Indian Journal of Trauma and Emergency Pediatrics
Volume 7 Number 2, April - June 2015

Marfan Syndrome: A Case Report and Review of Literature

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Abstract

Marfan Syndrome is autosomal dominant disorder, characteristically with cardiovascular, eye and skeletal, features. Mutation in fibrillin-1 on chromosome 15 is detected in 66–91% of cases.Some cases may be due to mutation in TGFbRI or TGFbR2. Prophylactic medical treatment to protect the aorta with regular follow-up helps prevent or delay serious complications. Prophylactic aortic surgery should be considered when the aortic root at the Sinus of Valsalva exceeds 5 cm.

Keywords: Marfan Syndrome; Fibrillin-1 TGFbR1 or TGFbR2.

Introduction

Marfan syndrome is a multisystem connective tissue disorder usually associated with mutation in fibrillin, and occasionally with mutation in TGFBR1 or 2. Because it is dominant, people who have inherited one affected FBN1 gene from either parent will have Marfan's syndrome. Hence, one affected parent is sufficient to pass on the disorder to the child. Being a connective tissue disorder, Marfan's syndrome affects almost all of the body's systems, including the skeletal, cardiovascular, nervous, skin, and pulmonary systems.

Case Summary

Eleven years girl brought by his parents to our OPD with complaints of diminishing of vision since birth. There was no history of trauma to eyes. Also he was not a known case of juvenile diabetes mellitus or juvenile hypertension. There was no history of any other eye complaint, delayed milestones, any surgery, respiratory illness, cardiac illness. In family history, his father was also suffering from similar complaints along with some cardiac problem and long limb deformities, details of which were not available. Her father died 6 years ago in same course of illness. Also her paternal grandmother was suffering from similar illness & she expired in same course. Her parents had family history of non-consanguineous marriage. He was a full term normal hospital delivery with good cry and adequate weight at birth. Our case was first issue of parents out of their 3 siblings (2 males & a female); none of them having any congenital anomaly or similar illness. We admitted the girl to our hospital in paediatric ward for further investigations & management.

On examination, her vital parameters were normal as per her age. In anthropometric examination, she was having extra long upper limbs & lower limbs. Her head circumference was 52cm,chest circumference – 59 cm, .height – 140cm, upper segment / lower segment ratio – 0.70 (reduced), arm span – 142cm, mid arm circumference – 16 cm & weight – 25.03 kg. All systemic examinations were within normal limits. Opinion from Ophthalmologist was taken which after fundoscopy stated that her vision was 6/36 for both the eyes & there was superotemporal displacement of lenses in both the eyes. No retinal detachment was there. There was no any spine deformity like scoliosis or chest deformity present.

The following investigations were done

Hb – 10.5 gm%; TLC – 6900 / cmm; (N– 46, L – 42,E – 07, M – 05.)

Serum electrolytes:

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Sodium – 138 mmol / L. Potassium – 4.4 mmol / L. Calcium – 9.8mg%.

Urine examination was normal.

X-ray chest was normal.

2D ECHO didn't show any cardiac anomaly.

Colour Doppler of aorta didn't reveal any abnormality.

We diagnosed this as Marfan's syndrome on following basis

- Family history of Marfan's syndrome was present.
- Superotemporal displacement of lens.
- Systemic Score: Total = 8.

  Wrist and thumb sign = 3

  Hind-foot deformity = 2

  Reduced elbow extension = 1

  Myopia >3 diopters = 1

  Reduced upper segment / lower segment ratio & increased arm / height & no severescoliosis = 1

Discussion

Marfan's syndrome is a genetic disorder of the connective tissue with autosomal dominant inheritance. People with Marfan's tend to be unusually tall, with long limbs and long, thin fingers. Marfan's syndrome is named after Antoine Marfan, the French pediatrician who first described the condition in 1896. The gene linked to the disease was first identified by Francesco Ramirez in 1991. [1]

Marfan's syndrome has a range of expressions, from mild to severe. The most serious complications are defects of the heart valves and aorta. It may also affect the lungs, the eyes, the dural sac surrounding thespinal cord, the skeleton and the hard palate.Marfan's syndrome affects males and females equally.

The initial assessment should include a personal history, detailed family history and clinical examination including ophthalmology examination and transthoracic echocardiogram.

