-10% of maternal mortality [American College of Cardiology/American Heart Association Task Force 2006; Kearney 1993; Almeda 2004; Arnold 2008; Ardehali 2007; Shirakawa 2002; Cini 2008]. The majority of cases reported occur in patients with known risk factors for aortic or coronary artery dissections, known prior to presentation. Over 50% of reported cases of aortic dissection in pregnancy are associated with Marfan or Ehler-Danlos syndrome [von Kodolitsch 2000; American College of Cardiology/American Heart Association Task Force on Practice Guidelines 2006; Mehta 2002; Erbel 2001; Heefner 1973] with the incidence of dissection in pregnancy in Marfan patients being 3%, and similarly there are documented aortic diameter thresholds at which intervention is recommended: 50 mm or an increase of 5 mm per year. Other causes include genetic disorder such as ACTA1 gene polymorphism. On the other hand, one of the main complications is thromboembolic events resulting from hypercoagulation state during pregnancy [Rensing 1999; Bates 2008; Salazar 1984; Weiss 1998; Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology 2003].

We presented successful surgical outcomes of three pregnant women who required urgent cardiovascular surgery because of pregnancy-related cardiovascular complications. Diagnostic and treatment strategies have also been described in this report. In two of three cases, women were operated without cesarean section using a normothermic ECC. According to the previously published cases with spontaneous coronary artery dissection [ESC Guidelines 2011; Chambers 1994; Parry 1996; Chandrasekhar 2009; Weiss 1998; Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology 2003; Regitz-Zagrosek 2008] and aortic dissection [Putnik 2011], operations using normothermic extracorporeal circulation were performed without any side effects in both the mother and fetus.

As a result of low blood flow to the intervillous space during CPB, fetal hypoxia can be seen. The exact cause for the reduced flow is not known but is thought to be insufficient blood flow or uterine artery spasm during extracorporeal perfusion. Therefore, we used levosimendan as an inodilator in the perioperative and postoperative period. Moreover, some authors have reported fetal arrhythmia to be caused by hypothermia rather than being related to maternal oxygenation and acid-base balance, whereas others have reported fetal arrhythmia after use of normothermic perfusion. The reduced fetal heart rate (FHR) during CPB has been reported to be increased [American College of Cardiology/American Heart Association Task Force 2006; ESC Guidelines 2011; Parry 1996], or temporarily restored by increasing maternal blood flow [American College of Cardiology/American Heart Association Task Force 2006; Kearney 1993; Chandrasekhar 2009; Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology 2003; Nasiell 2009; Butchart 2005] and, thus, increasing perfusion pressure. Frequently, FHR is increased temporarily as a result of the restored maternal circulation after discontinuation of ECC, before finally returning to baseline values.

Permanent fetal bradycardia is suggested as a result of high doses of narcotic analgesics [Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology 2003; Inanc 2009]. Furthermore, because of the classic inotropics and high dose narcotics decreasing uteroplacental blood flow and causing permanent bradycardia in the fetus, levosimendan as a potent inodilator was used per- and postoperatively in patients who underwent ECC.

In pregnant women, cardiac output is increased gradually resulting from increased total body volume and heart rate. The heart can increase its size by up to 30%, which is due to dilatation [Thistlethwaite 1998; Aliyary 2007; Almeda 2004]. In addition, pregnancy induces a series of hemostatic changes, with an increase in concentration of coagulation factors, fibrinogen, and platelet adhesiveness, as well as diminished fibrinolysis, which leads to hypercoagulability and an increased risk of thromboembolic events [Rensing 1999; Salazar 1984; Chambers 1994; Parry 1996]. In addition, obstruction to venous return by the enlarging uterus causes stasis and a further rise in risk of thromboembolism.

Coronary artery dissection is an unusual cause of acute coronary syndrome and about 26-38% of cases occur in late pregnancy, peripartum or postpartum [Almeda 2004; Arnold 2008; Ardehali 2007; Cini 2008; Koul 2001; Rensing 1999]. The condition mainly involves left main stem or left anterior descending artery or both [Arnold 2008; Ardehali 2007]. A small number of pregnant women with spontaneous coronary artery dissection have been reported previously in the literature [Aliyary 2007; Kearney 1993; Almeda 2004; Arnold 2008; Ardehali 2007]. The incidence has been reported to range from 0.1-1.1% [Aliyary 2007; Ardehali 2007; Cini 2008]. The cause of spontaneous coronary artery dissection in pregnant women remains unclear. The authors suggested that a medial eosinophilic angiitis, pregnancy-induced degeneration of collagen, and rupture of the vasal vasorum could be main reasons for dissection. Medical therapy, percutaneous coronary intervention (PCI), and CABG have been applied in the acute phase, but optimal therapy has yet to be determined [Almeda 2004; Arnold 2008; Ardehali 2007; Shirakawa 2002; Cini 2008]. We presented a pregnancy-related spontaneous LAD artery dissection, and successful management surgically using ECC without childbirth. We used levosimendan pre- and perioperatively to increase feto-placental blood flow during the operation. Previously published reports showed that revascularization surgery is the preferred mode of treatment in patients with left main stem dissection, multivessel dissection or complex lesions, or in patients with failed coronary intervention [Shirakawa 2002; Koul 2001]. Surgical myocardial revascularization has been shown to achieve good results [Badmanaban 2002; Thistlethwaite 1998; Aliyary 2007]. Maternal mortality during ECC is now similar to that in non-pregnant women who undergo comparable cardiac procedures [Badmanaban 2002; Thistlethwaite 1998], but fetal mortality remains high. Therefore, cardiac surgery is recommended only when medical therapy or interventional procedures fail and the mother's life is threatened, like in our case undergoing on-pump beating heart CABG.

