

A successful cesarean delivery without fetal or maternal morbidity in an Eisenmenger patient with cor triatriatum sinister, double-orifice mitral valve, large ventricular septal defect, and single ventricle who was under long-term bosentan treatment

Uzun süreli bosentan tedavisi altındaki kor triatriyatım sinister, çift girişli mitral kapak, geniş ventriküler septal defekt ve tek ventrikülü olan Eisenmenger sendromlu hastada fetal ve anne morbiditesi olmadan başarılı sezaryen doğum

Hacer Ceren Tokgöz, M.D., Cihangir Kaymaz, M.D.,# Nertila Poci, M.D.,#

Özgür Yaşar Akbal, M.D.,# Selçuk Öztürk, M.D.#

Department of Cardiology, Haydarpaşa Numune Training and Research Hospital, İstanbul, Turkey

#Department of Cardiology, Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital, İstanbul, Turkey

Summary– Presently described is successful cesarean delivery in a pregnancy superimposed on long-term bosentan treatment in an Eisenmenger syndrome patient with cor triatriatum sinister, double-orifice mitral valve, and large ventricular septal defect resulting in single functioning ventricle with double outlets. Cesarean delivery was performed at 27th week of gestation without maternal or fetal morbidity. The infant had no congenital cardiovascular abnormality or any probable teratogenic effect of bosentan treatment during pregnancy.

Özet– Bu yazıda, kor triatriyatım sinister, çift girişli mitral kapak, çift çıkışlı fonksiyonel tek ventriküle neden olan geniş ventriküler septal defekti olan ve uzun süreli bosentan tedavisi altındaki gebe bir Eisenmenger sendromlu hastada başarılı sezaryen doğum sunuldu. Sezaryen doğum gebeliğin 27. haftasında anne veya fetal morbidite olmadan gerçekleşti. Bebekte herhangi bir doğumsal kalp anomalisi ya da gebelik boyunca bosentan kullanımına bağlı teratojenik etki yoktu.

Eisenmenger syndrome is a form of pulmonary arterial hypertension associated with congenital heart disease. The congenital abnormality comprises large systemic-to-pulmonary shunt that eventually becomes pulmonary-to-systemic or bidirectional shunt. It is multisystem disorder with cyanosis and hematological changes, including secondary erythrocytosis, thrombocytopenia, and less frequently, leucopenia.^[1] Systemic vasodilation in pregnancy increases right-to-left shunt and worsens cyanosis, leading to low output state. This condition increases maternal mortality in peripartum period, as well as fetal and neonatal mortality and morbidity.^[2]

Abbreviations:

COC	Combined oral contraceptive
GA	General anesthesia
IUD	Intrauterine device
RA	Regional anesthesia

This case report is a description of peripartum management of a pregnant patient with Eisenmenger syndrome.

CASE REPORT

A 22-year-old female patient with previously diagnosed Eisenmenger syndrome was referred to our center in 2009 with progressive dyspnea occurring at 27th week of an unmonitored pregnancy. At admission, she had no symptom or complication other than dyspnea at rest.

She had previously been diagnosed with complex congenital abnormalities, including cor triatriatum sinister, double-orifice mitral valve, and large ven-

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Correspondence: Dr. Hacer Ceren Tokgöz. Abdurrahmangazi Mah., Sevenler Cad., Lagün Sitesi, E9, D: 3, Sancaktepe, İstanbul, Turkey.

Tel: +90 216 - 542 32 32 e-mail: hacerceren@yahoo.com

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tricular septal defect resulting in double outlet right ventricle without pulmonary stenosis.

With confirmed diagnosis of Eisenmenger syndrome and baseline World Health Organization (WHO) class III status, bosentan therapy (125 mg twice a day) had been initiated 1 year earlier. Due to unavailability of grown-up congenital heart disease unit or pulmonary hypertension referral center near the patient's residence, regular follow-up had not been possible.

Right heart catheterization performed at time of diagnosis (1 year earlier) revealed pulmonary arterial systolic pressure of 125 mmHg and pulmonary arterial mean pressure of 80 mmHg. Systemic systolic, diastolic, and mean pressures were 111, 69, and 71 mmHg, respectively. Vasoreactivity test performed with intravenous adenosine was negative. Baseline 6-minute walking distance was 435 m.

At admission, the patient was WHO class IV, with systemic arterial blood pressure of 110/70 mmHg, regular pulse rate of 100 bpm and blood oxygen saturation level of 93% in room air. Physical examination revealed jugular venous congestion with evident systolic "v" wave. Accentuated pulmonary closure sound with right-sided holosystolic murmur and left-sided diastolic murmur were also audible. Electrocardiogram revealed sinus rhythm with right ventricular hypertrophy and right axis deviation. Hemoglobin, hematocrit and platelet values were 15.4 g/dL, 43.8%, and $205 \times 10^3/\mu\text{L}$, respectively.

