Case Report

Emphysema, dilatation of ascending aorta and mitral valve prolapse in Marfan syndrome - A case report

Thajuddin MD[1*], E.A. Ashok Kumar[2]

[1]Post Graduate, [2]Professor
Department of Medicine, MNR Medical College and Hospital, Medak, Telangana, India
[*]Corresponding author email: **taj.md198@gmail.com**

International Archives of Integrated Medicine, Vol. 3, Issue 9, September, 2016.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 24-08-2016 **Accepted on:** 31-08-2016
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Thajuddin MD, E.A. Ashok Kumar. Emphysema, dilatation of ascending aorta and mitral valve prolapse in Marfan syndrome - A case report. IAIM, 2016; 3(9): 242-246.

Abstract

Marfan syndrome is an autosomal dominant, multisystem connective tissue disorder. Mutations are present in the *FBN1* gene on chromosome 15, which encodes for the connective tissue protein fibrillin, occasionally a mutation in TGFBR1 or 2. This disorder is characterized by skeletal, cardiovascular and ocular abnormalities. Pulmonary abnormalities occur in approximately 10% of patients, the commonest being spontaneous pneumothorax and emphysema**.** Cardiovascular abnormalities being Mitral valve prolapse (MVP), is a relatively frequent abnormality and Aortic dilatation. Aortic root dilatation is one of the cardinal features of Marfan syndrome. But aorta may be dilated anywhere in its course, most common being ascending aorta. In this case report, a 17 years old boy with Marfan syndrome presented with combination of emphysema, dilatation of ascending aorta, mitral valve prolapse, which is rare.

Key words

Marfan syndrome, Emphysema, Mitral valve prolapse, Dilatation of ascending aorta.

Introduction

Marfan syndrome is anautosomal dominant, multisystem connective tissue disorder, with an incidence of about 1 in 5,000 [1]. Mutations are present in the *FBN1* gene on chromosome 15, which encodes for the Connective tissue protein fibrillin, occasionally a mutation in TGFBR1 or 2, fibrillin-1 [2]. Fibrillin-1 is the main component of microfibrils, which, in turn, are constituents of elastic fibers. Microfibrils confer mechanical stability, contribute to growth factor regulation, and are thought to have a role in

tissue development and homeostasis [3]. Fibrillin-1 mutations are thought to lead to haploinsufficiency and/or dominant negative activity of the mutant fibrillin-1 protein. Tissues with abundant type I collagen are most prominently affected, including the skeletal, ocular, and cardiovascular systems [4]. 25% of cases arise from de novo mutation FBN 1 gene mutation on chromosome 15 [5]. This disorder is characterized by skeletal, cardiovascular and ocular abnormalities. Pulmonary abnormalities occur in approximately 10% of patients, although pulmonary symptoms are not main feature in the Marfan syndrome [6, 7]. Many cases have underlying pulmonary pathology, the commonest being spontaneous pneumothorax and emphysema [8-10]. Many cases who had no or mild pulmonary symptoms were found to have restrictive pattern and few obstructive pattern on PFT and some kind of emphysematous changes at autopsy. So far in literature many cases reported with histologically diagnosed cases of emphysema, the most common being distal acinar, but can occur any histological type[4]. Mitral valve prolapse (MVP), an abnormal displacement into the left atrium of a thickened and redundant mitral valve during systole, is a relatively frequent abnormality in Marfan syndrome, clinically presents as chest pain, palpitations, tachycardia and shortness of breath. Aortic root dilatation is one of the cardinal features of Marfan syndrome. But aorta may be dilated anywhere in its course, most common being ascending aorta. Other characteristic features include anterior chest deformity, long fingers, aortic root dilatation and dissection, lens dislocation and myopia. Less specific features include high arched palate, crowding of teeth and skin striae. In this case report a 17 years boy with Marfan syndrome presented with combination of emphysema, dilatation of ascending aorta, mitral valve prolapse which is rare.

Case report

A 17 years old male, presented with the complaints of breathlessness without exertion of 2 months duration, palpitation of one month duration and fever not associated with chills and rigors of one day duration. There was no history of running nose, cough, paroxysmal nocturnal dyspnoea, chest pain, haemoptysis, pedal oedema, syncopal attacks, joint pains, pain abdomen, vomiting or rash. He was not a known case of hypertension, diabetes, tuberculosis, bronchial asthma, epilepsy, hypo or hyperthyroidism .He is a non-smoker and non-alcoholic. He was born out of consanguineous marriage. He had one elder sibling who was apparently normal.

