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Cardiovascular Diseases During Pregnancy

Gebelik Seyrinde Kardiyovasküler Hastalıklar

ABSTRACT

Pregnancy-associated hemodynamic changes may cause severe complications in patients with cardiovascular diseases. It may also reveal previously undiagnosed conditions or worsen existing ones. To prevent maternal and fetal complications during pregnancy, a thorough evaluation of the pregnant woman's cardiac history, symptoms, functional capacity, and physical examination should be conducted, in line with current risk classification systems. In this case series, we present the course of pregnancy in four patients with severe cardiac pathology.

Keywords: Congenital heart diseases, pregnancy, cardiac function

ÖZET

Kardiyovasküler hastalığı olan kadınlarda, gebeliğe bağlı ortaya çıkan hemodinamik değişiklikler, ciddi komplikasyonlara sebep olabilir. Daha önceden tanı almamış hastalarda, gebelik kalp hastalığının aşikar hale gelmesine ya da bilinen hastalığın şiddetlenmesine neden olabilir. Gebelikte maternal ve fetal komplikasyonların önlenmesi için, güncel risk sınıflama önerilerine göre, gebelik öncesi öykü, semptomlar, fonksiyonel kapasite ve fizik muayene bulguları değerlendirilmelidir. Vaka serimizde, ciddi kardiyak patoloji bulunan 4 hastanın gebelik sürecini sunmayı amaçladık.

Anahtar Kelimeler: Doğumsal kalp hastalıkları, gebelik, kalp fonksiyonları

CASE REPORT
OLGU SUNUMU

Pregnancy causes significant hemodynamic changes. Increases in both plasma volume and red cell count lead to hypervolemia. Maternal cardiac output increases by 30% to 50% compared to its pre-pregnancy state, with the peak increase occurring at the 32nd week of pregnancy.[1,2] Circulating albumin concentration decreases by 12% to 18% from its baseline during pregnancy, reaching its lowest level at the 24th week of gestation.[3] Maternal heart rate progressively increases, peaking in the third trimester. Arrhythmias are not uncommon during pregnancy; left axis shift due to diaphragmatic elevation, ST depression, or inverted T waves may also be observed.[1,4] A decrease in systemic vascular resistance occurs, linked to reductions in both preload and afterload. Pulmonary artery pressure remains constant due to decreased pulmonary vascular resistance, which coincides with an increase in pulmonary blood flow.[1,4,5] Labor is associated with increased oxygen consumption and heightened preload due to uterine autotransfusion, potentially causing hemodynamic decompensation in patients with cardiac disease. These alterations may cause severe complications in patients with cardiovascular pathologies.[5] In this case series, we present four cases of patients with severe cardiac disease. Informed consent was obtained from all patients.

Case Report

Case 1

A 28-year-old female patient, who had undergone mechanical aortic valve replacement 10 years ago due to severe aortic stenosis related to acute rheumatic fever at the age of 11, was admitted to the cardiology outpatient department for routine yearly follow-up. She had no complaints, and her New York Heart Association (NYHA) functional capacity (FC) was Class II. She was taking metoprolol 50 mg once daily and warfarin. A targeted International Normalized Ratio (INR) level of 2.5 international units (IU) was achieved with 12.5 mg/day of warfarin. Her physical examination revealed a 3/6 systolic murmur in the aortic area, without any other pathological findings. Her electrocardiogram (ECG) showed sinus tachycardia and an incomplete right bundle branch block.

