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A pediatric case of mitral regurgitation: eyes open!

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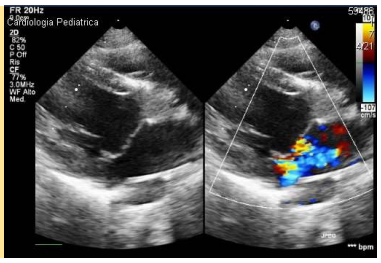
INTRODUCTION

Mitral valve disease is common at all ages. In the pediatric population, it can be congenital or acquired and may occur either isolated or associated with other heart lesions. Herein we reported the case of a 2-year-old girl with mitral valve disease.

ONSET

Her medical history revealed overall good health in the past. A few weeks before admission, she had a rash with **fever** that did not need antibiotic treatment, in concomitance with a streptococcal pharyngitis in her older sister. At physical examination, a **2/6 murmur** at the apex, that radiated to the axilla and mesocardium was present. ECG was normal. The echocardiogram revealed a **prolapse** of the anterior mitral leaflet and a **thickened** and **hyperreflective** posterior leaflet, that determined a **severe mitral regurgitation** (MR). Therefore, cardiological therapy with **ACE-inhibitors** and **diuretics** was started and the child was referred to our rheumatologists to exclude rheumatic disease. No other symptoms (arthralgia, chorea, illness) or clinical findings were present. Nevertheless, laboratory tests revealed **streptococcal sensitization indexes** (ASLO, anti- DNase B) and **erythrocyte sedimentation rate** (ESR) persistently high in serial blood samples.



According to the 2012 Australian guidelines for prevention, diagnosis and management of acute rheumatic fever (ARF) and rheumatic heart disease (RHD), **one Jones major criteria** (carditis – severe MR) and **two minor criteria** (fever and ESR>30mm/h) were fulfilled for diagnosis of rheumatic disease (see Table 1). In addition to the cardiological therapy, the girl started corticosteroids per os and antibiotic prophylaxis with benzylpenicillin 600.000 UI i.m. every 21 days.

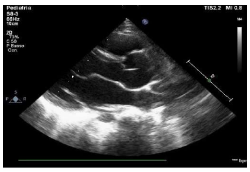
Initial episode of ARF	Two major or one major and two minor manifestations *plus* evidence of a preceding Group A Streptococcus infection	
Recurrent attack of ARF	Two major or one major and two minor or three minor manifestations	
Major manifestations	**High risk groups** Carditis Polyarthritis or aspetic monoarthritis or polyarthralgia Sydenham chorea Erythema marginatum Subcutaneous nodules	**All other groups** Carditis Polyarthritis Sydenham chorea Erythema marginatum Subcutaneous nodules
Minor manifestations	Fever ERS> 30mm/hr or CPR>30mg/L Prolonged P-R interval on ECG	Fever Polyarthralgia or aspetic monoarthritis ERS> 30mm/hr or CPR>30mg/L Prolonged P-R interval on ECG

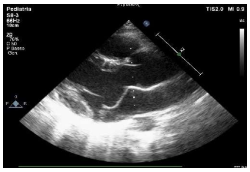
TABLE 1. The 2012 Australian guidelines for prevention, diagnosis and management of ARF and RHD.

FOLLOW UP

During follow up **MR** remained **severe** and **dilation of the aortic bulb** was also noticed. Because of failure of the treatment, the peculiar echocardiographic aspect, and the age at presentation, other causes of MR were ruled out. In the suspect of a possible collagenopathy the girl underwent a genetic examination. Family history of thoracic and abdominal aneurysm of the aorta also emerged. At a physical examination a slight diffuse **articular hypermobility** was found, so Next Generation Sequencing (NGS) for collagen genes was performed.

After one year follow up, patient began to complain of **fatigue** after moderate efforts. Therefore, she underwent a cardiac surgery for **mitral valvuloplasty**. The macroscopic aspect of the valve suggested a congenital anomaly and the biopsy showed a severe myxomatous degeneration. After these findings, rheumatic aetiology was definitively excluded, and penicillin prophylaxis was stopped. To complete the diagnostic process, the girl underwent an eye examination, that showed **ectopia lentis**, with a super-temporal dislocation of the crystalline.





Finally, the NGS analysis confirmed the diagnosis of collagenopathy. In fact, the molecular analysis showed a ""c.3772C>T, p.Pro1258Ser, **" de novo mutation of FBN1 gene in heterozygosis** which can be responsible of Marfan syndrome (MFS).

The presence of ectopia lentis and FBN1 gene mutation associated with aortic dilatation could make diagnosis of **Marfan syndrome, according to 2010 revised Ghent criteria** (see Table 2).

In the absence of family history
Ao (z ≥ 2) AND EL
Ao (z ≥ 2) AND FBN1 mutation
Ao (z ≥ 2) AND systemic score ≥7
EL AND FBN1 mutation with a known Ao
In the presence of family history
EL AND FH of MFS
Systemic score ≥7 AND FH of MFS
Ao (≥2 above 20 years old, ≥3 below <20 anni) AND FH of MFS

TABLE 2. The revised Ghent criteria.2010. Ao: Aorta; EL: Ectopia Lentis; FBN1: Fibrillin-1; FH: Family History; MFS: Marfan Syndrom

DISCUSSION AND CONCLUSION

In the pediatric population, MR may often occur in the context of a systemic disease, such as connective tissue diseases, rheumatic disease, and various congenital heart defects. A careful differential diagnosis is mandatory to choose the appropriate treatment. In this case we dealt with some confounding factors, but according to the most recent 2020 Australian guidelines, with modified Jones criteria that in low-risk population consider ERS a minor criterion if >=60 mm/h, this case would not have been considered an RHD. Therefore, other causes of MR could have been ruled out, maybe avoiding an unnecessary painful therapy for the patient.

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