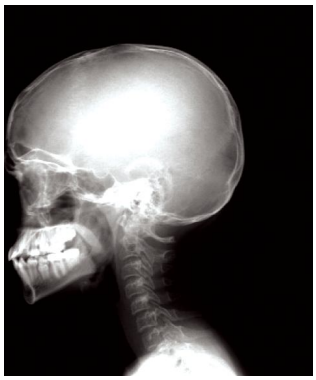
The aortic diameter at the Sinus of Valsalva should be related to normal values based on age and body surface area.The development of scoliosis and protrusioacetabulae is age dependent, commonly occurring following periods of rapid growth.X-ray for these features, depending on age, if a positive finding would make the diagnosis of Marfan syndrome[2].

A pelvic MRI scan to detect dural ectasia is indicated if a positive finding would make the diagnosis of Marfan syndrome [3].

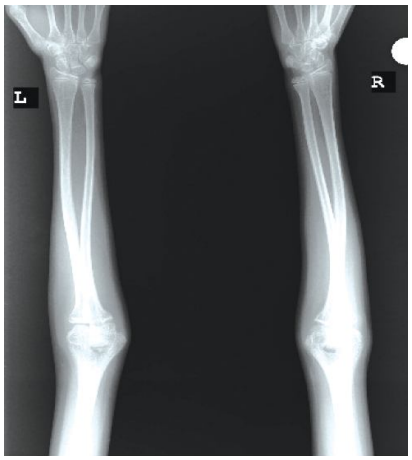
Sign and Symptoms

The constellation of long limbs, dislocated lenses and the aortic root dilation are generally sufficient to make the diagnosis of Marfan's syndrome with reasonable confidence.

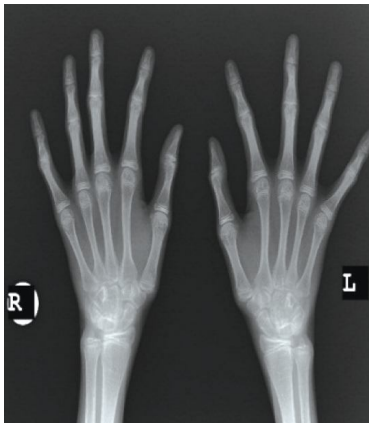
Skeletal system



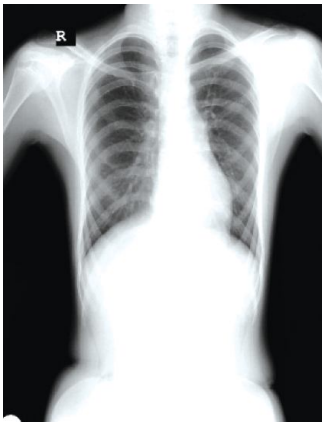
X-ray skull



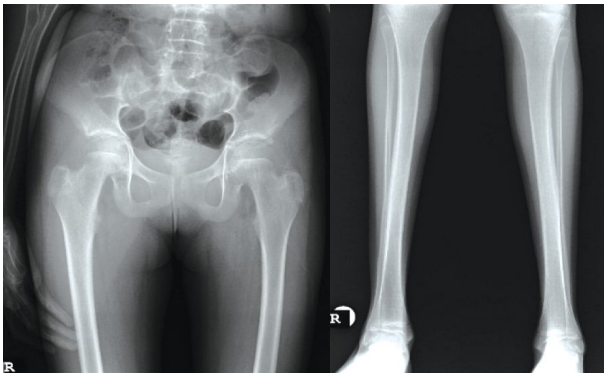
X-ray long bone (upperlimb)



X-ray showing long metacarpals



Chest x-ray PA view



X-ray HipX-ray long bone (lower limb)

Many individuals with Marfan's syndrome grow to above-average height. Some have long, slender limbs (dolichostenomelia) with long fingers and toes (arachnodactyly). An individual's arms may be disproportionately long, with thin, weak wrists. In addition to affecting height and limb proportions, Marfan's syndrome can produce other skeletal anomalies. Abnormal curvature of the spine (scoliosis), abnormal indentation (pectus excavatum) or protrusion (pectus carinatum) of the sternum are not uncommon.[4]Other signs include abnormal joint flexibility, a high palate, malocclusions, flat feet, hammer toes, stooped shoulders, and unexplained stretch marks on the skin. It can also cause pain in the joints, bones and muscles in some patients.

