Marfan syndrome: Report of two cases with review of literature

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Abstract

Marfan syndrome is a variable, autosomal dominant disorder of connective tissue whose cardinal features affect the cardiovascular system, eyes and skeleton. The minimal birth incidence is around 1 in 9800. About three quarters of patients have an affected parent; new mutations account for the remainder. The patient's prognosis depends on the severity of cardiovascular complications and is mainly determined by progressive dilation of the aorta. If signs of Marfan syndrome are recognized, it is important to refer to the correct health care professional for further testing to prevent associated complications. If not properly treated, premature death may be caused by the severe cardiovascular and pulmonary complications associated with Marfan syndrome. Therefore, it is important to identify this potentially life-threatening condition in general practice. This article reports two cases with a very typical features of Marfan syndrome.

Key words: Connective tissue disorder, Ghent criteria, Marfan syndrome

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Introduction

Marfan syndrome is a multisystem connective tissue disorder usually associated with mutation in fibrillin, and occasionally with mutation in TGFBR1 or 2. The minimal birth incidence is 1 in 9800.[1] About 27% of cases arise from new mutation. Marfan syndrome is a variable autosomal dominant disorder with characteristic cardiovascular, eye and skeletal features. Progressive aortic dilatation, usually maximal at the sinus of Valsalva, associated with aortic valve incompetence leads to aortic dissection or rupture and is the principal cause of mortality, but mitral valve prolapsed with incompetence may be significant, and lens dislocation, myopia, and arthritis associated with chronic joint laxity can cause substantial morbidity.[2]

The diagnosis is commonly considered in a young person with a tall, thin body habitus, long limbs, arachnodactyly, pectus deformities, and sometimes scoliosis. Other clinical findings such as a high arched palate with dental crowding, skin striae, recurrent hernia or recurrent pneumothorax may increase suspicion. Family history may be helpful, but around 27% of cases arise from new mutation.[3]

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.[4] Prophylactic medical treatment to protect the aorta with regular follow-up helps prevent or delay serious complications.

Case Reports

Case 1

A 25-year-old male reported to the department of Oral Medicine and Radiology (A.B. Shetty Memorial Institute of Dental Sciences, Mangalore, Karnataka, India) with a chief complaint of forwardly placed upper anterior teeth since childhood. Medical history of the patient revealed that

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the patient was on medication for epilepsy 8 years back but had discontinued since 7 years and the last epileptic attack occurred 1 year back. The family history of the patient was noncontributory.

On general examination, the patient was of tall stature, being 78 inches in height. Built of the patient was ectomorphic with long upper and lower extremeties and lower segment greater than the upper segment [Figure 1]. Outward bowing of the legs was noticed along with dry scaly skin. The first toe was greater than the other fingers and tapering [Figure 2]. Upper extremities showed long spidery fingers (arachnodactyly) with prominent finger joints [Figure 3]. The chest was flat with prominent ribs. Scoliosis and left kyphosis was also noticed. Stretch marks were noticed over the skin of shoulder, axilla, back of the trunk and buttocks [Figure 4].

Head and neck examination revealed a convex profile with long and narrow face [Figure 5]. The supraorbital ridges were prominent and downward sloping eyes were noticed. The nostrils were small and the nose appeared to be deviated to the left side. Intraorally, high arched palate [Figure 6] was noticed along with the collapsed maxillary arch. Teeth showed anterior crowding in both the arches with rotation of upper incisor teeth and anterior open bite.

A special clinical test for evaluation of hyperextensibility included thumb (steinberg) sign [Figure 7] and wrist (walker sign) which were both positive.

Later radiographic investigations were performed which included panoramic view, lateral cephalometric view, temporomandibular joint pen, and close views. Temporomandibular joint open and close views revealed hypermobility of the temporomandibular joint [Figure 8].

Both the clinical and radiographic findings were suggestive of Marfan syndrome. The patient was then referred for ophthalmologist and cardiac evaluation. Eye examination revealed bilateral ectopia lentis with retinal detachment.

