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RESEARCH ARTICLE

LOEYS-DIETZ SYNDROME VS MARFAN SYNDROME: HEREDITARY CONNECTIVE TISSUE SYNDROMES, A DIAGNOSTIC CHALLENGE. REPORT OF A CASE

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ABSTRACT

The diagnosis of Marfan syndrome (MFS) is based on clinical characteristics already defined in the Ghent nosology, and agreed by the opinion of international experts to recognize this syndrome. 9 These Ghent criteria are mentioned here, which include a set of Major and minor criteria in different body systems, and which have been shown to be applicable to this condition, since with these criteria the diagnosis has been confirmed in more than 95% of the patients, described in the literature. However, it is not always easy to reach the diagnosis, since some of the diagnostic criteria are not applicable to children. And failure to accurately recognize the variable clinical expression can delay follow-up and decision-making in these patients. This article describes a case report of a patient with clinical characteristics of Marfan syndrome, which are transposed with some characteristics of Loeys-dietz, in the absence of family history.

INTRODUCTION

Hereditary connective tissue syndromes (SHTC) affect various organs and systems including: cardiovascular, skin, joints,bone, eyes and lungs. The phenotypic decription of these Shtcs is b ased on the identification of mutations in various genes that encode structural proteins, modifying enzymes or components of the TGF signaling pathway. Two examples of SHTC are: Marfan syndrome (MFS) and Loeys-Dietz syndrome (LDS), they present age-dependent penetrance and phenotypic overlap of cardiovasular, skeletal and skin characteristics, MFS is caused by heterozygous mutations in FBN1, which encode the fibrillin-1 protein of ther extracelluar matrix (ECM); the most common cardiovascular phenotype involves aortic aneurysm and sinus of valsalva dissection. LDS is caused by mutations in TGBR1/ 2, SMAD2, 3, or TGFB2/3, all encodeing components of the TGFB signaling pathway. (1)

CASE REPORT

A 12-year-old female with no significant family history, known from the first year of life, with congenital heart disease, postoperative for patent ductus arteriosus (PCA / 2007). Postoperative aneurysms of the proximal portion of the aorta (Feb / 2019).

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In spectrum monitoring Marfán - Loeys Dietz; Exome study directed for 99 genes, identifying variant of uncertain clinical significance c.2933C> T (p.Pro978Leu) in the RYR1 gene. On physical examination, the patient presented a phenotype characterized by dolichocephaly, narrowing of the parietals, domed forehead, fascies in the helmet Greek, enophthalmos, telecanthus, bluish sclera with ota nevi, midface retrusion, short philtrum, microstomia, arched upper palate, bifid uvula, micrognathia, short neck, C2-C3 anterolisthesis, thoracoxyphosis, pectum carinatum, joint hypermobility +++, syndactum and camptodactyly of the 2nd, 3rd, 4th and 5th fingers, genu recurvatum, knee dislocation, bilateral clubfoot, brachydactyly, thin and lax skin.

