

Case Report

A 50-Year-Old Woman with Marfan's Syndrome

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Abstract

Marfan syndrome (MFS) is a systemic connective tissue disorder. It is an autosomal dominant disorder caused by mutations in the extracellular matrix protein fibrillin-1 gene located on chromosome 15. It has variable range of expressions. Cardiovascular manifestations in Marfan's syndrome patients include aortic and valvular diseases. Here we describe a 50-year-old female patient with Marfan syndrome who had aortic aneurysm with mitral and aortic regurgitation. Diagnosis was made on the basis of physical examination, color doppler study and family screening. She was previously being treated as a case of rheumatic valvular disease because her body habitus was overlooked. She was managed conservatively and advised to go for prophylactic surgery to prevent aortic dissection. She was also counseled about screening her children for transmission and expression of this disease.

Key words: Marfan's syndrome, Aneurysm, Regurgitation

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Introduction

Marfan syndrome (MFS) is an autosomal dominant (AD) inherited disorder of connective tissue. It is a multisystem disorder with manifestations typically involving the cardiovascular, skeletal and ocular systems. It occurs in all ethnic groups and has a prevalence of 1 in 100,000 population.^{1,2} In about 75% cases the defective gene on chromosome 15 is inherited³ from an affected parent. However, in about 25% cases it is due to new mutation. The patient under discussion had cardiovascular features including aortic aneurysm with mitral and aortic regurgitation though marfanoid features were overlooked for a long time. The objective of reporting this case is to emphasize the importance of physical examination after proper exposure to look for skeletal features in patients with aortic regurgitation with or without mitral regurgitation, specially in context of conservative rural Bangladeshi female patients.

Case report

A 50-year-old non-smoker, non-diabetic, normo-

tensive housewife presented on 18th February 2011 with shortness of breath on exertion and palpitation for one year. She did not give any history suggestive of rheumatic fever or any connective tissue disorder. She denied any form of sexual promiscuity in her life. On examination, she was breathless on mild exertion but neither cyanosed nor clubbed, her blood pressure (BP) was 140/30 mm Hg, pulse was 80 beats/min and regular in rhythm and respiratory rate was 22/min. Her jugular venous pressure was not raised. Precordium examination revealed a thrusting apical impulse at 5th intercostal space just lateral to the left midclavicular line. Both 1st and 2nd heart sounds were soft and there was no third or fourth heart sound. A prominent early diastolic murmur was heard along left sternal edge with patient leaning forward and breath held in expiration and there was a pansystolic murmur in the mitral area radiating to left axilla. Examination of other systems did not reveal any abnormalities.

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Fig 1



Fig 2

The patient was previously diagnosed as a case of rheumatic heart disease with combined aortic and mitral regurgitation and was treated with digoxin, diuretic and benzathine penicillin injection monthly as prescribed from a cardiac institute. As she used to wear traditional dress (long clothes) around her body, her physical appearance and body habitus could easily be overlooked. After

proper exposure her height and arm span (Fig 1) were recorded 5'6" and 5'8" respectively. She had high arched palate, mild scoliosis, flat feet and arachnodactyly with positive thumb sign. Her family members were screened by physical examination and her son was found to have marfanoid features (Fig 2) with faint aortic regurgitant murmur. Electrocardiogram (ECG) showed sinus tachycardia with borderline left ventricular hypertrophy. Color doppler study showed grade III aortic regurgitation and grade II mitral regurgitation. All the chambers were normal. Mitral valve was normal in appearance. Aortic valve cusps were normal with normal systolic opening. Ascending aorta was hugely dilated (60 mm). Left ventricular systolic function was fair with ejection fraction 52%.

Complete blood count, urine routine examination, serum creatinine, random blood sugar and antistreptolysin O were normal. Rheumatoid factor, venereal disease research laboratory (VDRL) and Treponema pallidum hemagglutination (TPHA) tests were negative. Chest radiography was unremarkable. Special tests including slit lamp examination of eyes and genetic testing could not be done due to limited resources.

Treatment

The patient was advised to take rest. She was prescribed salt restriction, β blocker and low dose angiotensin converting enzyme inhibitor (ACEI). After about three weeks she was found marginally better. She was given prophylaxis for infective endocarditis. Considering the aortic diameter she was advised to come for regular follow-up at cardiac center and counseled about prophylactic surgery on aortic root and ascending aorta with the aim of avoiding mortality associated with type A aortic dissection. As her son was found to have marfanoid features along with faint aortic regurgitant murmur, she was suggested for screening of other family members to receive genetic counseling and prophylactic treatment, if necessary.

Discussion

MFS is an autosomal dominant disorder of fibrous tissue due to mutation of fibrillin gene located on chromosome 15. The condition classically involves skeletal, ocular and cardiovascular systems in addition to skin, pulmonary and neurological complications. About 90% of patients with Marfan's syndrome will develop cardiac complications.²

Following the development of molecular detection of defective fibrillin gene (FBNI), diagnostic criteria for Marfan's syndrome as proposed by de Paepe et al⁴ revising the previous Berlin criteria were followed. For diagnosing MFS, the subject being examined must have a first-degree relative affected with the disease and involvement of two systems with a major sign. In absence of genetic criteria, there should be involvement of three systems, at least two with major signs.