Eyes

Lens dislocation in Marfan's syndrome; The lens was kidney-shaped and was resting against the ciliary body

Marfan's syndrome can also seriously affect the eyes and vision. Nearsightedness and astigmatism are common, but farsightedness can also result. Subluxation (dislocation) of the crystalline lens in one or both eyes (ectopialentis) also occurs in 80% of patients. In Marfan's syndrome, the dislocation is typically superotemporal whereas in the similar condition homocystinuria, the dislocation is inferonasal.[5]Sometimes eye problems appear only after the weakening of connective tissue has caused detachment of the retina. Early onset glaucoma can be another related problem.

Cardiovascular System

The most serious signs and symptoms associated with Marfan's syndrome involve the cardiovascular system: undue fatigue, shortness of breath, heart palpitations, racing heartbeats, or angina pectoris. Cold arms, hands and feet can also be linked to Marfan's syndrome because of inadequate circulation. A heart murmur, abnormal reading on an ECG, or symptoms of angina can indicate further investigation. The signs of regurgitation from prolapse of the mitral or aortic valves result from cystic medial degeneration of the valves, which is commonly associated with Marfan's syndrome. However, the major sign that would lead a doctor to consider an underlying condition is a dilated aorta or an aortic aneurysm. Sometimes, no heart problems are apparent until the weakening of the connective tissue (cystic medial degeneration) in the ascending aorta causes an aortic aneurysm or aortic dissection, a surgical emergency. An aortic dissection is most often fatal and presents with pain radiating down the back, giving a tearing sensation.

Lungs

Marfan's syndrome is a risk factor for spontaneous pneumothorax. In spontaneous unilateral pneumothorax, air escapes from a lung and occupies the pleural space between the chest wall and a lung. The lung becomes partially compressed or collapsed.[6] This can cause pain, shortness of breath, cyanosis, and, if not treated, it can cause death.

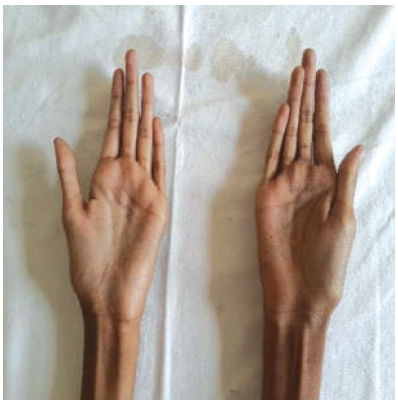
Central Nervous System

Dural ectasia, the weakening of the connective tissue of the dural sac encasing the spinal cord, though not life-threatening, can reduce the quality of life for an individual. It can be present for a long time without producing any noticeable symptoms. Symptoms that can occur are lower back pain, leg

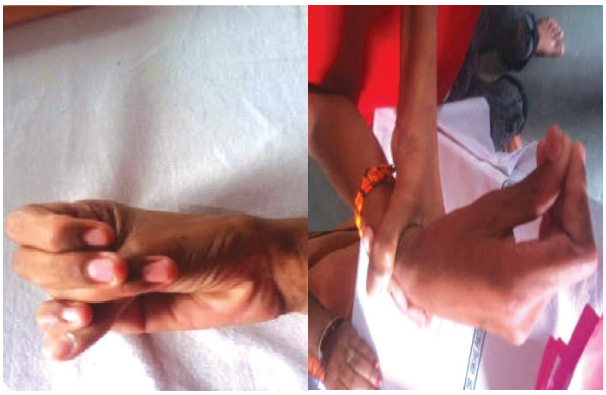
pain, abdominal pain, other neurological symptoms in the lower extremities, or headaches. Such symptoms usually diminish when the individual lies flat on his or her back. Other spinal issues associated with Marfan's syndrome include degenerative disk disease, spinal cysts and dysautonomia.

Diagnosis

Diagnostic criteria of Marfan's syndrome were agreed upon internationally in 1996. A diagnosis of Marfan's syndrome is based on family history and a combination of major and minor indicators of the disorder, for example: four skeletal signs with one or more signs in another body system such as ocular and cardiovascular in one individual.



