Correspondence to:
Andrej PREVEDEN
Jirečková 3
21000 Novi Sad
Serbia
andrej.preveden@mf.uns.ac.rs

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SUMMARY
Introduction The incidence of aortic dissection ranges 3–5 cases per 100,000 person-years. In women under the age of 40 who acquire aortic dissection, almost half of the cases happen during pregnancy.

Case outline We report a case of a 22-year-old pregnant woman in the 16th gestational week with a history of arterial hypertension and known aortic dilatation, who was admitted with aortic dissection. She underwent the Bentall procedure, in which her aortic valve, ascending aorta, and proximal part of the aortic arch were replaced using valved composite graft. On the next day, the evacuation abortion was made, since the fetus didn't survive the operation. Six years later, the patient stopped taking anticoagulation therapy and was admitted for prosthetic valve thrombosis, which was successfully treated with intravenous heparin. One year later, the patient died of a myocardial infarction due to coronary thromboembolism, confirmed on autopsy.

Conclusion Preconceptional counseling in women with a known aortic disease is of the utmost importance. Aortic dissection in pregnant women is an acute life-threatening condition for both mother and fetus that should be managed by a multidisciplinary team. After a mechanical heart valve implantation, lifetime oral anticoagulants are mandatory.

Keywords: aortic dissection; pregnancy; anticoagulation therapy; prosthetic valve thrombosis; coronary embolism

INTRODUCTION
Aortic dissection (AD) is not a common disease, its incidence ranges 3–5 cases per 100,000 person-years [1]. Although almost two thirds of patients are male, an important fact is that in women under the age of 40 who acquire AD, almost half of the cases happen during pregnancy [2, 3].

The most important risk factor is arterial hypertension, while the others include aortic dilatation and aneurysm, aortic coarctation, bicuspid aortic valve, and connective tissue diseases like Marfan syndrome [2, 4].

Hypertension is considered to be a common disorder during pregnancy. About 1% of pregnant women have preexisting hypertension and about 5% develop gestational hypertension [5].

CASE REPORT
In June 2008, a 22-year-old pregnant woman in the 16th gestational week (GW) was admitted with heavy back and chest pain of sudden onset. She had a history of hypertension for the last five years and had her regular checkups. The last transthoracic echocardiography (TTE) had been performed two years prior to her admittance, when the ascending aorta was found to be dilated with the inner diameter of 43 mm. The patient stopped taking her antihypertensive medications at the start of her pregnancy. Her ambulatory and home-monitored blood pressure (BP) did not exceed 135/95 mmHg.

Admission electrocardiogram (ECG) was normal. TTE revealed dilated ascending aorta (52 mm in diameter on the 2D parasternal long axis view), with a clearly visible intimal flap (Figure 1) that originated from the area of the right aortic cusp. Significant aortic regurgitation grade 3/4 was registered with color Doppler. Fetal echocardiography registered normal fetal heart activity with the frequency of 165 bpm.

An interdisciplinary team consisting of cardiologist, cardiac surgeon, anesthesiologist and...
gynecologist decided to perform an urgent operation, with the fetus left inside the uterus. The Bentall operation was carried out replacing the aortic valve, ascending aorta, and the proximal part of aortic arch with valved composite graft. Light microscopic analysis of the aortic tissue showed a presence of cystic medial necrosis with elastic fibers that were torn and moved apart, as well as a large amount of mucoid substance (Figure 2). The aortic valve had all three cusps, but they were myxomatously degenerated on histology.

The patient left the operating room in a stable condition, but fetal echocardiography on the first postoperative day (POD) showed no heart activity. The team of doctors met once again and decided to terminate the pregnancy, considering the intrauterine death of the fetus and the patient's general condition. The dead fetus and the placental tissue were removed by dilatation and curettage on the second POD. Autopsy and histopathology showed maceration of the fetus without any malformations and abnormalities.

