Marfan Syndrome Presenting with Aortic Aneurysm in Two Siblings at Childhood: Case Report

Çocukluk Çağındaki İki Kardeşte Aort Anevrizmasına Yol Açan Marfan Sendromu

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ABSTRACT The cardiovascular involvement of Marfan syndrome is usually referred as the most serious and severe clinical manifestation. However, it rarely occurs in children. This case report presents two siblings who have been initially diagnosed with aortic aneurysm which eventually turned out to be a manifestation of Marfan's syndrome. Cardiovascular surgery was preferred as the choice of treatment because there were evident aortic aneurysms in both siblings and the family history was positive for sudden cardiac death. After an aortic aneurysm is diagnosed in a child, the child should be examined carefully in aspect of Marfan syndrome. Moreover, the other family members should be screened for both Marfan syndrome and related cardiovascular involvement.

Key Words: Aortic aneurysm; child; Marfan syndrome

ÖZET Marfan sendromunun neden olduğu kardiyovasküler sistem tutulumu, hastalıkla ilgili olarak ortaya çıkan en ciddi ve ağır klinik tablolardan sorumludur. Bu olgu sunumunda, başlangıçta aort anevrizması saptanan ve daha sonra Marfan sendromu hastası oldukları belirlenen iki kardeş tanımlanmıştır. Aort anevrizması varlığı ve ani ölümle ilişkili aile öyküsü nedeniyle iki kardeşe kardiyovasküler cerrahi uygulanmış ve aort anevrizması onarımı yapılmıştır. Marfan sendromunun sebep olduğu kardiyovasküler sistem tutulumu, çocuklarda nadiren görülmese de herhangi bir çocukta aort anevrizması tanısı konulduğunda olguda mutlaka Marfan sendromu bulunup bulunmadığı araştırılmalıdır. Bundan başka, diğer aile bireyleri de hem Marfan sendromu hem bu sendromun kardiyovasküler sistem tutulumu bakımından ayrıntılı olarak taranmalıdır.

Anahtar Kelimeler: Aort anevrizması; çocuk; Marfan sendromu

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Firstly described by Antoine Marfan in 1896, Marfan syndrome is an autosomal dominant disorder of the connective tissue which leads to cardiovascular, skeletal, and ocular alterations.[1,2] The cardiovascular involvement of Marfan syndrome is generally referred as the most serious and severe clinical manifestation in adults, thus determining the survival. The most typical cardiovascular feature of this syndrome is the progressive dilatation of proximal aorta which usually results in aortic dissection and even aortic rupture.[3] However the cardiovascular symptoms of Marfan syndrome usually become prominent after the second or third decade of life. Up to date, only a few studies documented about the cardiovascular manifestations of Marfan syndrome in children.[4]

This case report presents two siblings who have been initially diagnosed with aortic aneurysm which eventually turned out to be a manifestation of Marfan syndrome.

CASE REPORTS

CASE 1

A seven year old girl was referred to the study center due to chest pain. It was learnt that the patient was under clinical follow up since she was diagnosed with atrial septal defect (secundum type) five years ago. Her past history revealed that the patient underwent surgery for congenital hip dislocation when she was 18 month old. It was also learnt that her parents were cousins and that her previously born sisters died because of cardiac and respiratory insufficiency (Figure 1). The body weight of the patient was 16 kg (3-10 percentile) while her body length was 116 cm (25 percentile). Physical examination showed exaggerated joint mobility despite the normal skin elasticity and a +++/6 systolic murmur was auscultated at the aortic area. A chest X-ray demonstrated the enlargement of aortic knob with a cardiothoracic index <0.5 while the echocardiographic examination indicated an aneurysmatic dilatation in ascending aorta. The diameter of as-