On examination, patient was thin built and tall in stature, height 165 cm, arm span 172 cm, upper segment 72 cm, lower segment 93 cm, poorly nourished, weight 40 kg, BMI 14.5, head circumference 52 cm, inter canthal distance was normal. No other skeletal deformities were noted. He had high arched palate, wrist sign positive, thumb sign positive, arachnodactyly was noted, hyper extensibility of fingers was present. Lens dislocation, Café au lait spots were absent. His temperature was 99.4^0 F, PR - 120/min regular, B P-110/70 mmHg, RR-16/min, and JVP was normal.

Examination of Respiratory system – Trachea was central in location, Barrel shaped chest, chest circumference was 70 cm at rest and 73 cm on full inspiration. Expansion of chest was 3 cm, right hemi thorax 35 cm at rest and 36.5 cm on full inspiration, left hemi thorax 35 cm at rest and 36.5 cm on full inspiration. AP diameter – 18 cm, Transverse diameter – 24 cm i.e. ratio was 3:4. Hyper resonant note was present all over the areas of lungs, liver dullness upper level was at the right 8^{th} inter costal space, Vesicular breath sounds heard over all the areas of lungs .

Examination of Cardio vascular system –Apex beat was felt in left 5^{th} inter costal space medial to mid clavicular line, JVP was normal, Apex impulse tapping type in the left 5^{th} inter costal space on mid clavicular line, On auscultation mitral area- loud S1 and normal S2, mid systolic click heard at third left parasternal area, normal

heart sounds were heard in all other areas. Per abdomen Examination -liver was palpable 2 cm below the costal margin, liver span was normal. Examination of CNS – no focal neurological deficit was noted.

On investigations

Complete blood picture: Hb - 11 gm%, RBC - 4.5 millions/mm^3, WBC - 8200/mm^3, DC – Neutrophils - 62%, Eosinophils - 2%, Lymphocytes - 34%, Monocytes - 2%, Basophils - 0%, Platelets - 1.6 lakhs/mm^3, ESR – 10 mm 1st hour, RBS - 109 mg/dl. Complete Urine Examination revealed Albumin - nil, Sugar - nil, Pus cells - 1 to 2 cells/mm^3, RBC - 2 to 3 cells/mm^3. ECG revealed heart rate of 110/mt, normal sinus rhythm, regular, Right Axis Deviation +, Right Ventricular Hypertrophy +, P mitrale and incomplete RBBB. X-ray chest PA view-showed increased rib spaces, hyper inflated radiolucent lungs. 2D ECHO- showed dilation of ascending aorta, mitral valve prolapse was present, no Mitral regurgitation, no Aortic Regurgitation. PFT-restrictive pattern/obstructive pattern, FEV1/FVC ratio was Predicted - 92.6, Pre test – 74.0, Post test -77.1, FEV 25% - 75% was Predicted - 3.75, Pre test – 1.43, Post test - 1.60, indicating small airway disease .X-ray left hand AP - View revealed Metacarpal Index of 10.1 Based on history, clinical examination and investigations patient was diagnosed as a case of Marfan syndrome with Emphysema, Ascending Aorta Dilatation and Mitral Valve Prolapse (**Figure – 1 to 5**).

Figure – 1: PFT-showing restrictive pattern.

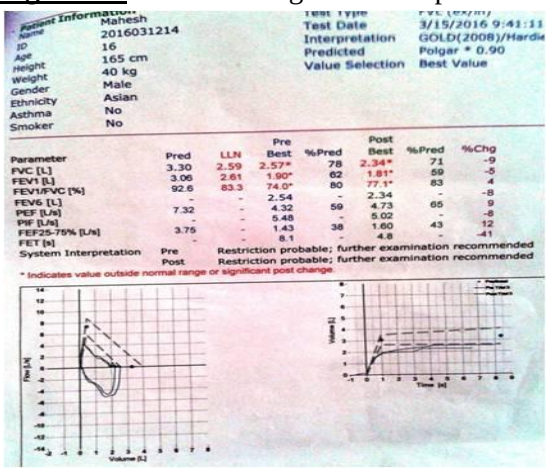


Figure – 2: 2D echo report showing MVP and Ascending Aorta dilatation.