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Transthoracic echocardiography (TTE) revealed a mean gradient of 20 mmHg across the mechanical aortic valve. Transesophageal echocardiography showed mild valve degeneration without any mass, vegetation, or thrombus. She was advised about the risks of pregnancy. After three months, she was admitted to the cardiology inpatient clinic at the 5th week of a twin pregnancy. She has already discontinued warfarin treatment two weeks prior. Low molecular weight heparin (LMWH), specifically enoxaparin 0.6 cc twice a day subcutaneously, was initiated and adjusted according to her weight. Her Anti-Factor Xa level was monitored weekly, with a target range of 0.8-1.2. After three weeks, her Anti-Factor Xa level was measured at 0.7, so the LMWH dose was increased from 0.6 cc twice daily to 0.8 cc twice daily. Weekly TTE assessments showed an increased gradient across the mechanical aortic valve, consistent with advancing gestational age and increased volume overload. At the same time, her B-type natriuretic peptide (BNP) level was 210 pg/mL. The Anti-Factor Xa levels were monitored weekly for 12 weeks and maintained between 0.8-1.2. In the 17th week of gestation, she was hospitalized to switch anticoagulant treatment. Low molecular weight heparin was discontinued, and warfarin was initiated. A targeted INR was achieved with 12.5 mg of warfarin daily. At the 29th week of gestation, she developed severe itching with urticarial lesions and was diagnosed with an atypical eruption of pregnancy. Her symptoms resolved with methylprednisolone lotion and antihistamine treatment. In the 31st week, she was hospitalized due to the risk of preterm delivery. Anticoagulant treatment was switched back to enoxaparin 0.8 cc subcutaneously twice daily, with close monitoring of Anti-Factor Xa levels. The LMWH dose was increased to 1 cc twice daily for the last three weeks. At 35 weeks, she delivered twin babies via Cesarean section (C/S) under epidural anesthesia with normal Apgar scores (both baby girls; 1st baby: 2,255 g, Apgar score 9/10; 2nd baby: 2,500 g, Apgar score 8/10). After delivery, the patient was stable and asymptomatic and was discharged on the 7th day postpartum. At a follow-up visit three months later, her INR level was 2.5 with 12.5 mg/day warfarin, and TEE findings were consistent with pre-pregnancy results. Both baby girls showed normal development, and no congenital anomalies were detected. The patient continued breastfeeding for six months without any complications.

ABBREVIATIONS

6MWT	Six-minute walking test
ACEI	Angiotensin-converting enzyme inhibitor
AV	Atrioventricular
BB	Beta blockers
BNP	B-type natriuretic peptide
C/S	Cesarean section
cC-TGA	Corrected transposition of the great arteries
CT	Computed tomography
ECG	Electrocardiogram
FC	Functional capacity
HF	Heart failure
INR	International Normalized Ratio
IU	International units
LMWH	Low molecular weight heparin
LVEF	Left ventricular ejection fraction
NYHA	New York Heart Association
PAP	Pulmonary artery pressure
TOF	Tetralogy of fallot
TTE	Transthoracic echocardiography
VSD	Ventricular septal defect
WHO	World Health Organization

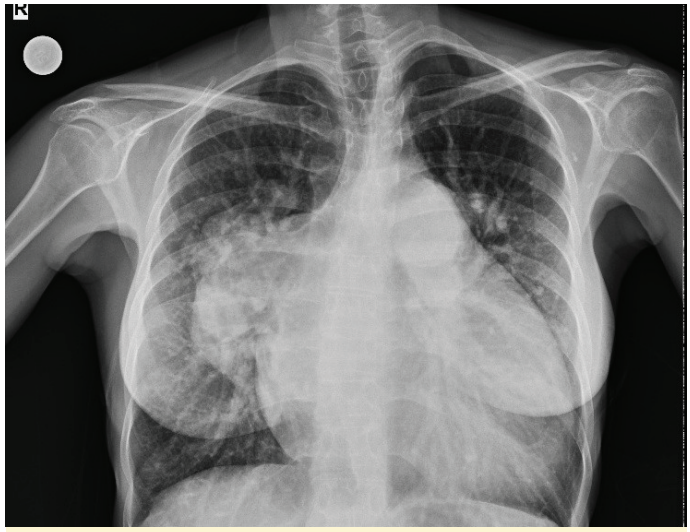

Figure 1. Increased cardiothoracic ratio with a dilated pulmonary artery on chest X-ray.

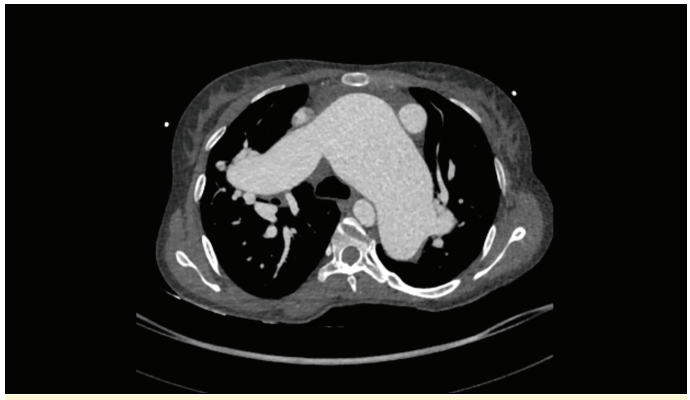

Figure 2. Dilated pulmonary trunk on computed tomography (CT) pulmonary angiography.