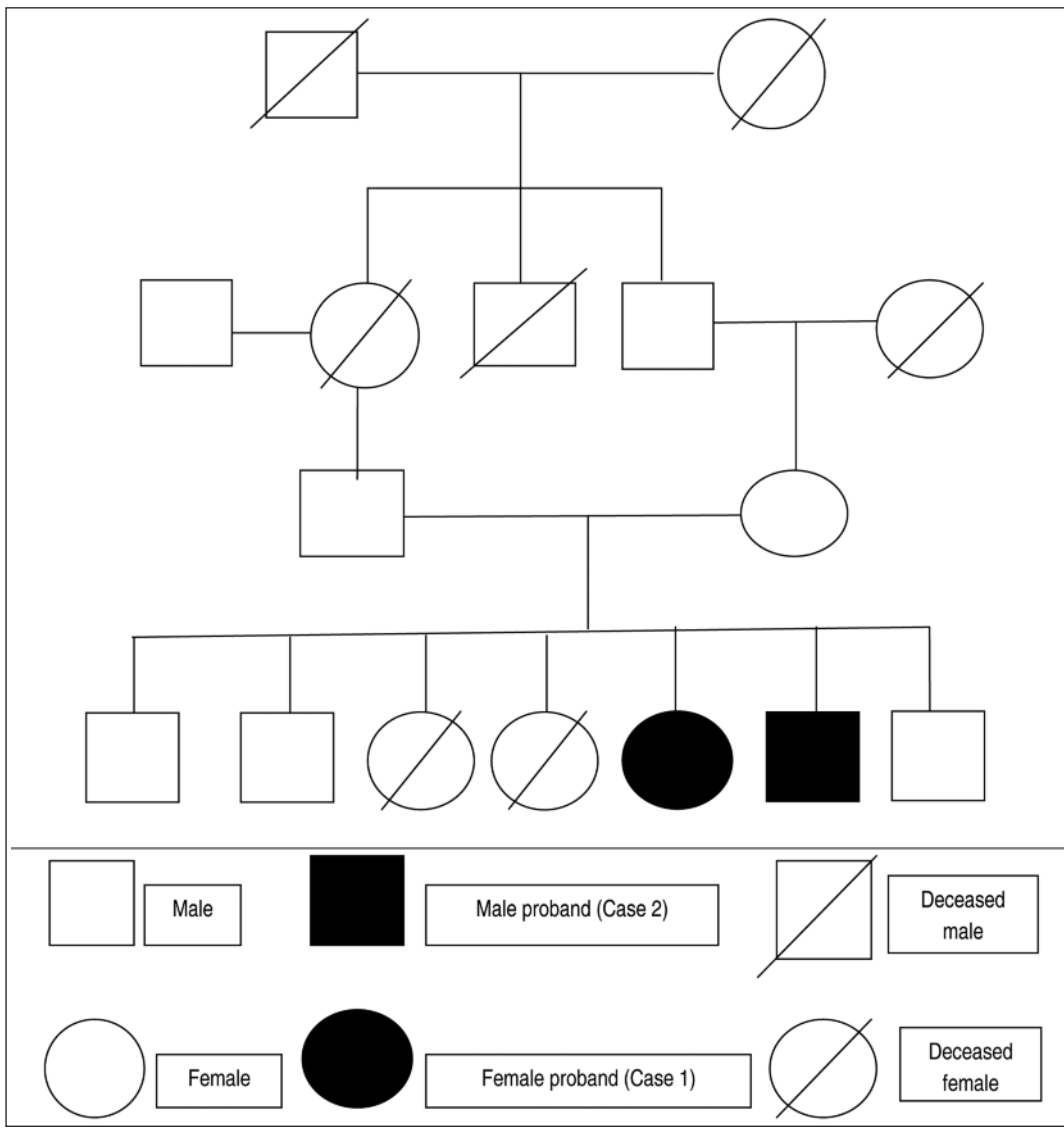

FIGURE 1: The pedigree of case 1 and case 2.