Further postoperative course was uneventful. Postoperative TTE showed normal prosthetic valve function with normal velocities [mean pressure gradient (PG) 8.5 mmHg]. Computerized tomography (CT) of the aorta on the 14th POD confirmed normal position of the tubular graft, but also an existing intimal flap in the aortic arch that extended all the way to the bifurcation of the aorta (Figure 3). After a 24-hour BP monitoring, the patient's antihypertensive therapy was adjusted. She was dismissed on the 20th POD in a good general condition with carvedilol, losartan and methyldopa. Acenocoumarol as an oral anticoagulant with a target internationalized normalized ratio (INR) of 2.0–3.0 was initiated.

Four months later, after heavy physical activity, the patient developed dehiscence of the sternal wound, which was hence resutured. The wound still failed to heal, so several weeks later another resuture had to be undertaken, after which the sternum was finally successfully managed.

The patient was free of symptoms on her medications for the next six years and went to checkups regularly, until July 2014, when she was admitted to the intensive care unit with severe shortness of breath and chest pain. Six days before she had carelessly stopped taking oral anticoagulant therapy.
TTE revealed severe dysfunction of the prosthetic valve with an echo formation measuring 15 × 10 mm in size, attached on the ventricular side with thrombus characteristics and a large embolic potential (Figure 4). The measurements showed obstruction across the valve with high PG (maximum PG 99 mmHg, mean PG 49 mmHg, V_max 5 m/s), along with a significant insufficiency that had a central regurgitation jet. Cinefluoroscopy revealed one completely immobile leaflet (Figure 5). CT scans of the aorta showed the progress of the false lumen in the descending aorta with a significant parietal thrombosis. The diameter of the descending aorta on CT was 45 mm in total, out of which only 5 mm was the true lumen, since the false lumen was 21 mm and the thrombosis 19 mm.

The patient was considered to have a high risk for a redo operation (EuroSCORE II was 18.97%), so she was treated conservatively with an intravenous unfractionated heparin (UFH) infusion. The UFH dosage had been adjusted in the 1,200-1,700 IU/h interval, depending on the values of APTT that was checked on a regular basis.

Further TTE exams showed graduate lysis of the previously registered echo mass, normalization of the prosthetic valve function, and a PG decrease. After 40 days of continuous intravenous UFH infusion and regular periodic TTE exams, oral anticoagulation therapy with acenocoumarol was continued. Because of the prolonged heparin use and its potential effect on heparin-induced thrombocytopenia (HIT), platelet count was checked regularly. Nonetheless, it remained normal the entire time. The patient was discharged from the hospital in a clinically stable condition with target INR between 2.0 and 3.0.

One year later, in April 2015, the patient was admitted as an emergency case once again because of chest pain and serious shortness of breath. The admission ECG raised a suspicion for a myocardial infarction (MI) (Figure 6) and laboratory tests revealed elevated cardiac enzymes. Shortly upon admission, the patient had cardiac arrest with pulseless electrical activity. Cardiopulmonary resuscitation was performed, but the patient died.

The autopsy discovered that the reason for the MI was a thromboembolus in the left anterior descending coronary artery (LAD) without any atherosclerotic changes. There were signs of acute transmural MI in the anterior and lateral wall of the myocardium. On the cross pathology, the area of the MI was pale yellow and soft, surrounded by a hyperemic zone. On the histologic section, cardiomyocytes were necrotic with the loss of nuclei and striations, the interstitium was edematous with the presence of a dense infiltrate of neutrophils (H&E, 20×).
DISCUSSION

AD in pregnant women can be explained by hormone-mediated and hemodynamic changes during pregnancy that increase the aortic wall stress. Tachycardia and rise in cardiac output are the most prominent ones, because of their effect on hemodynamic stress on the arterial walls. Stimulation of the estrogen receptors in aortic tissue causes connective fiber fragmentations and acid mucopolysaccharides reduction, leading to the reduced wall elasticity. The aortic stress can also be increased by the gravid uterus that compresses the aorta [6].