Case 2

A 34-year-old female patient was admitted to the cardiology outpatient clinic at 27 weeks of pregnancy. She had a complex congenital heart disease and was referred to our clinic. It was noted that she had been admitted to another hospital nine years prior with dyspnea. At that time, a chest X-ray demonstrated an increased cardiothoracic ratio with a dilated pulmonary artery (Figure 1). Transthoracic echocardiography revealed atrioventricular and ventriculo-arterial discordance, a 3.5 cm perimembranous ventricular septal defect, mild-to-moderate atrioventricular (AV) regurgitation, a systolic gradient of 50 mmHg across the aortic valve, and a systolic gradient of 100 mmHg across the pulmonary valve with a pulmonary artery aneurysm. Computed tomography (CT) of the thorax, performed seven years after the initial diagnosis and two years before pregnancy, revealed that the pulmonary artery measured 78 mm at its widest point (Figure 2). Right heart catheterization findings

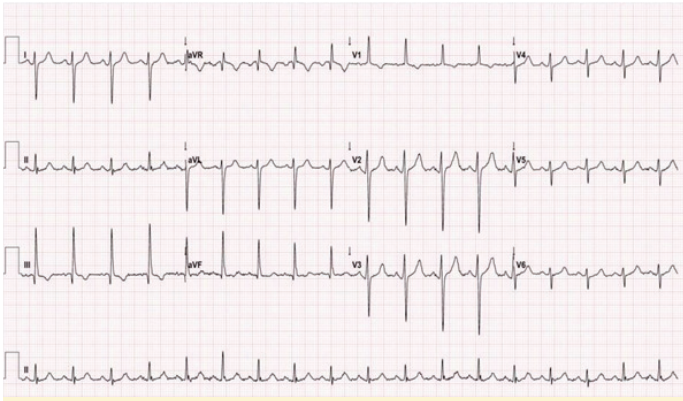

Figure 3. Right bundle branch block (RBBB) on electrocardiogram (ECG).

were consistent with TTE, confirming corrected transposition of the great arteries with ventricular septal defect (VSD) (cC-TGA), as well as aortic and pulmonary stenosis. At that time, the patient declined further procedures due to the high risk of surgical intervention and did not attend regular follow-up visits.

At her first admission to our cardiology department after becoming pregnant, she was asymptomatic. Physical examination revealed a 4/6 systolic murmur radiating to the left sternal border with a palpable thrill. Despite having a large VSD and pulmonary stenosis, she exhibited no cyanosis or clubbing in her extremities at rest. Her arterial oxygen saturation was 96%. An ECG showed atrial fibrillation, and LMWH in the form of enoxaparin 0.4 cc twice daily was administered during pregnancy. Although she experienced supraventricular tachycardia, her ventricular rate remained stable, and no additional treatment was required. Her laboratory parameters were within normal limits, except for a high pro-B-type natriuretic peptide (pro-BNP) level of 1650 pg/mL. She visited the cardiology outpatient department weekly for follow-up, and her functional capacity remained stable throughout the pregnancy. At 35 weeks of pregnancy, she was admitted with new-onset dyspnea. After obstetric evaluation, she was hospitalized due to the risk of cardiac decompensation. A Cesarean section was performed under epidural anesthesia, resulting in the delivery of a baby boy (2,255 g, Apgar score 9/10) without complications. She was discharged on the 7th day post-delivery under LMWH therapy. One month later, she was re-hospitalized with dyspnea and swelling in her abdomen and both legs. It was discovered that she had discontinued her medications to breastfeed, despite being advised against breastfeeding. Her pro-BNP level had risen to 10,650 pg/mL. Transthoracic echocardiography showed increased dilatation of the right heart chambers and decreased right ventricular function. Pulmonary thromboembolism was ruled out via CT pulmonary angiography. Intravenous (IV) diuretic treatment was administered until compensation was achieved, and she was discharged on the 6th day with oral diuretic therapy. The patient was once again advised not to breastfeed. One month after discharge, enoxaparin was discontinued, and apixaban 5 mg twice daily was prescribed.

