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Case Report

Spontaneous Pneumothorax Revealing Marfan Syndrome

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Abstract

Marfan syndrome is a multisystem connective tissue disorder with distinct physical characteristics. It is an autosomal-dominant, heritable disorder which affects many organs. An early diagnosis, medication to protect the aorta, and prophylactic surgery to replace the enlarged aortic root lead to a relatively normal life expectancy. We report case of an18-year-old boy who had a Marfan syndrome revealed by spontaneous pneumothorax. The patient met the Ghent diagnostic criteria of Marfan syndrome through the musculoskeletal features as well as the aorta aneurysm.

Keywords: *Marfan Syndrome; Pneumothorax; Pectus Carinatum*

Abbreviations

MFS: Marfan Syndrome; MRI: The Magnetic Resonance Imagery; TGF-β: Transforming Growth Factor Beta; TGFBR1: Transforming Growth Factor Beta Receptors Type 1; TGFBR2: Transforming Growth Factor Beta Receptors Type 2; TAA/D: Thoracic Aortic Aneurysm and Dissection; FBN1: Glycoprotein Gene Fibrillin-1

Introduction

Marfan syndrome is a multisystem connective tissue disorder with distinct physical characteristics. It shows an autosomal dominant pattern of inheritance and 25 - 30% of cases show sporadic mutation [1]. Marfan syndrome patients have a risk for spontaneous pneumothorax that is 10 times higher than the general population with an associated prevalence that is between 4 and 11% [2].

Case Presentation

An 18-year-old young man presented to the emergency department with a sudden onset of pain in the left anterior portion of the chest and severe dyspnea. He had no prior medical or surgical history. On physical examination, the patient had a pectus carinatum (pigeon chest) (Figure 1) and a probable pneumothorax of the left hemithorax. The chest x-ray confirmed the diagnosis (Figure 2). A closed chest tube drainage was performed, and the left lung re-expanded completely over the next few days. The patient was a 166 cm tall and thin. The musculoskeletal examination showed extremely long, slender fingers and toes with widened space between the hallux and second toe (Figure 3) and a positive wrist (Figure 4) and thumb sign (Figure 5). The cutaneous examination found stretch marks in the axillary region and the back (Figure 6). Marfan syndrome (MFS) was suspected. The chest computed tomography showed a small left pneumothorax, apical emphysema, an aneurysm of the aorta and a diaphragm hernia (Figure 7). The patient was referred to the cardiology department for a cardiovascular evaluation which found an enlargement of the aortic root so the patient was given atenolol. An echocardiogram is to be done annually to monitor the aortic root dilatation. The magnetic resonance imagery (MRI) of the rachis did not find any ectasia of the dura mater. The clinical geneticist confirmed that the patient met the Ghent diagnostic criteria for MFS.