Maternal transthoracic and transesophageal 2-dimensional echocardiography and color Doppler im-



Figure 1. Transesophageal 2-dimensional echocardiography revealed cor triatriatum sinister, double-orifice mitral valve, large ventricular septal defect, and double outlet right ventricle. VSD: Ventricular septal defect.

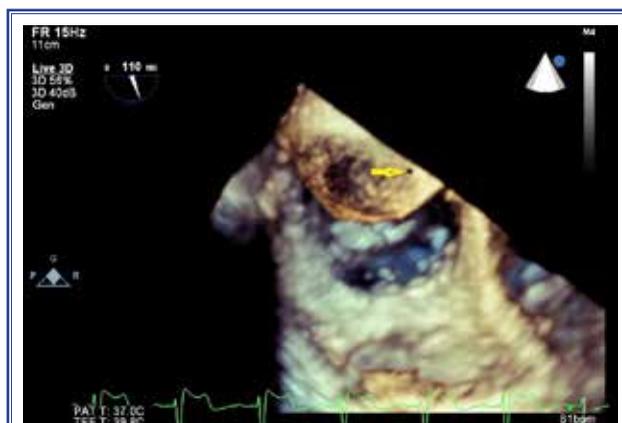


Figure 2. Real-time 3-dimensional transesophageal echocardiography showed defect on membrane of cor triatriatum sinisterum.

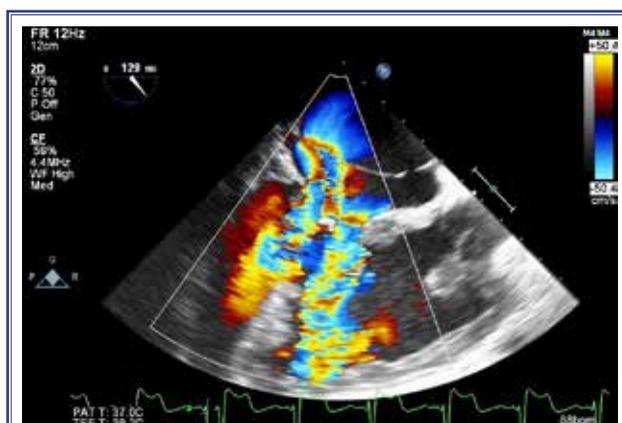


Figure 3. Color Doppler imaging of transesophageal 2-dimensional echocardiography illustrated cor triatriatum sinisterum, double-orifice mitral valve, large ventricular septal defect, and double outlet right ventricle.

aging confirmed severe pulmonary hypertension concomitant with cor triatriatum sinisterum, double-orifice mitral valve, large ventricular septal defect, and double outlet right ventricle (Figures 1, 3). Diameter of pulmonary artery was 32 mm. In the left atrium, maximum and mean gradients on membrane of cor triatriatum sinisterum were measured at 10 and 5 mmHg, respectively. Real-time 3-dimensional transesophageal echocardiography showed defect in membrane of cor triatriatum sinisterum as illustrated in Figure 2. Systolic function of ventricle was normal.

After hospitalization, she continued to receive bosentan. Council of cardiology and obstetrics decided to terminate the pregnancy with cesarean section. Interdisciplinary approach of members of cardiology, cardiovascular surgery, obstetrics, anesthesiology, in-

tensive care, and perinatology departments yielded successful cesarean delivery performed under general anesthesia (GA), following 3 days of corticosteroid treatment to augment fetal lung maturation. In present case, we continued bosentan therapy during postpartum period, as well as diuretic therapy to avoid volume overload. Our patient did not receive anticoagulation treatment during pregnancy or peripartum period because of high bleeding risk, nor were pharmacological agents (e.g., intravenous epoprostenol, nitric oxide) added to treatment.

The infant was born without any sign of congenital cardiovascular abnormality or probable teratogenic effects due to bosentan treatment during pregnancy.

Following routine postnatal care and 30 days follow-up in perinatal intensive care unit, both the baby and the mother were discharged without any problem. Bosentan treatment was maintained.

