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Mitral Valve Prolapse in Marfan syndrome: Case Report and Review of Literature

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Abstract **Case Report**

Mitral valve prolapse, an abnormal displacement into the left atrium of a thickened and redundant mitral valve during systole, is a relatively frequent abnormality in humans and may be associated with serious complications. One of the possible consequences of this condition is that the malfunctioning mitral valve allows backflow of blood in the left atrium, which, when severe, leads to left ventricular enlargement and failure. Besides severe mitral regurgitation, mitral valve prolapse has been associated with serious complications such as bacterial endocarditis and sudden death. Marfan syndrome is an autosomal dominant systemic disorder of the connective tissue. Patients affected by the Marfan syndrome carry a mutation in one of their two copies of the gene that encodes the connective tissue protein fibrillin-1. Marfan syndrome affects most organs and tissues, especially the skeleton, lungs, eyes, heart, and the large blood vessel that distributes blood from the heart to the rest of the body. We report a case of Marfan syndrome in a 30 years old patient presenting with mitral valve prolapse, tricuspid regurgitation associated with severe ocular, musculoskeletal abnormalities.

Keywords: Connective tissue disease, marfan syndrome, mitral valve prolapse.

INTRODUCTION

Marfan syndrome (MFS) is one of the most common inherited disorders of connective tissue [1,2]. It is an autosomal dominant condition with a reported incidence of 1 in 3000 to 5000 individuals. There is a wide range of clinical severity associated with MFS with classic ocular, cardiovascular and musculoskeletal abnormalities, while some patients demonstrate significant involvement of the lung, skin and central nervous system. The diagnosis of MFS relies essentially on the fulfillment of clinical diagnostic criteria as outlined by the revised Ghent score [3].

Mitral valve prolapse (MVP) is generally sporadic but is also associated with a variety of congenital disorders of connective tissue including Marfan syndrome, Ehler-Danlos syndrome, osteogenesis imperfecta, dominant cutis laxa pseudoxanthoma elasticum, and the MASS syndrome (mitral valve prolapse, aortic root dilatation, skeletal changes, and skin changes), among others. It has been estimated that only 0, 25% of patients with mitral valve prolapse have Marfan syndrome. This percentage may be somewhat higher if the newer and more stringent criteria for MVP are used, but it is unlikely that more than 1-2% of patients with MVP have an associated connective tissue disorder [4].

CASE REPORT

A 36 year old male, with no previous medical history, presented to our department with dyspnea and atypical chest pain associated to palpitations at rest, had been in his usual state of health until 2 months before his admission. There were no associated autonomic symptoms, pre-syncope or syncope. The patient did not have a family history of a similar problem. On examination, the patient was comfortable at rest, The patient was normotensive, with a blood pressure of 113/61 mmHg, with an irregular pulse and tachycardia of 120 beats per minute. The first heart sound was soft with a murmur of mitral regurgitation graded as 4/5. There were no clinical features of infective endocarditis or cardiac failure. Respiratory examination revealed pectus carinatum and was otherwise normal.

Our patient was extremely tall 203 cm and very thin with typical musculoskeletal features of Marfan syndrom these included arachnodactyly with

positive wrist and thumb signs, hindfoot valgus with plain flat feet dolichostenomelia **(Fig.1)**, increased arm span/height, scoliosis, downslanting palpebral fissures, and micrognathism. His total systemic score was 11 based on the revised Ghent nosology.

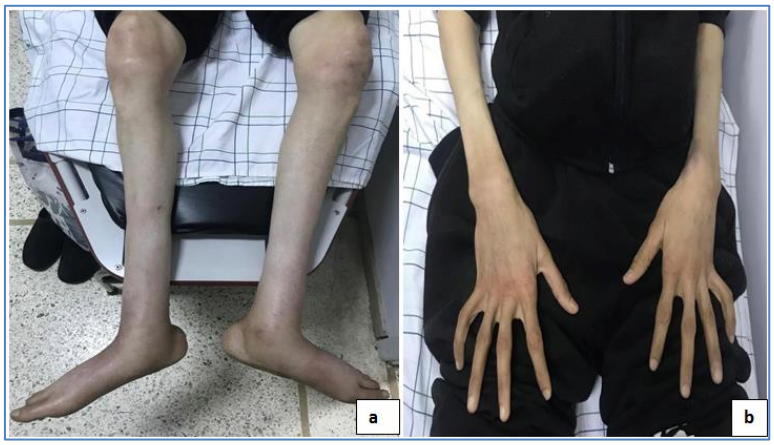

Fig-1: Typical clinical signs in Marfan syndrome: (a) Dolichostenomelia and Hindfoot valgus with plain flat feet and (b) Arachnodactyly

Ophthalmology examination conducted by an ophthalmologist revealed a right dense cataract with lens subluxation but no dislocation. The left eye had a clear lens with no subluxation or dislocation. Laboratory tests were within normal limits (full blood count, urea and electrolytes, calcium, magnesium and phosphate, liver function tests, troponin T, creatine kinase). A skin biopsy was realised, showing a decreased elastin content and fragmentation of elastic fibres.

