Research Paper Medical Science

MARFAN'S SYNDROME WITH UNUSUAL PRESENTATION

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ABSTRACT

Marfan syndrome (MFS) is an autosomal dominant disorder caused by mutations in the gene encoding the extracellular matrix (ECM) protein fibrillin1 and TGFBR1 or 2. It is primarily associated with skeletal, cardiovascular and ocular pathology, displaying near-complete penetrance but variable expression. We hereby reporta case of an adolescent male with Marfans syndrome with progressive changes in cardiovascular system.

KEYWORDS Fibrillin 1; Marfans syndrome ; TGFBR1 or 2.

INTRODUCTION :

Marfan syndrome is an autosomal dominant, multisystemic connective tissue disease, associated with a mutation in fibrillin1,2, and occasionally a mutation in TGFBR1 or 23,4,5. The cardinal manifestations of this condition involve the cardiovascular, ocular and skeletal systems. The most serious complication in patients with Marfan syndrome presents progressive aortic root dilation that may lead to aortic dissection, rupture or aortic regurgitation, which used to be the main cause of death in this patient category prior to the era of successful preventive therapies. To make the diagnosis of Marfan syndrome more consistent and of more prognostic value, the Berlin diagnostic criteria of 1988 were revised and the clinical features codified as the Ghent nosology in 1996. Prophylactic medical treatment to protect the aorta with regular follow-up helps prevent or delay serious complications2.

CASE REPORT :

A 16 yr old adolescent from keralapura presented to Opd of-ShriAdichunchanagiri institute of medical science, B G Nagara, Karnataka with the complaints of cough with expectoration, more at night and increased in lying position and giddiness of 4 days duration and an episode of syncope 2 days before admission while travelling in bus, with loss of consciousness for 1- 2 min, hehad palpitations from the past 3 months. No history of chest pain or breathlessness . His father was also diagnosed as Marfan's syndrome and undergone cardiac surgery 4 yrs back.Hence the child was also taken to Hassan Govt Hospital, where 2D-ECHO was done and said to be normal. After 2 years child was taken toJayadeva Institute of Cardiology Bangalore, Echosuggested dilated aortic root and was advised for follow up. During follow up visit 2D ECHO was suggestive of aortic root dilatation, Mitral valve prolapse with Mitral regurgitationand was advised for follow up scan after 6 months. On follow up visit 1 month back ECHO showed aortic root dilatation, Mitral Valve Prolapse with moderate MR with mild PAH.

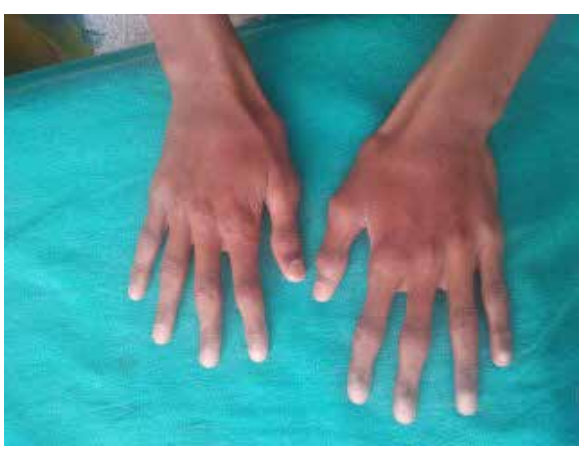
The child was born to a non-consanguineous married couple with father diagnosed as Marfan's 5 years back and had undergone cardiac surgery 1 year back as ECHO was suggestive of severe ARwith ascending aortic aneurysm. CT aortogram was suggestive of annulo-aortic ectasia with ascending aortic aneurysm.

On physical examination the boy was thin built and of tall stature with height corresponding to more than 95th centile (fig 1). There was pectusexcavatum (fig 2) and an arm span of 180cm, with ratio of 1: 1.5 and with reduced upper segment to lower segment ratio. The child had arachnodactyly (fig 3) with presence of characteristic wrist (fig 4) and thumb sign (fig 5). There was dolicocephaly with high arched palate and pesplanus (fig 6).

On ocular system examination the child had sever myopia with flat cornea and increase in axial length of the globe.

