

Preventative Valve-Sparing Aortic Root Replacement and Pregnancy Outcome in Marfan Syndrome

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ABSTRACT

In Marfan syndrome, with dilatation of the aortic root secondary to an underlying connective tissue defect, pregnancy can cause hemodynamic stress leading to the development of an aortic aneurysm and even a fatal aortic dissection. In the presence of existing aortic root enlargement and a family history of aortic dissection, preventative elective surgery is suggested. Aortic root replacement with or without a valve-sparing procedure is superior to total aortic root replacement with prosthetic valve/tube graft. It provides excellent survival with low rates of aortic – valve related complications.

Key words: Marfan syndrome, valve-sparing aortic root replacement, pregnancy outcome

Introduction

In Marfan syndrome, the myxoid degeneration of the aortic root is often associated with idiopathic dilatation of all parts of the aortic root: aortic annulus, sinuses of Valsalva and sino-tubular junction. When a woman with Marfan syndrome and annuloaortic ectasia coinciding with an aneurysm or an aortic diameter greater than 5.5 cm, considers pregnancy, prophylactic aortic grafting should be done¹. Both short-term and long-term follow-up of patients with Marfan syndrome are more favorable and superior in those who had repair with the reimplantation technique compared to those patients who had repair with the remodeling (Bentall procedure). The David-I procedure, repair of the aortic root aneurysm and preservation of aortic native valve with reimplantation into vascular graft, is the operation of choice in young females with Marfan syndrome expecting pregnancy. This method helps to avoid the need for long-term anticoagulation and may reduce the risk of stroke or endocarditis. The current study presents the surgical procedure and pregnancy outcome of a woman with annulo-aortic dilatation in the setting of Marfan's syndrome.

Case Report

A 25 year-old primigravida with Marfan syndrome presented at her 33rd week of gestation to our hospital. There was a positive history of Marfan syndrome in her

close family. Her mother and brother died from cardiovascular complications of Marfan syndrome at ages of 26 and 22, respectively. The patient had a 6 cm aneurysm of her aortic root affecting the sinuses of Valsalva. The rest of her ascending aorta, above the sino-tubular junction was normal but the aortic wall was thin. She also had moderate mitral and mild aortic and tricuspid regurgitation with normally developed aortic valve leaflets. However, there was one stress fenestration of the commissure between the non coronary and right coronary leaflets. The coronary arteries were normal, coming from corresponding sinuses. Her clinical presentation was typical for Marfan syndrome and she was not on any medications. Two years prior, she underwent a valve-sparing aortic root replacement with a 28 mm prostheses, David-I operation (Deutsches Kinderherzzentrum, Herz- und Thoraxchirurgie, Sankt Augustin, Universität Bonn, Bonn). Immediate postoperative echocardiographic assessment was satisfactory. It showed normal aortic root diameter, minimal aortic and moderate mitral regurgitation. Left ventricular size and function were normal. The fractional shortening was within normal limits, 30–32%. Following surgery, the patient remained asymptomatic, and was treated with atenolol and diuretics to reduce risk of aortic dissection and post-operatively pleural effusion². She stayed in close consultation with her cardiologist and took pre-pregnancy counselling at the regional

genetic center. She conceived a year and a half after the surgery and was in permanent antenatal care of her gynaecologist and cardiologist. The pregnancy course was uneventful except for mild shortness of breath and fatigue during her second trimester. Because of her comorbidities, her cardiologist recommended a delivery by caesarean section. At admission in our hospital, her height was 168 cm and weight was 57 kg. She had a long thin face, limbs and digits, high arched palate, arachnodactyly, hypermobile joints and lens subluxation. Blood pressure was 110/65 mmHg. ECG showed sinus rhythm and a heart rate of 80 bpm. During her hospital stay, repeat echocardiography showed a normal aortic diameter, moderate dilatation of the left atrium with normal contractility and severe mitral regurgitation secondary to mitral valve prolapse. Ejection fraction was normal up to 70%. The pressure in the right ventricle and pulmonary artery was normal. At the 37th week of gestation, fetal echocardiography showed normal fetal anatomy and normal fetal heart function. At the 39th week of pregnancy, an elective caesarean section was performed under general anaesthesia. She gave birth to a healthy boy weighing 3130 g with an Apgar score 10/10. Blood was taken from the umbilical cord and was sent for genetic analysis. Physical examination of the newborn was not suggestive of Marfan syndrome and his cardiologic and ophthalmologic examinations were within normal limits. The patient's operative and postoperative course was uncomplicated.