Our patient had neither a positive family history of aortic diseases nor the other Marfan features like spine or chest deformities that would indicate the presence of this syndrome [7, 8]. Previously diagnosed hypertension and dilated aorta were the risk factors that immediately raised the suspicion for the right diagnosis in this case. Hypertension in pregnancy is often related to preeclampsia and eclampsia, however in this case it was present from before and there was no proteinuria [9]. The latest discoveries suggest that the loss of nocturnal BP drop (the so called non-dipping pattern) may be the main cause of cardiovascular dysfunction and hemodynamic impairment in pregnancy, rather than just hypertension by itself [10].

Most of the antihypertensive drugs are avoided during pregnancy because of their side effects on the fetus. Drugs that are recommended are methylodopa, nifedipine, and labetalone, while angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are contraindicated [11]. According to the current guidelines, antihypertensive therapy in pregnant women who are without any symptoms and signs of organ dysfunction is recommended when the BP levels reach > 160 mmHg for systolic or > 110 mmHg for diastolic BP, and may be considered for BP ≥ 150/95 mmHg [9, 11]. Considering that our patient did not have BP levels above 140/90 mmHg during pregnancy according to the history data and home-based measurements, stopping her antihypertensive therapy was justified and according to guidelines.

Dilated ascending aorta in our patient was noticed two years prior to her pregnancy, 43 mm in diameter on TTE. An indication for elective surgery of the ascending aortic aneurysm is the diameter ≥ 55 mm, but for patients with Marfan syndrome or other risk factors, this threshold can be lowered to 45 mm according to the current guidelines [12]. As a separate recommendation, it is stated that lowering this threshold even more may be considered in the case of planned pregnancy, but thresholds are not specified.

TTE should be performed monthly or every other month during pregnancy in patients with known dilated ascending aorta to identify the potential progress of the aortic diameter, and if indicated undertake surgery on time, thus preventing potential unwanted incidents [13]. Unfortunately, our patient hadn’t had a TTE exam during the pregnancy, so possible progressive dilatation of her ascending aorta couldn’t have been recognized.

Management of AD involving ascending aorta (Stanford type A) is an urgent surgery, because of high mortality in patients who are not operated on, which reaches 50% in the first 48 hours [12, 13]. In the case of acute AD during pregnancy, management protocols depend on the gestational age. If the pregnancy is older than 28 GW (third trimester), it is indicated to deliver the baby with caesarean section first, and then perform surgery of the aorta [14]. Our patient was in the 16th GW and the caesarean section was not an option, so the urgent surgery of the aorta was undertaken immediately.

Echocardiography is a basic diagnostic modality for aortic diseases. However, a negative TTE does not rule out AD. Other imaging techniques such as transesophageal echocardiography (TEE), CT, and magnetic resonance have a greater field of view and may provide additional information important for the operation [15], but in this case the diagnosis of the dissection and the decision for surgical treatment was made using solely TTE, which, according to the literature, has a sensitivity and specificity of 75% and 90%, respectively [4]. Precious time was saved by skipping TEE and CT scan, and the negative effects of CT radiation and contrast agents were avoided.

The patient survived the cardiac surgery, but the stress on the fetus was apparently too strong and it died, so the evacuation abortion was undertaken the next day. There is a limited number of similar cases in the literature. Majority of them describe the dissection in the third trimester, which is in fact the most vulnerable period [16, 17, 18]. Only two case reports describe the surgical repair of Stanford type A AD before the third trimester with maternal and fetal survival in both of them [19, 20]. Liu et al. [21] reported five cases of Bentall operation in Stanford type A AD during pregnancy, only one of which happened before the third trimester (22 GW), with both mother and fetus diseased.

There are multiple possible reasons for the fetal death. The main ones being the dissection itself, with the intimal flap potentially compromising the placental perfusion, as well as the factors associated with the operation, including cardiopulmonary bypass and circulatory arrest. Hypothermia during bypass has also shown to worsen the fetal prognosis [22].

The tissue sample of the ascending aorta that was sent to light microscopic histopathology showed cystic medial necrosis, which is a typical finding in Marfan syndrome [7]. Considering the significantly higher burden of acute aortic syndromes in Marfan patients, recognizing this syndrome in our patient could have improved her follow-up. She had an aneurysm of the ascending aorta, which is a major criterion for Marfan syndrome diagnosis, yet criteria on other organ systems (skeletal, ocular, respiratory, skin) were not fulfilled [8].