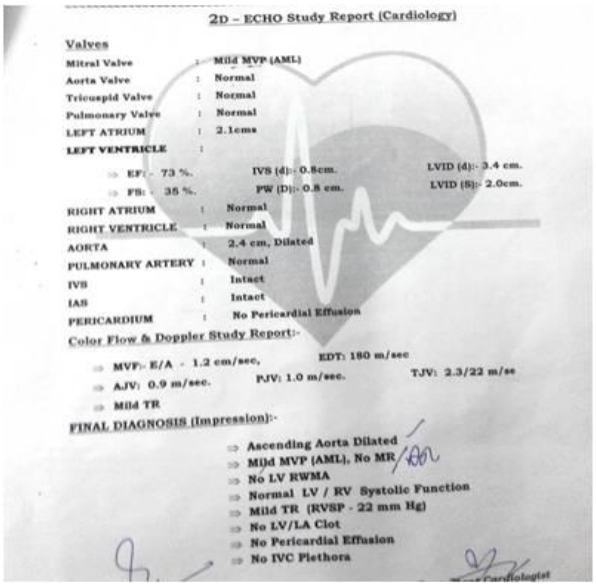


Figure – 3: X-ray left hand AP and Lateral. Metacarpal index was 10.1.

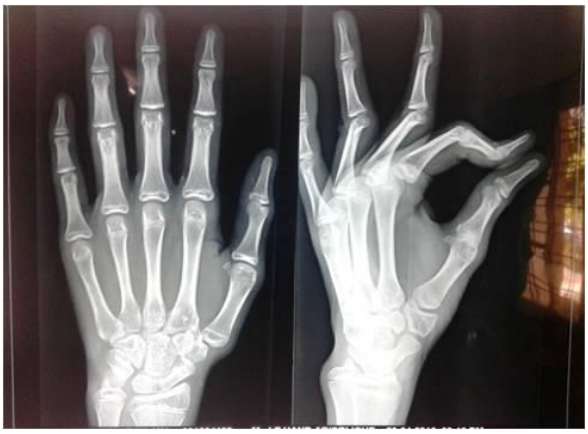


Figure – 4: X-ray chest PA view showing Emphysematous changes.

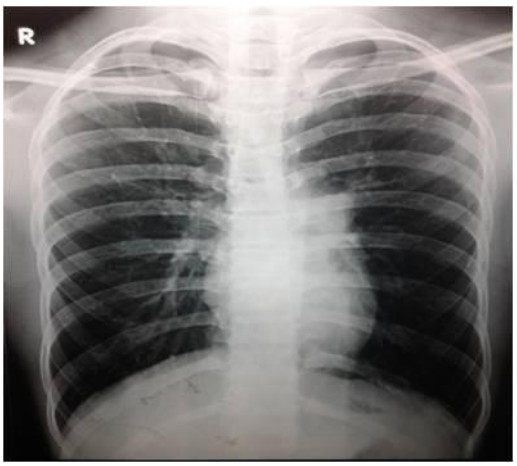
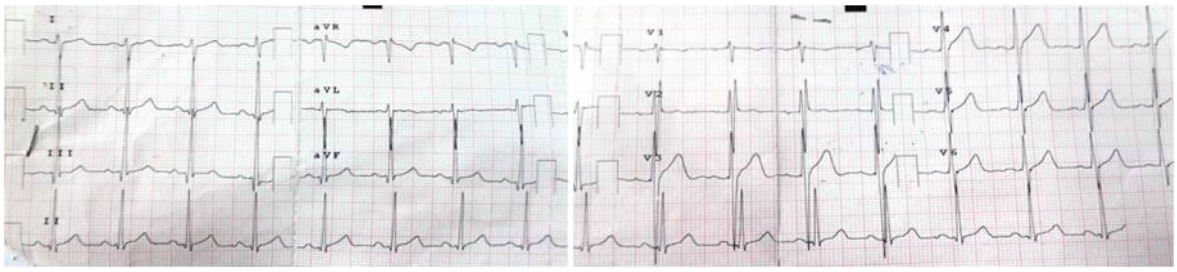


Figure – 5: ECG - within normal limits.