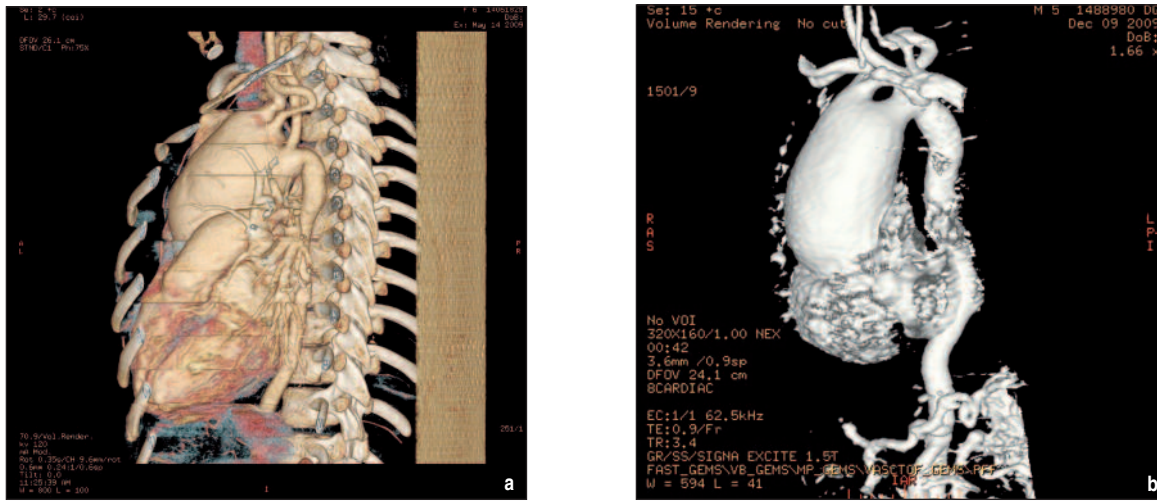

FIGURE 2: a) Three-dimensional computed tomography angiography reveals an aneurysmatic dilatation of the ascending aorta in the first case. **b)** Three-dimensional magnetic resonance angiography demonstrates an aneurysmatic dilatation of the ascending aorta in the second case.

cending aorta was measured as 3.4 cm by echocardiography and 5.1 cm by computed tomography (CT) angiography (Figure 2a). Due to the presence of exaggerated joint mobility and aortic aneurysm, Marfan syndrome was suspected and a homozygous mutation was detected at the intron 56 locus of the fibrillin gene (located in chromosome 15) by means of FISH testing. Afterwards an ophthalmological examination was made and no pathological findings were specified. Since there was a family history of sudden cardiac death, cardiovascular surgery was planned to treat the aortic aneurysm and avoid aortic dissection. During the operation, the supracoronary walls of the aort were repaired with a 22 mm wide Dacron graft after the pouch in the ascending aorta is excised and a 2 cm gap within the atrial septum was sutured. Histopathological evaluation demonstrated the prominent loss of elastic fibers in the aortic wall (Figure 3). The patient recovered the postoperative period without any complications. Up to date, she has had no cardiovascular symptoms and she has been in good health.

CASE 2

A five year old boy was called for a checkup visit after his sister was diagnosed with Marfan syndrome presenting with aortic aneurysm (Case 1). His medical history revealed nothing particular except pes planus. The body weight of the patient was

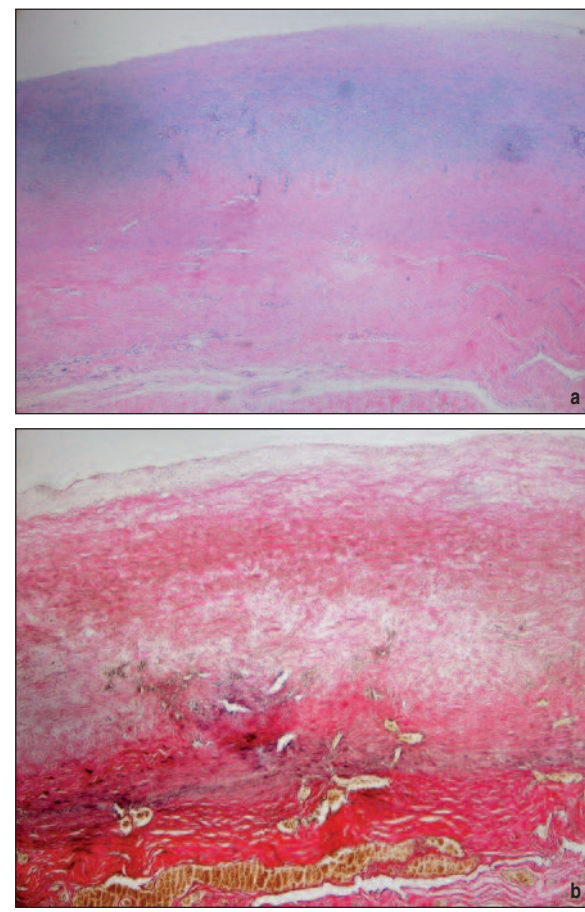

FIGURE 3: a) Degenerative alterations in tunica intima and tunica media layers of the aortic wall in first case (hematoxylene eosine stain, x40 magnification) **b)** The lack of regular black staining indicates the loss of elastic fibers in the aortic wall of the first case (Verhoeff's elastic stain, x40 magnification).