The patient was released from hospital with a combined antihypertensive therapy including losartan. A number of studies on animal and human models have demonstrated that losartan improves endothelial function and has a positive effect on aortic root stabilization [23].

The necessity of a lifetime anticoagulation therapy after mechanical valve implantation is clearly demonstrated in this case [24]. The patient had stopped taking oral anticoagulants for an unknown reason, and during that period of...
time she was not protected with a low-molecular-weight heparin. This led to valve thrombosis in only a few days, causing its malfunction and resultant heart failure.

The diagnosis of prosthetic valve thrombosis was based on the findings of TTE and cinefluoroscopy. TTE provided a proper diagnostic assessment with 2D echo when an echo mass (15 × 10 mm) attached at the ventricular side of the prosthetic valve was registered. High velocity and elevated transprosthetic gradients were measured with Doppler echo.

Usually, urgent surgery is the treatment of choice in such critically ill patients with obstructive valve thrombosis [24]. Therapeutic strategy in this case was mainly influenced by the risk assessment, which was too high for a redo operation, so being aware of the prosthesis location, the presence of a valvular obstruction, and the patient’s clinical status, heparin infusion was started. This led to prosthetic valve function recovery after two months. The prolonged heparin use did carry an increased risk of complications like hemorrhage and HIT; however, they were fortunately avoided. From the aspect of HIT, low-molecular-weight heparin might have been a better choice over UFH. Recent studies show lower incidence of HIT with the use of low-molecular-weight heparin in comparison to UFH, without a significant difference in therapeutic effect [25].

Nine months later, the cause of death was a massive transmural MI. The autopsy showed that the MI was caused by thromboembolism in the LAD. There were no atherosclerotic plaques in coronary arteries. The reported incidence of thromboembolism after Bentall operation is around 0.7% events per year, which is mainly associated with inadequate anticoagulation [26]. The main cause of coronary thromboembolism is atrial fibrillation [27]. Although our patient was in sinus rhythm, she did have a few other risk factors, including previous cardiac surgery, non-infected thrombi on prosthetic valve, and intraluminal thrombosis inside the chronic dissection of the descending aorta, which are all described as rare but possible causes of coronary thromboembolism [27, 28]. There is scarce data in literature describing coronary thromboembolism after Bentall operation [29, 30]. As in our case, coronary thromboembolism was also caused by prosthetic valve thrombosis due to inadequate coagulation in the described cases.

In conclusion, we can say that even though this pregnancy could have been classified as a high-risk one, considering the patient’s hypertension and known aortic disease, the follow-up was not as thorough as it should have been and the preconceptional counseling failed. Taking everything into account, it might have been wise to consult the patient against pregnancy. BP levels during pregnancy probably haven’t been monitored regularly since the antihypertensive therapy was discontinued, which might have contributed to the damage of the aorta. In the setting of acute chest pain and distress in pregnancy, AD should always be suspected.

Echocardiography is rapid, accurate, and cost-effective in the diagnosis and follow-up of aortic diseases. In contrast to the poor pregnancy follow up, the reaction of the multidisciplinary team managing AD was prompt and appropriate to this life-threatening condition, saving the woman’s life but unfortunately losing the baby. Mandatory lifetime oral anticoagulants after a mechanical valve implantation is clearly demonstrated in this case.

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REFERENCES


Трудница преживела дисекцију аорте, а касније умрла због коронарне емболије – јединствен случај несарарадњивог болесника

Андреј Преведен1,2, Голуб Самарџија1,2, Стаменко Шушак1,2, Александар Реџек1,2
1Универзитет у Новом Саду, Медицински факултет, Нови Сад, Србија;
2Институт за кардиоваскуларне болести Војводине, Сремска Каменица, Србија

САЖЕТАК
Увод Често се дисекција аорте среће у пет почетних година од 40 година, а касније се један месец. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду.

Приказ болесника Приказ болесника уређен је у више глави. У глави једноствености и допуном аорте, у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду. У овој раду, касније се дисекција аорте у каснијем периоду.