Discussion

Marfan syndrome is an autosomal dominant, multisystem connective tissue disorder, Mutations are present in the *FBN1* gene on chromosome 15, which encodes for the Connective protein fibrillin, occasionally a mutation in TGFBR1 or 2. 25% of cases arise from denovo mutation FBN 1 gene mutation on chromosome 15. This disorder is characterized by skeletal, cardiovascular and ocular abnormalities. Pulmonary abnormalities occur in approximately 10% of patients, although pulmonary symptoms are not the main feature in the Marfan syndrome. Many cases have underlying pulmonary pathology, the commonest being spontaneous pneumothorax and emphysema. The pulmonary histologic changes in Marfan syndrome have been described in a number of small series and case reports. These include widespread or patchy cystic changes, emphysema, and spontaneous pneumothorax; focal pneumonia or bronchiectasis, bullae, congenital pulmonary malformations (particularly middle lobe hypoplasia), and apical fibrosis have also been described [4, 11]. However, no literature exists that has reported a critical microscopic examination of these tissues for histologic similarities. As medical and surgical treatments continue to improve, patients with Marfan syndrome are living longer and experiencing age-related disease. In addition, the inheritance of Marfan syndrome does not preclude the presence or development of a second pulmonary disease process. It will be important in the future to be able to separate true Marfan- related pulmonary changes from those attributable to other pathologic processes Fibrillin is an important component of the microfibrillar system that acts as a scaffold for elastogenesis. The pathophysiology comes out of degeneration of elastic fibers in Marfan syndrome seem to explain the majority of manifestations of this condition. Stiffness and reduced distensibility of the aorta in response to increased pulse pressure, is the important consequence of elastin degeneration. Recently, another hypothesis has emerged trying to explain the pathophysiology behind Marfan syndrome. Transforming growth factor beta, a cytokine that regulates cell morphogenesis, is thought to contribute to the Marfan syndrome phenotype. Abnormal fibrillin causes failure of the sequestration of the inactive latent precursor of TGF beta, resulting in excessive activation of TGF beta, and thus producing the phenotype of Marfan syndrome. Many cases who had no or mild pulmonary symptoms were found to have restrictive pattern and few obstructive pattern on PFT and some kind of emphysematous changes at autopsy. Many cases reported with histological diagnosed case of emphysema, most common being distal acinar, but can occur any histological type. . Mitral valve prolapse (MVP), an abnormal displacement into the left atrium of a thickened and redundant mitral valve during systole, is a relatively frequent abnormality in Marfan syndrome, clinically presents as chest pain, palpitations, tachycardia and breathless [12, 13]. Aortic root dilatation is one of the cardinal features of Marfan syndrome. But aorta may be dilated anywhere in its course, most common being ascending aorta. Other characteristic features include anterior chest deformity, long fingers, aortic root dilatation and dissection, lens dislocation and myopia [14, 15]. Less specific features include high arched palate, crowding of

teeth and skin striae. In this case report a 17 years boy with Marfan syndrome presented with emphysema, dilatation of ascending aorta, mitral valve prolapse, which is rare.

References

1. Rangasetty UC, Karnath BM. Clinical signs of Marfan syndrome. Hosp physician, 2006; 42(4): 33-38.
2. Bolieau C, Jondeau G, Mizuguchi T, et al. Molecular genetics of Marfan syndrome. Curr Opin Cardiol., 2005; 20: 194-200.
3. Ramirez F, Dietz HC. Marfan syndrome: from molecular pathogenesis to clinical treatment. Curr Opin Genet Dev., 2007; 17: 252-258.
4. Tanoue LT. Pulmonary involvement in collagen vascular disease: a review of the pulmonary manifestations of the Marfan syndrome, ankylosing spondylitis, Sjögren's syndrome, and relapsing polychondritis. J Thorac Imaging., 1992; 7: 62-77.
5. Collod-Beroud G, Boileau C. Marfan syndrome in the third millennium. Eur J Hum Genet., 2002; 10: 673-681.
6. Paepe AD, Devereux RB, Dietz HC, et al. Revised diagnostic criteria for the Marfan syndrome. Am J Med Genet., 1996; 62: 417-426.
7. Loeys BL, Dietz HC, Braverman AC, et al. The revised Ghent nosology for the Marfan syndrome. J Med Genet., 2010; 47: 476-485.
8. Wood JR, Bellamy D, Child AH, et al. Pulmonary disease in patients with Marfan syndrome. Thorax, 1984; 39: 780-784.
9. Dwyer EM, Troncale F. Spontaneous pneumothorax and pulmonary disease in the Marfan syndrome. Ann Intern Med., 1965; 62: 1285-1292.
10. Hall JR, Pyeritz RE, Dudgeon DL, et al. Pneumothorax in the Marfan syndrome: prevalence and therapy. Ann Thorac Surg., 1984; 37(6): 500-4.
11. Sharma BK, Talukdar B, Kapoor R. Cystic lung in Marfan's syndrome. Thorax, 1989; 44: 978-979.
12. Arthur E. Weyman and Marielle Scherrer-Crosbie Marfan syndrome and mitral valve prolapsed. J. Clin. Invest., 2004; 114: 1543–1546.
13. Huggon IC, Burke JP, Talbot JF. Contractural arachnodactyly with mitral regurgitation and iridonesis. Arch Dis Child, 1990; 65: 317-19.
14. Kim M Summers, Jennifer A West, Annette Hattam, Denis Stark, James J McGill, Malcolm J West. Recent developments in the diagnosis of Marfan syndrome and related disorders. MJA, 2012; 197: 494 – 497.
15. IAMS H.D. Diagnosis and management of marfan syndrome. Curr. Sports Med. Rep., 2010; 9(2): 93-98.