Marfan syndrome in adulthood: a case report

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ABSTRACT
Marfan syndrome is an autosomal dominant connective tissue disorder, caused by a defect in the fibrillin-1 gene, which plays an important role in the formation of elastic tissues. It is diagnosed on clinical grounds, some of which depend on growth. Our purpose is to describe an atypical case of Marfan syndrome in a 44 year-old-male patient, with no history of health problems, who arrives at the Emergency Department with shortness of breath, abdominal pain and great pedal edema. On physical examination, heart murmur, elevated jugular venous pressure and congestive hepatomegaly were found. Chest radiograph, transthoracic echocardiogram, and ophthalmologic examination were performed, after which Marfan syndrome was diagnosed, according to the clinical picture and the revised Ghent criteria.

Key words: Marfan syndrome, Aortic regurgitation, Aortic aneurysm, skeletal disturbances, Lens subluxation

INTRODUCTION
Marfan syndrome is the most common inherited multisystem connective tis-
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 Skeletal disorder. This autosomal dominant disease has an incidence of 2-3 per 10,000 individuals, without predilection of gender, race or ethnic group. It has been demonstrated that the cause of this disease is a change in the FBN1 gene, which encodes the fibrillin-1 protein, a component of a microfibrils network serving as a frame to elastin deposition and assembly of elastic fibers. In this gene, over 500 mutations have been described and almost all are unique for an individual or family affected, giving rise to a hereditary defect in the fibrillin-1 and causing a formation of abnormal elastic fibers, with the consequent dysfunction of the tissues that present it. Furthermore, it has been postulated that normal fibrillin would inhibit growth of the long bones and elastic fibers through its tension would control the growth of these; therefore, since there is an alteration in these structures an exaggerated bone growth would occur, typical of the disease.

Its complications affect the eyes, lungs and musculoskeletal system; but the high mortality of untreated cases results almost exclusively from cardiovascular complications, including aortic dissection and its rupture.

Advances in the understanding of the causes of Marfan syndrome, its early diagnosis and the subsequent medical or surgical therapy has led to the marked improvement in the prognosis of the affected population, compared to previous decades. Early identification of asymptomatic patients is essential to reduce the frequency of fatal aortic accidents. This paper aims to present the case of an adult patient with no history of health problems that started with a clinical picture of global heart failure and, at admission, a Marfan syndrome was diagnosed. Its importance is given by the lateness of diagnosis, which was only achieved in collaboration with the Cuban Brigade.

**CASE REPORT**

44 year-old-male patient, with no history of health problems, who arrives at the Emergency Department of Hospital do Prenda with shortness of breath, which began two weeks ago, first on exertion, and then it forced him to rise at night when he was sleeping, relieved by sitting, with approximately one hour duration. He also complained of abdominal pain in the right upper quadrant and increased volume of lower limbs up to half of both thighs.

**Positive data on physical examination**

- Height: 2.10 meters, long arms and fingers. Arachnodactyly. Positive wrist/thumb sign. Joint laxity, flat feet, and decreased adipose tissue (Figure 1).
- **Pectus carinatum**, with decreased thorax expansion, superficial polypnea, respiratory rate of 34 beats per minute and crackling rales in both lung bases, more pronounced on the left hemithorax.
- Irregular and bounding pulse.

![Figure 1. Skeletal characteristics of the patient. A. Above-average height, elongated arms, decreased adipose tissue. B and C. Arachnodactyly, wrist/thumb positive sign, joint laxity.](image)
Apex beat was visible, palpable and displaced outside the midclavicular line. First noise decreased in the apex, sisto-diastolic murmur in the left sternal border with prevalence of the diastolic component (grade IV/VI) with neck irradiation. Elevated jugular venous pressure. Blood pressure: 100/70 mmHg.

- Soft and palpable abdomen, painful on palpation in the right upper quadrant, with hepatomegaly of 4 cm below the costal margin. Presence of hepatotheracic reflux.
- Soft, cold and painless edema in the lower extremities to the middle of both thighs, with presence of pitting edema.

It was decided to admit the patient with the diagnosis of overall heart failure, and drug treatment was started, with which the clinical picture improved. Given the phenotypic characteristics of this patient and auscultatory findings suggestive of aortic valve disease, it was decided to perform other complementary tests:

1. **Echocardiography (Figure 2):** Dilated ascending aorta, with pearly appearance, 77 mm diameter, non-dilated aortic annulus and normal aortic arch (34 mm) were observed. Severe aortic regurgitation which fully occupied the outflow tract of the left ventricle with 80 ml regurgitant volume and effective regurgitant orifice area of 0.95 cm². Dilated left ventricle with mild global hypokinesia and decreased systolic function (ejection fraction 40%).

2. **Eye exam:** Slit lamp: clear cornea is observed in both eyes, anterior chamber with increased depth, lens subluxation and iridodonesis.

Given these findings it was concluded that the patient presented Marfan syndrome. He was told about the possibility of surgical treatment of aortic valve disease and he agreed. During hospital stay the patient had a cardiac arrest and died.

**COMMENT**

Marfan syndrome is caused by the alteration in the microfibrils, usually caused by mutation of FBN1 gene encoding fibrillin-1, and is located on chromosome 15q21; all of which was first described by Dietz et al. in 1991. Fibrillin-1, an extracellular glycoprotein essential for fibrogenesis is the major component of the microfibrils of 10-12 nm, which forms, together with elastin, the elastic fibers found in tissues. FBN1 mutations increase susceptibility of fibrillin-1 for *in vitro* proteolysis, with the fragmentation of microfibrils as a result.

Diagnosis is mainly based on clinical findings. There are three forms of presentation closely related to age, and to well-defined clinical conditions and prognosis: neonatal, child and classic. The latter is the most common and recognized, and occurs in children, adoles-
cents and adults. In accordance with the new diagnostic criteria for Marfan syndrome published in 2011, arising from the review of the classical Ghent criteria, the patient phenotype characterizes the diagnosis of this syndrome from other diseases with similar phenotypes.

Skeletal disorders are the most common and earliest to detect, and therefore are the ones to first establish the suspicion of the disease. They are progressive with age and are completed in adolescence. The most frequent are: extreme height, pectus excavatum or carinatum, arachnodactyly, scoliosis, joint hypermobility and high arched palate. Cardiovascular injuries determine the prognosis of Marfan syndrome, since they cause the highest mortality, between 70-95% of cases, aortic dilatation has been the most specific and frequent problem. Its incidence depends on the age, 40-80% in children and 80-100% in adults.

Ocular involvement is common (70%) and progressive. The more specific lesion for diagnosis is lens subluxation; however, you must also identify refraction errors to preserve the maximum visual function.

When considering the diagnostic criteria described above, this patient presented:
1. Family and genetic history: Physical examination on first-degree relatives was performed without finding evidence of the disease.
2. Skeletal System:
   - Pectus carinatum: 2 points.
   - Flat foot: 1 point.
   - Wrist/thumb sign: 3 points.
3. Cardiovascular system: dilated ascending aorta with severe aortic regurgitation (presence of major criterion).

By clinically excluding Ehlers-Danlos and Loeys-Dietz syndromes, and considering that there was no family history of the disease, the presence of dilated aortic root and lens subluxation allows the diagnosis of Marfan syndrome.

In the literature revised all clinical types of this syndrome are mentioned, but diagnosis of the disease is usually performed during childhood and adolescence. The interesting thing in this case is its late diagnosis in a patient who had several admissions for heart failure and did not have a complete and accurate assessment. At present genetic counseling is provided to other family members.

REFERENCES