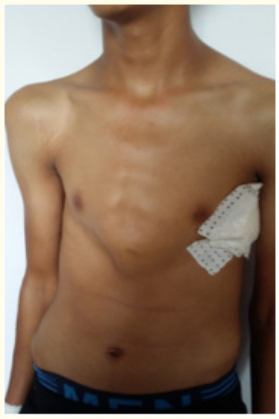

Figure 1: *Pigeon (pectus carinatum).*

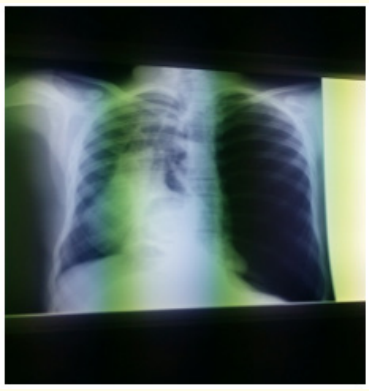

Figure 2: *Chest X-ray showing evidence of left Pneumothorax.*

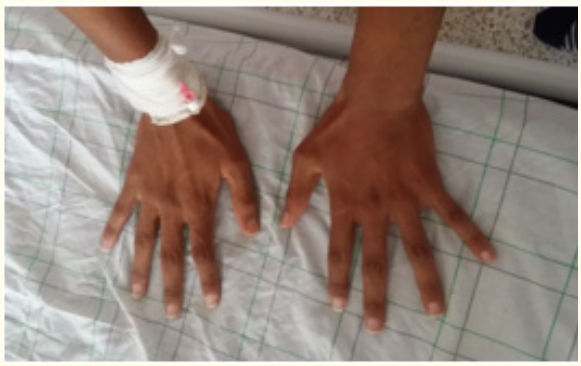

Figure 3: *Long digits on hands (dolichostenodactyly).*

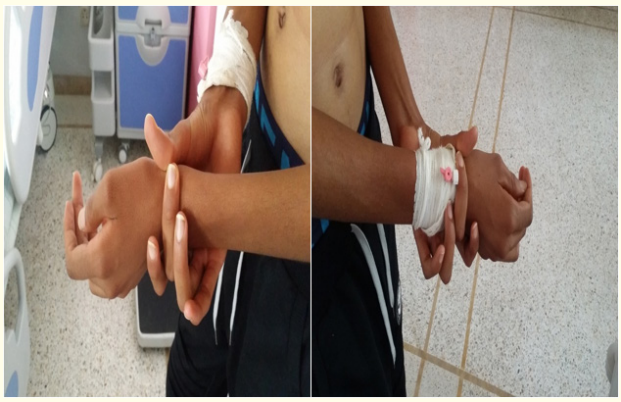

Figure 4: *Wrist sign: the thumb and fifth finger overlap when grasping the wrist of the opposite hand.*

Figure 5: *Thumb sign: the thumb protrudes beyond the edge of the palm.*

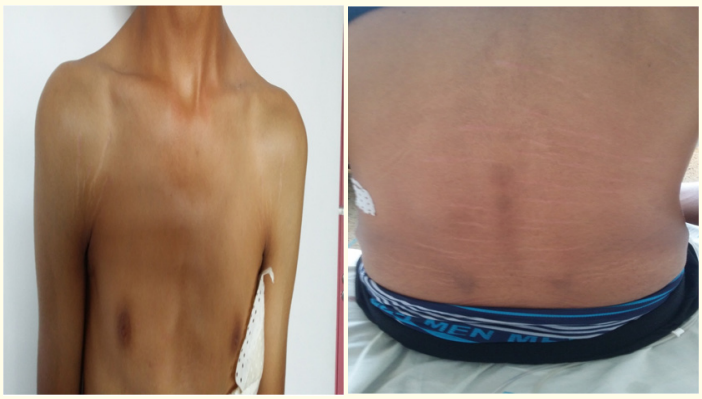

Figure 6: *Stretch marks in the axillary region and the back.*

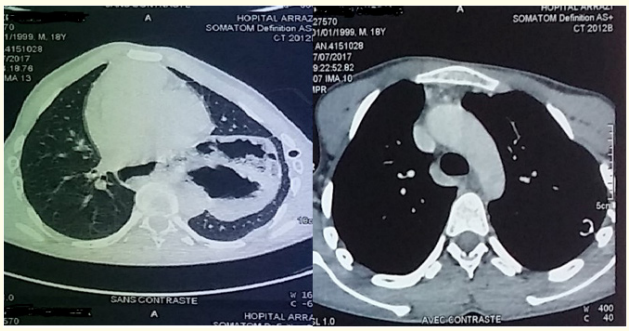

Figure 7: *The chest computed tomography showed a small left pneumothorax, apical emphysema, an aneurysm of the aorta and a diaphragm hernia.*

Discussion

Marfan syndrome is an autosomal-dominant, heritable disorder of the connective tissue. It affects many organs and, if untreated, results in premature death primarily due to aortic dissection. The cause is a mutation in the gene FBN1, which encodes the large glycoprotein, fibrillin-1. This condition can result in disproportionate tall stature, displacement of the ocular lens, aortic aneurysm, hypermobile joints, scoliosis, and pneumothorax, among many other features. Early diagnosis, treatment with medication to protect the aorta and prophylactic surgery to replace the enlarged aortic root lead to a relatively normal life expectancy [3].

First identified in 1902, the syndrome was named after Antoine-Bernard Marfan, a professor in pediatrics from Paris, who described a 5-year-old child with long arms and legs and numerous skeletal abnormalities. MFS has a worldwide prevalence of approximately 1 per 3,000 to 5,000 individuals [4]. This prevalence is likely underestimated because the symptoms unravel with aging. Many of the subtle physical characteristics may go undiagnosed by pediatric health care professionals unfamiliar with the underlying genotype. Although the inheritance is autosomal dominant and can commonly be recognized in a family pedigree, about 25% of diagnoses are due to sporadic de novo mutations that are difficult to identify and may not be reported in the MFS universal mutation database. Genetic variants in transforming growth factor beta (TGF-β) receptors type 1 (TGFBR1) and type 2 (TGFBR2) genes have been associated with different hereditary connective tissue disorders sharing thoracic aortic aneurysm and dissection (TAA/D). Mutations in both TGFBR1/2 genes have been described in patients with TAA/D and Marfan syndrome (MFS), and they are associated consistently with Loeys-Dietz syndrome. The existing literature shows discordant data resulting from mutational screening of TGFBR1/2 genes in patients with MFS. The aim of the study was to investigate the role of TGFBR1/2 genetic variants in determining and/or modulating MFS clinical phenotype [5].