Cardiac evaluation included color Doppler echocardiography

Figure 1: Tall stature and long-arm span

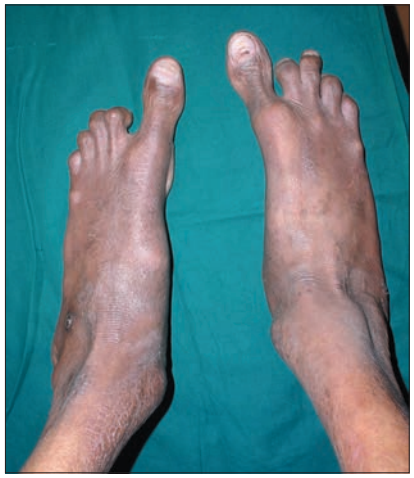

Figure 2: Dry scaly skin with long and tapering first toe

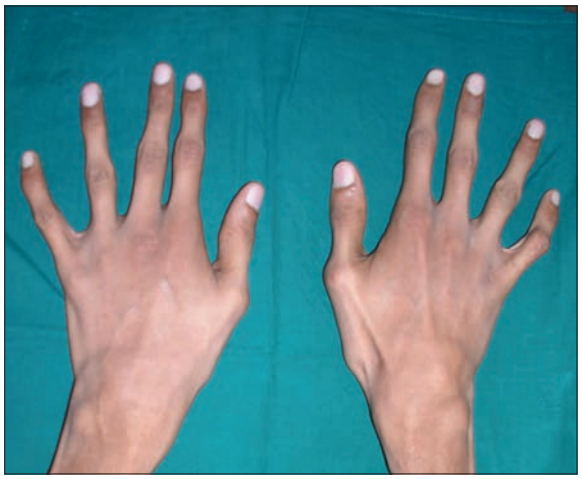

Figure 3: Long spidery fingers (arachnodactyly)

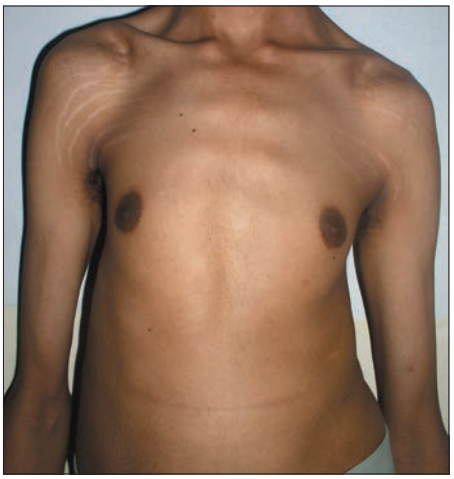

Figure 4: Stretch marks on skin of shoulder and axilla

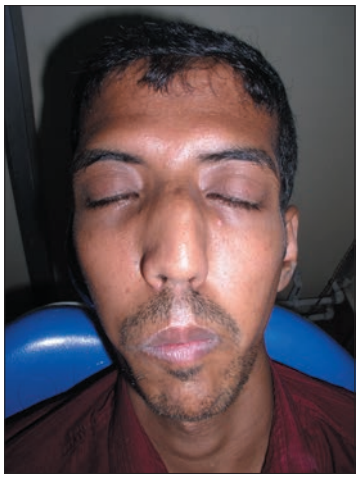

Figure 5: Extraoral photograph showing long and narrow face, prominent supraorbital ridges nostrils and small