Case 3

A 22-year-old female patient was admitted to the cardiology outpatient department at the 25th week of pregnancy. She was referred to our clinic due to a heart murmur and cyanosis. Her medical history revealed only mild cyanosis and dyspnea on heavy exertion. At the time of admission to our clinic, her NYHA functional capacity was Class II. Physical examination revealed a pulse rate of 100 beats per minute, oxygen saturation of 85% at rest, central cyanosis, clubbing of all fingers, and a 4/6 pansystolic murmur radiating to the left sternal border. Her hemoglobin and hematocrit levels were 13.3 g/L and 40.5%, respectively. Electrocardiography showed sinus rhythm with an incomplete right bundle branch block (Figure 3). Transthoracic echocardiography revealed normal left ventricular function, a large non-restrictive 14 mm VSD, a dilated coronary sinus due to a persistent left superior vena cava, a maximum systolic gradient of 82 mmHg (mean 44 mmHg) across the pulmonary valve, and right ventricular hypertrophy with normal function. Her six-minute walking test (6MWT) distance was 350 meters, and her O2 saturation dropped from 77% to 48% during the test. Her pro-BNP level was within normal limits (67 ng/mL). A Holter ECG demonstrated an incomplete right bundle branch block (RBBB). Obstetric evaluation and fetal echocardiography were normal. It was decided to follow the patient weekly in the cardiology outpatient clinic. At the 34th week of gestation, she was admitted with presyncope and palpitations and was hospitalized for further evaluation. No arrhythmias were detected during her hospital stay. It was determined that she had vasovagal symptoms, particularly associated with standing up or vascular access attempts, during which her cyanosis worsened. Fluid balance was regulated, and nasal oxygen was administered at 2 L/min. Obstetric evaluation remained normal, and subsequent follow-up continued in the hospital. Due to a urinary tract infection, the patient received IV antibiotic therapy. After the treatment was completed and the patient's symptoms resolved, a C/S was performed under epidural anesthesia at the 36th week of pregnancy (delivered a baby boy, 2,310 g, Apgar score 8/10). She was discharged on the 5th postoperative day without complications. The necessity of surgery for her VSD with pulmonary stenosis was explained to her, but she expressed a desire to postpone the operation due to the pandemic. Since she had no complaints during breastfeeding, it was decided that she could continue breastfeeding.

Case 4

A 31-year-old woman, who had given birth by elective C/S at 38 weeks to a healthy baby boy four days prior, was admitted to the cardiology outpatient department with dyspnea. Her medical history included a diagnosis of Ewing sarcoma, for which she had received chemotherapy and radiotherapy 19 years ago. Ten years after her cancer treatment, she presented to the cardiology clinic with palpitations, and TTE revealed a reduced left ventricular ejection fraction of 45%, with otherwise normal findings. She was started on beta blockers (BB) and an angiotensin-converting enzyme inhibitor (ACEI). After using this treatment for six months, she discontinued it due to pregnancy. That pregnancy was carried to term with a C/S delivery at 39 weeks, resulting in the birth of a healthy baby. Six months after delivery, her medication regimen was restarted. Ten years later, during the follow-up at the 8th week of her second pregnancy, TTE again showed an LVEF of 45%, and she was advised to attend regular follow-ups for mild heart

failure (HF). Despite these recommendations, she stopped all medications and did not attend follow-up appointments. At 38 weeks of gestation, a C/S with epidural anesthesia was performed at another hospital, and she was discharged after two days without complaints. On the 3rd postoperative day, she developed worsening dyspnea and was then readmitted to the emergency unit, where she was referred to the cardiology clinic. She had no history of hypertension, diabetes mellitus, drug use, smoking, or alcohol consumption. She experienced orthopnea, and physical examination revealed tachycardia and bilateral rales in the basal areas of the lungs. Electrocardiography on admission demonstrated sinus tachycardia at 98 beats per minute and an incomplete left bundle branch block. A chest X-ray showed cardiomegaly with pulmonary edema. Transthoracic echocardiography revealed a left ventricular ejection fraction (LVEF) of 30% and a maximum systolic pulmonary artery pressure of 70 mmHg. Computed tomography pulmonary angiography was normal. She was transferred to the coronary intensive care unit, where she received supplemental oxygen, intravenous furosemide infusion, beta blockers, angiotensin-converting enzyme inhibitor, and spironolactone. Her symptoms and hypoxemia resolved, and she was discharged after seven days. At her six-week postpartum follow-up, TTE demonstrated an LVEF of 45% with normal systolic pulmonary artery pressure (PAP) while on BB, ACEI, spironolactone, and oral furosemide. She was advised not to become pregnant again due to the increased risk of mortality and morbidity. Given the potential side effects of her medications, she was also advised not to breastfeed.