16 kg (10-25 percentile) while his body length was 106 cm (10-25 percentile). Physical examination showed bilateral pes planus, exaggerated joint mobility despite the normal skin elasticity and a +++/6 systolic murmur auscultated at the aortic area. A careful ophthalmological examination revealed nothing particular. A chest X-ray demonstrated an evident aortic knob alongside with a cardiothoracic index >0.5 whereas the echocardiographic examination indicated an aneurysmatic dilatation in ascending aorta and aortic regurgitation. The diameter of ascending aorta was measured to be 3.9 cm by echocardiography and 4.8 cm by magnetic resonance (MR) angiography (Figure 2b). Since there was a family history of sudden cardiac death, cardiovascular surgery was planned to treat the aortic aneurysm and to avoid aortic dissection.

DISCUSSION

Mitral valve prolapse and aortic root dilation have been respectively addressed as the most frequent cardiovascular alterations in children with Marfan syndrome. Aortic root dilatation in association with aortic dissection is the most common cause of morbidity and mortality. Unless the severe form of the disease presents with either pathological cardiac murmurs or heart failure or there is a family history, patients with Marfan syndrome usually remain asymptomatic until they reach the third decade of life, when the diagnosis is generally made. The severe form of this clinical entity generally occurs sporadically.[5-7] Differential diagnosis of an ascending aorta aneurysm includes congenital aortic dilatation (idiopathic, secondary to aortic stenosis or in relation with an arteriovenous fistula), infections (bacterial, fungal, viral, spirochetal) and certain vasculitic syndromes (such as Ehlers-Danlos syndrome, Takayasu arteritis, Behçet's disease and Kawasaki disease).[8]

In the present case report, two siblings with aortic root dilatation (and one with aortic regurgitation) are described. The previous loss of two sisters due to sudden cardiac death strongly indicated positive family history of the reviewed siblings. The absence of clinical signs and symptoms associated with the aforementioned birth defects, vasculitic syndromes and infections also suggested the diagnosis of Marfan syndrome.

In a similar case report by Leite et al., two siblings with the cardiovascular manifestations of Marfan syndrome were investigated. Both of the reviewed patients (aged 9 and 8 respectively) had severe aortic dilation with mild to moderate regurgitation, and one of them had even aortic dissection. Also the family of history of both siblings was strongly positive.[9] When both case reports are considered, it can be suggested that familial form of the disease may also present with serious cardiovascular complications. To the best of our knowledge, the present case report describes the youngest siblings that were both diagnosed with Marfan syndrome related aortic aneurysm during early childhood.

Once the syndrome is diagnosed, cardiovascular examination should be made to determine the risk factors for aortic dissection. These risk factors include aortic diameter greater than 5 cm, aortic dilatation extending beyond the sinus of Valsalva, rapid rate of aortic dilatation (45% per year, or 1.5 mm/year in adults), and family history of aortic dissection.[9] Aortic diameters can be measured by echocardiography, CT and MR angiography. As for the present cases, there is a discrepancy between the aortic diameters that were assessed by echocardiography and other imaging methods. Such a discrepancy may be attributed to the technical adequacy of echocardiographic equipment, skillfulness of the echocardiographer and the time interval (of three months) between the implementation of different imaging procedures.

As indicated by the present study, it should be kept well in mind that Marfan syndrome can lead to severe aortic dissection and aneurismal dilatation even during early childhood. When there is a high risk for aortic dissection or rupture, prophylactic aortic root surgery should be considered as was the case in the reviewed siblings. The mortality rate for emergent surgery of acute aortic dissection or aneurysm rupture is 8 times greater than that of elective surgery which is currently lower than 2%. Therefore it would be reasonable to plan prophylactic surgery in case there is a valid indication.[9,10]

Since the cardiovascular alterations seem to be closely related with the mutant fibrillin gene, all of the affected individuals should be assessed genetically so that the asymptomatic relatives can be identified. Another issue to be emphasized is the necessity of genetic counseling for the parents of children with Marfan syndrome. Consequently more case reports and even series are needed to clarify the clinical progress and outcome of familial Marfan syndrome so that an optimal management protocol can be established in future.

Acknowledgement

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