Discussion

Marfan syndrome is an autosomal dominant disorder with a prevalence of about 1–5 in 10,000. It is caused by a mutation in the fibrillin-1 gene (FBN1), located on the long arm of chromosome 15. The FBN1 gene is the major constituent of microfibrils, which are components of the extracellular matrix that are widely dispersed and perform numerous functions^{3–5}.

Mutation of the FBN1 gene produces abnormal protein products which contribute to defective connective tissue. Even with the discovery of the genetic and biochemical bases of the condition, the diagnosis of Marfan syndrome outside families with a classic phenotype remains entirely clinical^{6,7}. Marfan syndrome demonstrates variable expressivity, pleiotropy, and a high rate of new mutation. The condition is characterized by musculoskeletal, cardiovascular and ocular manifestations. The most common cardiovascular features are mitral valve prolapse and dilatation of aortic root. If not treated, associated clinical problems of mitral and aortic regurgitation with aortic dissection, results in death for most patients in their fourth and fifth decades of life⁸. The most common cause of death in adolescents or adults with Marfan syndrome are rupture of fusiform aneurysms of the ascending aorta, ascending aorta dissection and rupture and congestive heart failure from aortic/or mitral regurgitation. Beta blocker therapy, endocarditis prophylaxis,

aorta and aortic valve surgery have probably improved longevity⁹. Nevertheless, improved medical and surgical management of such patients has added an average of 10–15 years to the expected life duration¹⁰. In addition to the maternal risk associated with pregnancy in the Marfan syndrome, there is a 50:50 risk of having the child who will inherit the syndrome. Furthermore, the hyperdynamic and hypervolemic state of pregnancy increases the risk of aortic dissection. The incidence of dissection is highest during the third trimester of pregnancy and the first month postpartum¹¹. Before pregnancy, women with Marfan syndrome should be assessed for cardiovascular problems. The cause of the increased incidence of aortic dissection during pregnancy is unclear, but the combination of genetic predisposition to dissection and the hemodynamic stress during pregnancy may have a role. Also, high levels of estrogen may cause inhibition of collagen and elastin deposition in the aorta too^{12,13}. Finally, it has been shown that progesterone accelerates deposition of noncollagenous proteins in the aorta of the rats¹⁴.

Factors that can predispose patients to either aortic aneurysm or aortic dissection include systemic arterial hypertension, coarctation of aorta, pregnancy and trauma⁸.

The risk of aortic dissection or other cardiac complications is low when aortic root diameter does not exceed 40 mm and when a cardiac function is not compromised. If the diameter of the aortic root exceeds 40 mm, there is a 10% risk of dissecting aneurysm of the aorta^{12,15}. Surgical repair is generally recommended when the diameter reaches 55 to 60 mm and probably earlier if there is rapid progression or a family history of aortic dissection or rupture¹⁶. The risk of pregnancy in women who have had replacement of the aortic root is still unknown.

Conclusion

Treatment strategies for aortic root dilatation in patients with Marfan syndrome include both medical and surgical approaches. An aortic root diameter ≤ 40 mm is considered to be associated with a favorable outcome of pregnancy. Prophylactic therapy with beta blockers and hidralazine has been advocated¹⁴. If aortic root diameter is greater than 40mm and family history is positive for aortic dissection, as was the case with our patient, then an elective root replacement surgery is recommended before pregnancy. In our case, surgical treatment prior to pregnancy and appropriate preconception counseling were imperative for good maternal^{17,18} and fetal outcome. Additionally, in patients with aortic root dilatation, moderate/severe mitral regurgitation, aortic aneurysm or other cardiac abnormalities, caesarean section should be the preferred method of delivery because it minimizes the hemodynamic stress present in vaginal delivery. Successful pregnancy can be expected after a more physiological valve-sparing aortic root replacement.

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ISHOD TRUDNOĆE NAKON PREVENTIVNE ZAMJENE AORTNOG KORIJENA UZ OČUVANJE AORTNE VALVULE KOD MARFANOVOG SINDROMA

SAŽETAK

Kod Marfanovog sindroma s dilatiranim aortnim korijenom kao posljedicom defektnog vezivnog tkiva, trudnoća predstavlja kemedinamski stres koji može dovesti do razvoja aneurizme aorte ili čak fatalne aortne disekcije. Kod takvih pacijenata s verificiranom dilatacijom aortnog korijena i pozitivnom obiteljskom anamnezom za aortnu disekciju, preporuča se učiniti elektivni kirurški zahvat zamijene aortnog korijena s očuvanjem valvule, koji je superioran u odnosu na cjelovitu zamjenu aortnog korijena protetskom valvulom/cjevnim graftom. Takav zahvat osigurava izvrsno preživljenje s niskom razinom komplikacija posebice tijekom izloženosti stresogenim faktorima kao što je trudnoća.