Because pregnancy affects the coagulation state of circulation, it increases the risk of thrombosis of mechanical prosthetic valves or deep veins [Nasiell 2009; Butchart 2005; Chan 2000; Abildgaard 2009]. Warfarin, as an oral anticoagulant, is the most effective drug for the prevention of prosthetic heart valve thrombosis, but the treatment for pregnant women using a high dose warfarin causes highest risk to the fetus [ESC Guidelines 2011; Nasiell 2009]. Coumadin was started in the second trimester of our patient to provide prosthetic valve thrombosis. However, at the third trimester, she was referred to our clinic because of dispnea, orthopnea, and hypotension. Therefore, after cesarean section, we operated immediately under ECC. Prior to discharge in our case, we stopped the LMWH when the INR was over 2.5.

Abildgaard et al reported an incidence of thromboembolic complications in 7.1% of pregnant women with mechanical heart valve who were anticoagulated with low molecular weight heparin (LMWH) during the entire pregnancy; 3.6% for LMWH during first trimester and warfarin in the following two, and 2.4% for nine months oral anticoagulant [Chan 2000]. Given the high teratogenic risk of oral anticoagulant and the elevated rate of miscarriages associated with warfarin derivatives in the first trimester of pregnancy, these drugs should only be used in cases at a very high risk of thromboembolic events, leaving LMWH as the first option for anticoagulation of MPHV in this period [ESC Guidelines 2011; Nasiell 2009; Butchart 2005]. During the second and third trimester, oral anticoagulants seem safe for the fetus [ESC Guidelines 2011; Abildgaard 2009; Inanç 2009; Regitz-Zagrosek 2008]. The ACC/AHA and The European Society for Cardiac Surgery recommend the use of thrombolysis when surgical risk is high or surgery is not possible (7) (24) (28). There is a limited number of pregnant patients who underwent ECC due to mechanical heart valve thrombosis (Inanç 2009; Ozdemir 2009; Kim 2007]. We presented successful mitral valve replacement in a young pregnant patient with prosthetic valve thrombosis [Dogan 2012].

Asymptomatic aortic dissection has been reported in 6.4% of patients with acute aortic dissection. In these patients, hospital mortality was significantly higher. Indeed, because hemodynamic instability developed in our patient with type-I aortic dissection, an ascendant aortic aneurysm with a 47-mm diameter and evidence for intimal flap were detected incidentally using a transthoracic echocardiography. According to our experience, we suggest that the clinicians should be familiar with aortic dissection in pregnant patients without any risk if she has hemodynamic deterioration at each trimester. We hope that progressive dilatation could be presented due to hypertension and volume overloading in our case. When the fetus is viable, cesarean delivery followed directly by aortic surgery is recommended [Kim 2007]. Cesarean section should be performed in a hospital in which cardiothoracic surgery and neonatal intensive care facilities are available.

Conclusion

The cardiovascular complications must be considered when a pregnant woman presents with hemodynamic deterioration, or the pregnant woman has a history of prosthetic

heart valve replacement. Full physical examination including cardiac functions and an aortic pathology should be evaluated by teams including an obstetrician, cardiologist, and anesthetist. In women at high risk, noninvasive methods such as echocardiography and magnetic resonance imaging might be utilized in young females to screen for rare but life-threatening cardiovascular conditions that can occur in every trimester. If cardiac complication occurs at the 28 weeks gestational age, a cesarean section followed by a cardiac surgery is currently the best modality for surgical treatment. When gestational age is lower than 26 weeks, cardiac surgery may be considered without cesarean section in pregnant women with aortic or coronary artery dissection using normothermic ECC. During ECC, FHR and uterine tone should be monitored in addition to standard patient monitoring. To provide adequate uteroplacental blood flow, we suggest levosimendan administration per- and postoperatively in these particular patients.

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