Discussion

According to the World Health Organization (WHO)[6] classification, women in Class III-IV are at high cardiovascular risk during pregnancy.[5] This includes those with mechanical valves, unrepaired cyanotic congenital heart disease, and mild-to-moderate left ventricular (LV) dysfunction, which are classified under WHO Class III. These patients face a significantly increased risk of morbidity and mortality.[7] Pregnancy and delivery are associated with heart failure, arrhythmias, thromboembolic, and hemorrhagic complications in patients with mechanical heart valves. While warfarin is the standard treatment for mechanical valves, its use during the 6th-12th gestational weeks may cause severe embryopathy.[8] The risk of fetal complications is dose-dependent, with maternal warfarin doses greater than 5 mg per day increasing the risk.[9] Thromboembolic complications during low molecular weight heparin use are often due to subtherapeutic anticoagulation levels.[10,11]. Peak and trough levels of Anti-Xa should be carefully managed, with a target peak level of 1-1.2 U/mL and a trough level greater than 0.6 U/mL.[6,8,10,11] If the required daily warfarin dose is less than 5 mg, guidelines recommend its use during the first trimester of pregnancy. Apart from this, switching to dose-adjusted LMWH or IV unfractionated heparin is required.[6,12] The risk of thromboembolic complications with LMWH is lower in patients with a mechanical valve in the aortic position. In our patient, close and careful management of Anti-Xa levels, along with the aortic position of the mechanical valve, resulted in better maternal and fetal outcomes.

Unrepaired congenital heart disease is associated with symptomatic heart failure, worsening systemic atrioventricular valve regurgitation, arrhythmias, and endocarditis in pregnant patients. Conduction system disturbances and supraventricular arrhythmias are common in pregnant patients with corrected transposition of the great arteries (cC-TGA).[13,14] Our patient with cC-TGA and normal systemic ventricular function without hypoxemia experienced favorable outcomes during pregnancy. However, after delivery, she experienced worsening heart failure symptoms, which were resolved with furosemide treatment. She also had atrial fibrillation with a normal ventricular rate, likely due to conduction disturbances.

Ventricular septal defect with pulmonary stenosis is associated with maternal and fetal complications.[15,16] The coexistence of VSD and pulmonary stenosis may lead to a misdiagnosis of tetralogy of fallot (TOF). Anterocephalad deviation of the outlet septum is the morphological marker for differential diagnosis, causing infundibular stenosis of the pulmonary valve.[17] Our patient experienced vasovagal symptoms and presyncopal attacks but no actual syncope. Her Holter ECG demonstrated normal sinus rhythm. It was thought that the patient's young age and normal right ventricular function contributed to a favorable pregnancy outcome.

Left ventricular systolic dysfunction is an important predictor of worse maternal and fetal outcomes.[6] Our patient's left ventricular systolic dysfunction developed due to the chemotherapy and radiotherapy she received for Ewing sarcoma in childhood. She had no complaints after her first pregnancy and was treated with BB and an ACEI until her second pregnancy. Throughout her second pregnancy, she was asymptomatic. However, on the second postoperative day, her condition worsened due to volume overload related to childbirth, and TTE revealed a reduced LVEF of 30% with increased pulmonary artery systolic pressure of 70 mmHg. Due to delivery, the patient's initially mild HF progressed to severe HF, leading to pulmonary edema. In the coronary intensive care unit, her symptoms improved with furosemide, ACEI, BB, and spironolactone treatment. After six weeks, her LVEF returned to its pre-pregnancy level. It is important to note that in pregnant women with reduced left ventricular function, acute heart failure may develop due to the increased volume load in the first days following delivery. Close follow-up and treatment of these patients is required, even if the pregnancy itself is uneventful.

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