DISCUSSION

Pregnancy in patients with Eisenmenger syndrome is associated with high risk of intrauterine fetal death and maternal mortality.^[3-12] In these patients, maternal mortality is reported to be up to 50%, and it has remained unchanged in the past 5 decades.^[4,6-10] Furthermore, risk of maternal mortality is unpredictable on individual basis.^[8-12] Due to increased and fixed pulmonary arterial resistance, hemodynamic alterations during labor, delivery, and puerperium cannot be compensated for. Primary probable mechanisms of clinical deterioration in Eisenmenger pregnancy are hypervolemia, fixed pulmonary arterial resistance, and systemic arterial vasodilatation, resulting in increased right-to-left shunting, systemic arterial desaturation followed by low-cardiac output, reduced cerebral blood flow, preeclampsia, and thromboembolism.^[3-10] Though cesarean delivery has been reported to be associated with higher maternal mortality than vaginal delivery in patients with pulmonary arterial hypertension, it is an appropriate approach in patients with Eisenmenger syndrome.^[2,6-10] We preferred cesarean section in present case because the patient was not at full term. There are no data about safety of regional anesthesia (RA) vs GA in this group of patients. Both types of anesthesia can have detrimental effects on right ventricle function.^[11] There have been a few reports of successful cesarean section in patients with Eisenmenger syndrome under GA.^[11] However, there is consensus that

RA is safer than GA in patients who undergo planned obstetric surgery procedure.^[11] We achieved successful cesarean delivery in our patient under GA. As result of increased maternal cyanosis during pregnancy, intrauterine fetal loss has ranged from 75% to 85%. Premature birth rate with intrauterine growth retardation is also reported to be frequent.^[3-10] Reported perinatal mortality is as high as 28%.^[3-10]

It is recommended that pulmonary arterial hypertension patients should avoid pregnancy (Class I, Level C).^[1] Our patient had been advised to avoid pregnancy, but she had failed to achieve effective contraception, resulting in unintended pregnancy. Barrier contraceptive methods are appropriate for Eisenmenger patients, but with unacceptably high failure rate.^[1] Women with Eisenmenger syndrome are at risk of paradoxical embolism and stroke if they develop venous thrombosis while using combined oral contraceptive (COC).^[13] For this reason, these patients should be discouraged from COC use. Progestogen-only methods (e.g., pills, subdermal implants) are safer alternative for Eisenmenger patients; however, it should be emphasized that bosentan may reduce efficacy of orally administered progestogen.^[13] Intrauterine device (IUD) method of contraception can cause vasovagal reaction in Eisenmenger patients; therefore, IUD should be implanted in hospital setting in the presence of a cardiologist.^[13]

Today, intravenous prostacyclin (epoprostenol), sildenafil and tadalafil, and nebulized and intravenous iloprost may also be used in peripartum period.^[12] These therapies are needed in order to reduce pulmonary resistance and to stabilize right ventricular function. Diuretics are appropriate if the patient shows signs of high jugular venous pressure and right ventricular dysfunction.^[12]

In our case, we continued therapy with bosentan during peripartum period, as well as diuretic therapy to avoid volume overload. There was no teratogenic effect of bosentan on the fetus and pregnancy was terminated early.

In case of continuation of pregnancy in Eisenmenger patient, the patient should be regularly followed and hospitalized early with strict bed rest and monitoring as needed.^[12]

Termination of pregnancy is a decision made by team, including cardiologist, cardiovascular surgeon,

obstetricians, anesthesiologist, and intensive care and perinatology specialists. Patients with high right ventricular systolic pressure have increased maternal mortality rate in 6-month postpartum period. Regular follow-up at 6 months postpartum is appropriate.^[10]

Low-dose heparin during bed rest in pregnant patients with Eisenmenger syndrome is probably reasonable, as there is risk of paradoxical embolism caused by deep venous thrombosis. Use of anticoagulation is controversial because of bleeding risk in these patients.^[12] Our patient did not receive anticoagulation treatment during pregnancy or peripartum period due to high bleeding risk.

Furthermore, bosentan treatment in Eisenmenger pregnancy is another uncertainty. It has been labeled Category X for teratogenic risk as result of convincing evidence showing teratogenicity in animal studies.^[14] Teratogenic effects caused by bosentan include malformations of the head, mouth, face, and large blood vessels, and these effects are dose-dependent.^[14] Although bosentan was teratogenic with oral dose of 2 times maximum recommended human dose (on mg/m² basis) in rats, there were no teratogenic effects observed in rabbits in doses of up to equivalent of 10.5 g/day in 70 kg person.^[14] However, as teratogenic risk of bosentan in human pregnancies cannot be excluded, pregnancy screening at monthly intervals has been recommended.^[1,14,15]

The unique feature of present case with Eisenmenger patient was success of cesarean delivery without fetal or maternal morbidity in unmonitored pregnancy complicated by long-term bosentan treatment and complex underlying congenital cardiac pathology as demonstrated in 2- and 3-dimensional real-time echocardiography (Figures).

Absence of fetal or maternal mortality or morbidity in this case confirms importance of multidisciplinary teamwork. However, lack of infant morbidity, growth abnormalities, and probable neonatal problems consistent with bosentan teratogenicity in this case should not encourage pregnancies in any patient with pulmonary hypertension, regardless of specific type of ongoing treatment.

Effective contraception and periodic pregnancy screening are still critically important issues in this special patient group.

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