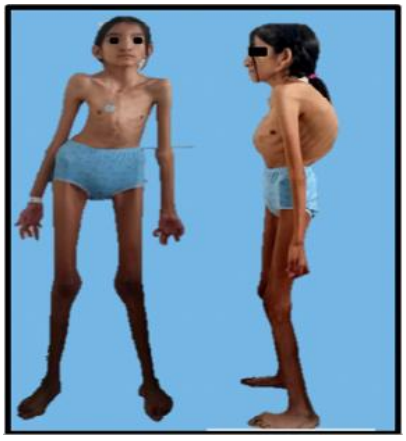

Figure 1. Phenotype of the patient

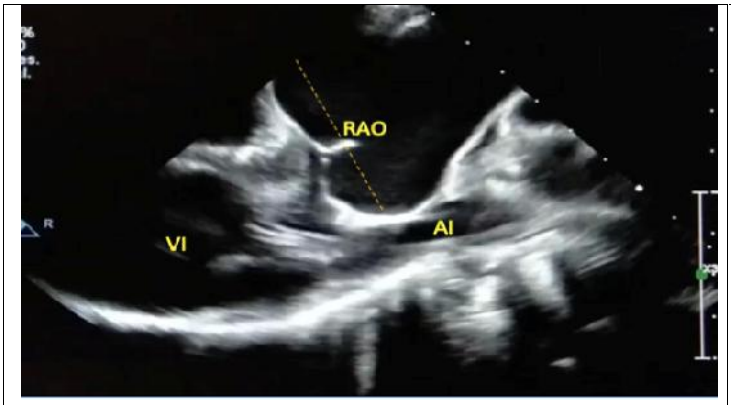

Figure 2. Aortic root dilation, 46 mm (sz + 12) by echocardiography

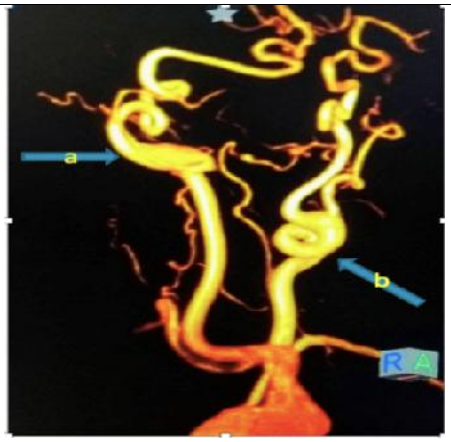

Figure 3. a) Fusiform aneurysm in the cervical segment of the right internal carotid artery after a 7 x 12 mm bifurcation. b) Left common carotid artery with complete loop at the level of the 4.7 mm bulb in Angioresonance

Table 1. Revised Ghent criteria for the diagnosis of Marfan syndrome and related diseases ([10,11,12,13,14])

In the absence of a family history: (1) Ao (Z ≥2) AND EL = MFS * (2) Ao (Z ≥2) Y FBN1 = MFS (3) Ao (Z ≥2) Y Syst (≥7pts) = MFS * (4) EL AND FBN1 with known Ao = MFS EL with or without Syst AND with an unknown FBN1 with Ao or without FBN1 = ELS Ao (Z <2) AND Syst (≥5 with at least one skeletal feature) without EL = MASS MVP Y Ao (Z <2) Y Syst (<5) without EL = MVPS In the presence of a family history: (5) EL Y FH of MFS (as defined above) = MFS (6) Syst (≥7 pts) AND FH of MFS (as defined above) = MFS * (7) Ao (Z≥2 above 20 years, ≥3 below 20 years) + FH of MFS (as defined above) = MFS *

Table 2. Systemic characteristics score ([10,11,12,13,14])

• Wrist and thumb sign - 3 (wrist or thumb sign - 1) • Pectus carinatum deformity - 2 (pectus excavatum or asymmetry of the thorax - 1) • Hindfoot deformity - 2 (simple flat foot - 1) • Pneumothorax - 2 • Dural ectasia - 2 • Protrusio acetabuli - 2 • Reduced US / LS 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, descending palpebral fissures, malar hypoplasia, retrognathia) • Skin stretch marks - 1 • Myopia> 3 diopters - 1 • Mitral valve prolapse (all types) - 1 Maximum total: 20 points; a score ≥7 indicates systemic compromise. US / LS, upper segment / lower segment ratio.

findings should be correlated with the clinical status of the patient. LDS can be distinguished from MFS by the presence of hypertelorism, bifid uvula or cleft palate, aneurysms and tortuosities at different vascular levels, mainly the aortic and cervical with a more aggressive and lethal behavior. [2.3]

DISCUSSION

The American and European College of Genetics and Medical Genomics recommend, as with other clinical tests, that the findings should be correlated with the clinical status of the patient. LDS can be distinguished from MFS by the presence of hypertelorism, bifid uvula or cleft palate, aneurysms and tortuosities at different vascular levels, mainly the aortic and cervical with a more aggressive and lethal behavior. [2.3]

Conclusion

Hereditary connective tissue syndromes constitute a diagnostic challenge due to the superposition of vascular, skeletal, craniofacial, cutaneous, ocular signs and symptoms, and

vascular aneurysms, highlighting the importance of molecular diagnosis.[1,2] Follow-up should be carried out by means of a multidisciplinary team; cardiovascular treatment is aimed at reducing hemodynamic stress with angiotensin II receptor antagonists and selective ß-1 blockers. The prognosis is poor with a life expectancy of less than 30 years.[1]

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