In addition to routine chest radiography and ECG, echocardiography is considered. Several reports have documented the accuracy and usefulness of echocardiography in the detection of aortic root dissection or dilatation or both⁵ which is particularly useful in deciding whether cardiac surgery should be performed or avoided.⁶

Management

The diagnosis, follow-up plan and treatment strategy for MFS require a multidisciplinary team which should include geneticist, ophthalmologist, cardiologist and orthopedic surgeon.

Ectopia lentis, which can lead to glaucoma, is a major diagnostic criterion of MFS. There may be retinal detachment and cataract. Yearly assessment by an ophthalmologist is essential. Severe scoliosis often requires surgical stabilization. In many patients, pectus deformity causes restrictive lung disease. A recent report described a significant increase in forced vital capacity after surgery with improvement most prominent in patients over 11 years of age.⁷

Given its impact on prognosis, the monitoring of patients with MFS is mainly directed toward the control of aortic disease. Treatment of patients with MFS with aortic involvement rests on following three main strategies: pharmacological treatment, prophylactic aortic surgery and advice about change in lifestyle.

Pharmacologic treatment

β blocker: Various retrospective studies have shown important role of β blocker in prevention of progression of aortic dilatation in patients with MFS^{8,9} which is attributed to reduction of aortic wall stress by negative chronotropic and inotropic effects.¹⁰ Current recommendation advises early use of β blocker in all patients with MFS independent of aortic diameter.¹¹

Renin-angiotensin system blocker: Over past few years, role of renin angiotensin system in pathogenesis of aortic dilatation has been growing.¹² The beneficial effect with treatment of ACEI is attributed to control of BP and reduction of stiffness of aortic wall¹² though its molecular mechanism is independent of control of BP.¹³

Doxycycline: A small dose of doxycycline which inhibits protease has been shown to prevent fragmentation of elastic fiber and prevents aortic rupture in mice model.¹⁴ Though not formally tested in aortic aneurysm, its use has shown beneficial effect.¹⁵

Prophylactic surgery on aorta: To avoid mortality associated with type A aortic dissection, prophylactic surgery on aortic root has the greatest therapeutic impact on survival of patients with MFS.¹⁶ Risk correlates positively with aortic diameter and therefore elective surgery is recommended when ascending aortic diameter is greater than 50 mm or even earlier if other risk factors are present.¹⁷ To avoid anticoagulant related risks, replacement of aortic root with preservation of aortic valve, if normal, is the present technique.¹⁸ Close monitoring and β blocker are continued after surgical repair in all patients.¹¹ For mitral valve prolapse (MVP), surgical repair is preferred if technically feasible¹⁹ avoiding long term risk of anticoagulation.

Endocarditis prophylaxis: National Marfan Foundation advocates use of endocarditis prophylaxis for patients with MFS who have valvular regurgitation.²⁰

Obstetric complication and treatment: During pregnancy, there is extra load on cardiovascular system and in MFS patients, heart failure may be precipitated.²¹ There is increased risk of aortic type A dissection typically in 3rd trimester and associated with high fetal mortality and with maternal mortality of around 50%.²¹ Nevertheless, according to the European Society of Cardiology pregnancy is not contraindicated in patients with an aortic root diameter of <40 mm.²² Patients with an aortic diameter \geq 40 mm who wish to have children are recommended to undergo elective aortic replacement surgery.²²

Advice about lifestyle: As physical exercise increases the stress on the wall of the aorta which can contribute to aortic dissection, strenuous exercise should be avoided.²³

Genetic counseling: As MFS is an AD disease, couples with one affected partner have a 50% risk of transmission to offspring which should be explained to affected patient. Preimplantation diagnosis^{21,24} or prenatal diagnosis²¹ with therapeutic abortion are important options that can prevent transmission of this condition.

Prognosis

The first long-term survival study by Murdoch²⁵ in 1972 on MFS patients who did not undergo aortic surgery showed that mean age of death was 32 years and 90% of all deaths resulted from cardiovascular causes² of which aortic rupture was responsible for 80%. However, with earlier diagnosis, better medical management and introduction of prophylactic aortic repair surgery, life expectancy has greatly increased by several decades and approaching to that of general population.²⁶

Conclusion

Although rheumatic fever is still the most common cause of aortic and mitral regurgitation in Bangladesh, the presence of pure regurgitant murmur demands complete physical examination of the patient to look for marfanoid features so that proper management including family screening may be offered to the patient before it is too late. Furthermore, there is an active area for more trials and research to improve pharmacological treatment to delay aortic aneurysmal progression in these patients.

Consent

Written informed consent was obtained from the patient for publication of the case report with accompanying pictures.

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