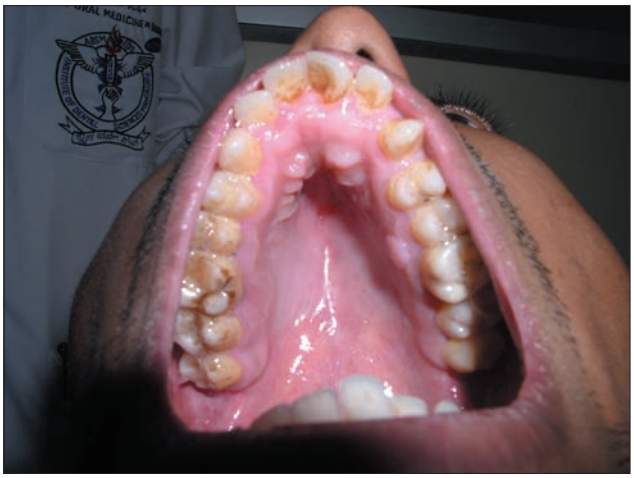

Figure 6: Intraoral photograph showing high arched palate

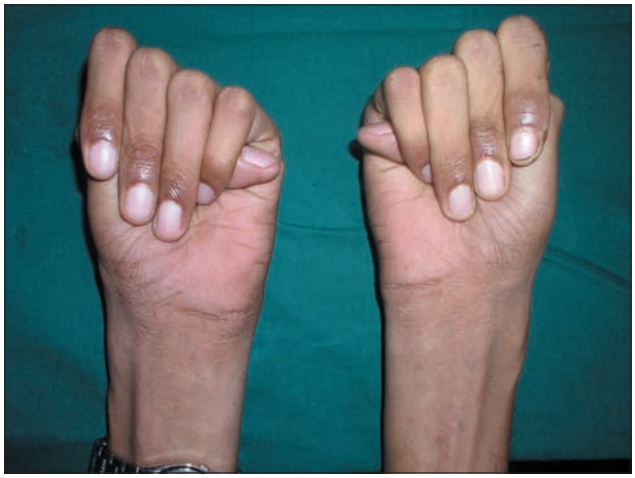

Figure 7: Positive thumb (steinberg) sign

Figure 8: TMJ open and close view showing hyperextensibility of temporomandibular joint

which revealed mild aortic annulus and root dilation with trivial mitral regurgitation, tricuspid regurgitation, and aortic regurgitation.

Dental treatment rendered to the patient involved the restoration of decayed teeth, extraction of the root stumps under antibiotic prophylaxis (cap amoxicillin 2 g given orally 1 hour before the procedure) and orthodontic treatment.

Case 2

An 11-year-old male patient reported to our department with a complaint of forwardly placed upper front teeth. Medical history revealed that patient had diminished vision when he was 5 years of age for which an ophthalmologist was consulted. All the relevant investigations were carried out and it was diagnosed as the case of subluxation of lens for which patient underwent eye surgery thrice. But it was not of much relief and was followed by bilateral retinal detachment. No history of other systemic symptoms. The family history revealed that patient's father and grandmother had similar eye problems and his father died of heart attack 6 years back.

On general examination, the patient had tall stature with the lower segment of the body greater than the upper segment and long, slender limbs, thin body habitus with increased arm span-to-height ratio [Figure 9], long, slender fingers [Figure 10], pectus carinatum [Figure 11], kyphosis, and reduced extension of elbows. The patient had positive wrist (Walker's sign) and positive thumb (Steinberg) signs.

Facial examination revealed a convex profile, elongated face, and TMJ hypermobility.

Radiographic investigations were performed which included panoramic view, lateral cephalometric view, and TMJ open and close views. TMJ open and close views revealed hypermobility of the temporomandibular joint.

Figure 9: Tall stature and long arm span

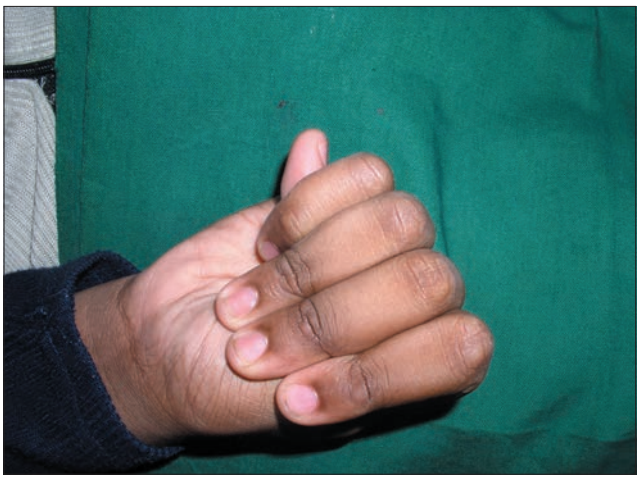

Figure-10: Long spidery fingers (arachnodactyly)

Figure 11: Deformed chest - pectus carinatum

Later, the patient was referred to a physician for a complete check-up but no abnormality was detected.

Depending upon the history and clinical features, diagnosis of Marfan syndrome was made.