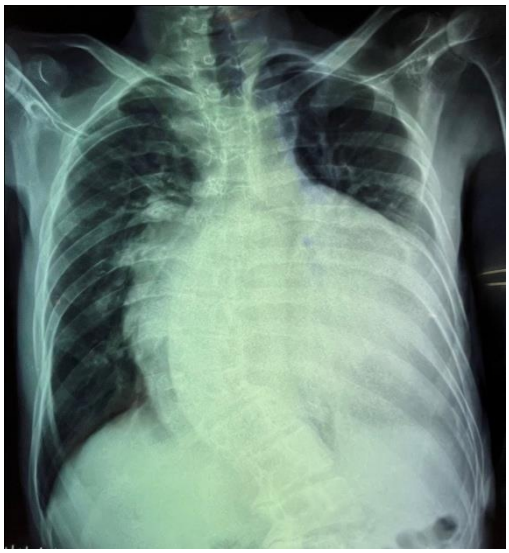

Fig-2: Chest X-ray showing cardiomegaly, double-density sign and scoliosis

Electrocardiogram showed an atrial fibrillation with ventricular rate of 119 bpm, chest X-ray **(Fig.2)** revealed an increased cardiothoracic ratio and scoliosis.

Transthoracic echocardiography demonstrated prolapse of the anterior mitral valve leaflet (A1,A3) with severe mitral regurgitation with no vegetation, enlarged left and right atrium, normal aortic root diameter of no evidence of dissection, and secondary tricuspid regurgitation. The ejection fraction was 62% and dilated left ventricular end diastolic and systolic diameters. Computerised Tomography (CT) and angiographic sequences didn't either show dilatation of the aorta. The pulmonary arterial system was within normal limits. The lung fields were clear and the cranio-cervical junction was normal with no subluxation. There was no abdominal aneurysm. The patient was proposed for surgery for his mitral valve and tricuspid valve repair with annuloplasty ring. Consent was obtained from the patient for publication of the case.

DISCUSSION

Marfan syndrome is almost exclusively inherited in an autosomal dominant manner with most patients harboring mutations involving the gene (FBN1) encoding the connective tissue protein fibrillin-1 [5]. In less than 10% with typical marfan phenotype, no mutations in FBN1 is identified and mutations in a gene encoding for transforming growth factor- beta receptors (TGFBR) maybe responsible [6]. While most individuals with MFS have an affected parent, about 25 % have MFS as a result of a de novo mutation.

Mitral valve prolapse is found in many, but certainly not all, patients with Marfan syndrome, it was suggested many years ago that isolated MVP may also be due to a mutation of *FBN1* [7]. However, despite the availability of literally millions of patients for study, no convincing association has been found to date. Occasional families with MVP have been identified and an underlying gene defect reported. In patients with X-linked myxomatous valvular dystrophy, a rare disorder associated with severe MVP, the defect has been linked to chromosome Xq28 [8]. The first locus for non-syndromic MVP has been mapped to chromosome 16p11.2–p12.2 in 2 of 4 patients at a French surgical

center [9]. A second locus for autosomal dominant MVP has been mapped to chromosome 11p15.4 [10]. Thus, even within families with an autosomal dominant mode of inheritance, there appears to be significant genetic heterogeneity.

The most common complication of MVP is severe regurgitation due to progressive degeneration of the valve and chordae, with myxomatous infiltration (thickening of the mitral layers with glycosaminoglycan accumulation), and fibroelastic and collagen alterations [11-13]. In about 75% of cases, there is sudden deterioration because of chordal rupture [14]. The cumulative risk of severe mitral regurgitation and valve rupture is minimal in individuals younger than 50 years of age but then rises steeply, with the risk in men being greater than in women beyond the age of 60. Using current prevalence data, it can be estimated that by the age of 70, approximately 11% of men and 6% of women with classic MVP will need mitral valve replacement [13].

The role of mechanical stress in the evolution of MVP is also important. The mitral valve opens and closes more than 3 billion times during the course of the normal human lifespan. During each closure period, it must withstand the full force of ventricular contraction. Because of the normal orientation of the leaflets, this force is unevenly applied, affecting the posterior leaflet more than the anterior leaflet, and prolapse of the posterior leaflet is more common (observed in two-thirds of cases, with prolapse of both leaflets occurring in the remaining third). This pattern of involvement and the fact that the valve disruption occurs late in life are consistent with the important role of physiologic stress in the development of MVP.

CONCLUSION

Marfan syndrome is one of the most common inherited disorders of connective tissue and it merits consideration because of the wide variety of ocular, cardiovascular, musculoskeletal and vascular abnormalities occurring in a single patient.

Declaration of conflicting interests

The author(s) declare(s) that there is no conflict of interest

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