Diagnostic criteria [4]

The diagnostic criteria of MFS have evolved thanks to the recent technological advancements in genetics. The criteria were established first in 1986 at the International Nosology of Heritable Disorder of Connective Tissue Meeting in Berlin. A more elaborate set of diagnostic criteria, labeled the Ghent criteria, was developed in 1996 to redefine the diagnosis of MFS. In 2010, a group of experts convened in Belgium to further change the Ghent diagnostic criteria in order to focus the differential diagnosis based on clinical evidence, family history, and genetic testing. The likelihood of identifying a mutation in FBN1 in a patient with MFS using the Ghent criteria is 95%. Diagnostic criteria verify the presence of defects in systemic features (Table 1). The new diagnostic criteria are divided into two subcategories depending on absence or presence of MFS in the family history (Table 2). In the absence of a family history there are four possible combinations for unequivocal diagnosis of MFS. The first is that both aortic root dilatation/dissection and ectopia lentis are present. The second is that both aortic root dilatation/dissection and an FBN1 mutation are confirmed. The third is an aortic root dilatation/dissection and a score

of 7 points or greater in systemic features (Table 1). The last way to confirm the diagnosis of MFS in the absence of a family history is the presence of ectopia lentis and a mutation of the FBN1 gene known to cause aortic disease. There are additional subtle signs of MFS that are not part of the scoring of systemic features such as a long, narrow face; crowded teeth due to the high arched palate. Other features include: nearsightedness; glaucoma at an early age; cataracts; detached retina and hernias and breathing problems such as snoring or sleep apnea [4]. Neurologic complaints can be found when the patient is older and the connective tissue that covers the brain and spinal cord weakens and stretches, which can cause numb, weak lower extremities and abdominal pain. Anywhere in the body where connective tissue is located can be affected. These symptoms may present as the chief complaint of the patient [4].

MFS features	**Points**
Wrist AND thumb sign	3
Wrist OR thumb sign	1
Pectus carinatum (pigeon chest)	2
Chest asymmetry or pectus excavatum (hollow chest)	1
Hindfoot deformity (forefoot abduction and lowering of midfoot)	2
Pes planus (flat footed)	1
Pneumothorax (collapsed lung)	2
Dural ectasia (widening of the membrane around spinal column on CT or MRI)	2
Protrusio acetabuli (deep hip socket)	1
Reduced US/LS ratio (without severe scoliosis) AND increased arm/height	2
Scoliosis or kyphosis (curvature of the spine)	1
Reduced elbow extension (< 170_)	2
Skin striae (without weight gain or pregnancy)	2
Myopia >3 diopters (moderate)	2
Mitral valve prolapse (all types)	1
Facial features (3/5 present)	1
Enophthalmos (eyeball recession into orbit)	1
Retrognathia (underdevelopment of maxilla or mandible)	1
Malar hypoplasia (small cheek bones)	1
Dolichocephaly (long head)	1
Down-slanting palpebral fissures (down-slanting eyes)	
Note: CT, computed tomography scan; LS, lower segment; MFS, Marfan syndrome; MRI, magnetic resonance imaging; US, upper segment.	
Score greater than 7 indicates systemic involvement. Maximum total points = 20.	
A Lower segment (LS) is measured from the top of the symphysis pubis to the floor. The upper segment (US) is calculated by subtracting the lower	

Table 1: *Scoring of systemic features of MFS.*

Positive family history	Negative family history
A positive family history of MFS and one of the following: • Ectopia lentis • Systemic feature score > 7 • Aortic diameter with a Z-score of > 2 (above 20 years of age) or > 3 (below 20 years of age)	An absent family history of MFS and one of the following: • Enlarged aortic diameter + ectopia lentis • Enlarged aortic diameter + FBN1 mutation • Enlarged aortic diameter + systemic feature score > 7 • Ectopia lentis + FBN1 mutation known to cause aortic disease

Table 2: *Diagnostic criteria for MFS in the absence of a positive or negative family history.*

Conclusion

Marfan syndrome might be a rare cause of pneumothorax, albeit, it should be considered when treating patients for recurrent spontaneous pneumothorax or rib cage abnormalities. The early detection of this autosomal-dominant, heritable disorder of the connective tissue can significantly improve the prognosis of cardiac abnormalities which are the main life-threatening feature of the disease [6].

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