Long metacarpals



Thumb sign Wrist sign

Revised Ghent Nosology

According to the US National Marfan Foundation, in 2010 the Ghent Nosology was revised, and new diagnostic criteria superseded the previous agreement made in 1996.

The seven new criteria can lead to a diagnosis.

In the absence of a family history of MFS:

1. Aortic root Z-score > / =2 AND ectopialentis
2. Aortic root Z-score > / =2 AND an FBN1 mutation
3. Aortic root Z-score > / =2 AND a systemic score >7 points
4. Ectopialentis AND an FBN1 mutation with known aortic pathology

In the presence of a family history of MFS (as defined above)

1. Ectopialentis
2. Systemic score > / =7
3. Aortic root Z-score > / =2

Points for systemic score

Wrist AND thumb sign = 3 (wrist OR thumb sign = 1)

Pectus carinatum deformity = 2 (pectus excavatum or chest asymmetry = 1)

Hindfoot deformity = 2 (plain pes planus = 1)

Dural ectasia = 2

Protrusio acetabula = 2

Reduced upper segment / lower segment ratio AND increased arm / height AND no severe scoliosis = 1

Scoliosis or thoracolumbar kyphosis = 1

Reduced elbow extension = 1

Facial features (3 / 5) = 1 (dolichocephaly, enophthalmos, downslanting palpebral fissures,

malar hypoplasia, retrognathia)

Skin striae = 1

Myopia >3 diopters = 1

Mitral valveprolapse (1D 4) = 1

Differential diagnosis

Many disorders have the potential to produce the same type of body habitus (i.e. shape) as Marfan syndrome. Distinguishing among these "marfanoid" disorders can be facilitated by genetic testing, and by evaluating signs and symptoms other than body habitus. Among the disorders capable of producing a marfanoid body habitus are:

- Congenital contractural arachnodactyly or Beals syndrome
- Ehlers–Danlos syndrome
- Homocystinuria
- Loeys–Dietz syndrome
- MASS phenotype

- Shprintzen–Goldberg syndrome
- Stickler syndrome
- Multiple endocrine neoplasia, type 2B

Management

There is no cure for Marfan's syndrome, but life expectancy has increased significantly over the last few decades, and clinical trials are underway for a promising new treatment. At present (2011), the syndrome is treated by simply addressing each issue as it arises and, in particular, preventive medication even for young children to slow progression of aortic dilation if such exists.

Regular checkups by a cardiologist are needed to monitor the health of the heart valves and the aorta. The goal of treatment is to slow the progression of aortic dilation and damage to heart valves by eliminating arrythmias, minimizing the heart rate, and minimizing blood pressure. Beta blockers have been used to control arrythmias and slow the heart rate. Other medications might be needed to further minimize blood pressure without slowing the heart rate, such as ACE inhibitors and angiotensin II receptor antagonists. If the dilation of the aorta progresses to a significant diameter aneurysm, causes a dissection or a rupture, or leads to failure of the aortic or other valve, then surgery (possibly a composite aortic valve graft or valve-sparing aortic root replacement) becomes necessary. New valve-sparing surgical techniques are becoming more common [7].

The skeletal and ocular manifestations of Marfan's syndrome are usually treated in the typical manner for the appropriate condition, such as with various kinds of pain medication or muscle relaxants. It is also common for patients to receive treatment from a physiotherapist, using TENS therapy, ultrasound and skeletal adjustment. This can also affect height, arm length, and life span. A physiotherapist can also help improve function and prevent injuries in individuals with Marfan's.[8] The Nuss procedure is now being offered to people with Marfan's syndrome to correct 'sunken chest' or (pectus excavatum).

A small pneumothorax might resolve without active treatment in one to two weeks. Recurrent pneumothoraces might require chest surgery. Moderately sized pneumothoraces might need chest drain management for several days in a hospital. Large pneumothoraces are likely to be medical emergencies requiring emergency decompression. Angiotensin II receptor antagonistlosartan, which appears to block TGF-beta activity, can slow or halt the formation of aortic aneurysms in Marfan syndrome.

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Indian Journal of Trauma and Emergency Pediatrics

Red Flower Publication Pvt. Ltd.

48/41-42, DSIDC, Pocket-II

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