Systemic examination: upon assessment of the precordium a hyperdynamic apex beat was felt in the 5thintercostal space at the midclavicular line. Late systolic murmur 3/6 with mid systolic click was heard in the mitral area. The murmur increased in intensity on valsalvamaneuver and persistent hand grip. Loud P2 was heard in the pulmonary area. S1 and S2 heard in the aortic area with normal split. Other systems being normal

Figure 1: Mafans sundrome in faher and child
Figure 2 (pectusexcavatum)
Indicating Autosomal dominant inheritance



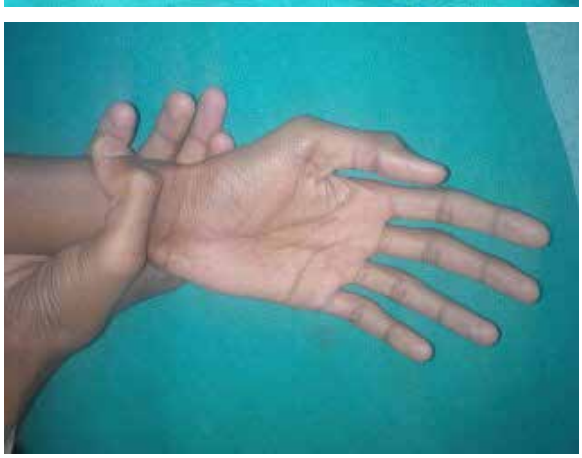


Figure 3Arachnodactyly (long and slender fingers)
Figure 4 Walker Murdoch Sign (Wrist Sign)

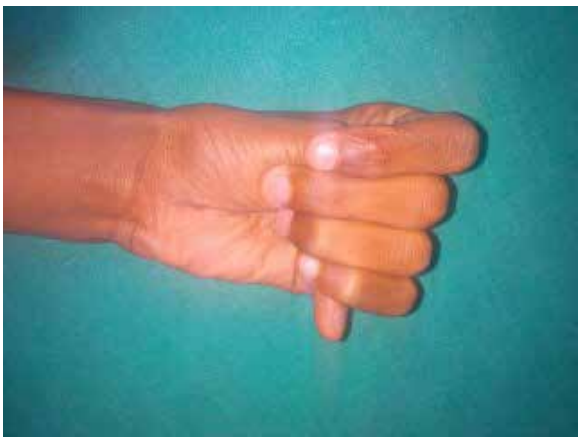


Figure 5 Steinberg sign (Thumb Sign)
Figure 6 Pes Planus

DISCUSSION :

MFS is associated with abnormal biosynthesis of fibrillin-1, a 350-kd ECM protein that is the major constituent of microfibrils. The fibrillin-1 *(FBN1)* locus resides on the long arm of chromosome 15 (15q21).[1] The minimal birth incidence is around 1 in 9800. About three quarters of patients have an affected parent; new mutations account for the remainder[2]. The most life threatening complication of Marfan syndrome is aortic aneurysm which can lead to aortic dissection, rupture or both[6]. Other cardiovascular complications include mitral valve prolapse, aortic regurgitation, tricuspid valve prolapse, and dilation of the main pulmonary artery.[7] Management focuses on preventing complications and genetic counseling. It requires a multidisciplinary team involving a geneticist, ophthalmologist , cardiologist and an orthopaedic surgeon. Most therapies currently available or under investigation aim to diminish aortic complications.

Activity restriction : Strenuous physical exertion, competitive athletics, and particularly isometric activities such as weight lifting are associated with an increased risk of aortic complications or ocular problems such as retinal detachment and should be discouraged.

Drugs : Based on the putative role of hemodynamic stress in aortic dilatation in MFS, β-blockers have traditionally been considered the standard of care, due to their negative inotropic and chronotropic effects. Numerous studies conducted in vivo managed to establish a direct link between the administration of angiotensin receptor blockers (ARBs) and the inhibition of TFGβ signalling. Calcium channel antagonists (e.g., verapamil) and angiotensin converting enzyme (ACE) inhibitors (e.g., enalapril) offer alternative therapeutic options.

Surgery: The severity of aortic disease is in relation to the extent of aortic dilation, the length of the dilated segment and

the location of the aortic involvement. Echocardiogram is recommended six months following the initial examination to determine the rate of aortic dilation and afterwards annually if aortic size is stable. In instances of aortic dilation of more than 45mm,more frequent imaging of the aorta should be considered[8]. Surgical outcome is more favorable if undertaken on an elective rather than an urgent or emergent basis. Therefore, aortic root surgery in MFS should be recommended for patients with an aortic root diameter ≥50 mm and considered for those with a rapid rate of enlargement (>5-10 mm/yr) or a family history of early aortic dissection. Preserving the native aortic valve at the time of repair is desirable to avoid the need for lifelong anticoagulation with warfarin.

Emerging studies: Several studies have shown the ability of antibodies that antagonize TGF-β to modulate the manifestations of MFS in mice, including defective pulmonary alveolar septation, myxomatousatrioventricular valves, skeletal muscle myopathy, and aortic root aneurysms. Currently, therapeutic delivery of TGF-β neutralizing antibody is not available for humans. However, a humanized anti–TGF-β1 monoclonal antibody (CAT-192) is currently under investigation for treatment of other TGF-β-related disorders, and its use remains a potential strategy for treating MFS.

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