Discussion

In 1991, fibrillin-1 gene mutation on chromosome 15 was identified as a cause of Marfan syndrome, but molecular testing was not as diagnostically useful as was originally hoped.[7] Fibrillin-1 mutation causes some Marfan-like disorders with a better prognosis. Recently, mutations in the transforming growth factor b-receptor 2 (TGFBR2) gene on chromosome 3 and in the TGFBR1 gene on chromosome 9 were found in some families with apparent Marfan syndrome. These "Marfan syndrome type 2" families seem less likely to have ectopia lentis.[3]

Most patients who have Marfan syndrome are usually diagnosed incidentally when they present for a routine physical examination. Marfan syndrome primarily involves the skeletal, ocular, and cardiovascular systems. Typically, patients with Marfan syndrome present with tall stature, ectopia lentis, aortic root dilatation, and a positive family history. Less frequently, the diagnosis is made when a patient presents with complications of the syndrome, such as aortic dissection, or with involvement of the pulmonary, skin/integument, or nervous systems.[2] Presentation of the disease varies greatly, even among family members. Some persons with Marfan syndrome experience only mild effects, whereas others have severe problems as seen in the present two cases. Case 1 presented with bilateral ectopia lentis with retinal detachment and cardiovascular manifestations whereas case 2 presented with bilateral ectopia lentis.

Skeletal manifestations are the cardinal signs of Marfan syndrome and usually gain the attention of a physician. The most common features include tall stature with the lower segment of the body greater than the upper segment and long, slender limbs, or dolichostenomelia; thin body habitus with increased arm span-to-height ratio; long, slender fingers, or arachnodactyly; deformities of the chest, such as pectus carinatum or pectus excavatum, scoliosis and highly arched palate with crowded teeth and dental malocclusion. Other less common manifestations include hypermobility of joints, flat foot (pes planus), reduced extension of elbows (<170°), and elongated face (dolichocephalia). Most of the features were seen in the present two cases except hypermobility of joints and flat foot (pes planus). Patients should be examined for arachnodactyly; positive wrist or Walker's sign (the distal phalange of the first and fifth fingers of the hand overlap when wrapped around the opposite wrist); and positive thumb or Steinberg sign (the thumb projects beyond the ulnar border while completely opposed within the clenched hand which were positive in both the cases).[1]

Cardiovascular manifestations are the most serious complications and determine the prognosis and survival in Marfan syndrome. Abnormalities include aortic root dilatation, aortic regurgitation, aortic dissection, and aortic aneurysm, which most commonly involves

the ascending aorta but can involve the descending aorta.[4] Mild aortic annulus and root dilation with trivial mitral regurgitation, tricuspid regurgitation, and aortic regurgitation was noticed in the first patient.

Ectopia lentis (subluxation of lens) is a hallmark feature of Marfan syndrome which is present in approximately 60% to 80% of patients[5] and was also noticed in the present cases. Ectopia lentis is usually bilateral, symmetrical, and upward. The diagnosis can be made by looking for iridodonesis (tremor of iris), phacodonesis (abnormal movement of lens), and a deep anterior chamber in the nondilated eye.[5]

Striae may occur over the shoulders and buttocks as noticed in the first case. Pulmonary manifestations include spontaneous pneumothorax and apical blebs. Marked dilatation of the dural sac may be seen frequently in computed tomography or magnetic resonance imaging scans, but the condition is usually asymptomatic.[1]

The diagnosis can be established by a comprehensive clinical evaluation and diagnostic criteria have been established. The Ghent criteria are based upon family/genetic history, involvement of organ systems (primarily skeletal, cardiovascular, and ocular), and whether the clinical sign is major or minor.[6] Major criteria are specific for Marfan syndrome and are rarely present in the general population. According to these criteria, Marfan syndrome in a patient with unequivocal family history is diagnosed when there is major involvement in one organ system (skeletal, cardiovascular, or ocular) and involvement of a second organ system. If the patient has no first-degree relative who is unequivocally affected by Marfan syndrome, the patient must have major criteria in at least two different organ systems and involvement of a third (skeletal, cardiovascular, and ocular) to be diagnosed with Marfan syndrome.[8]

Conclusion

Marfan syndrome is an inheritable connective tissue disorder and is rare as compared to acquired connective tissue disorders. Marfan syndrome is one of the most common single gene defects with a prevalence of around 1 in 9800 population. It is characterized by diverse clinical manifestations. Genetic testing is nonspecific, and the diagnosis is based on clinical criteria. Despite the morbidity and mortality associated with Marfan syndrome, appropriate medical and surgical management can improve and extend the lives of many patients, and advancing research holds the promise of further improvements in the future.

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