MARFAN SYNDROME IN INFANCY – A RARE CONDITION WITH POOR PROGNOSIS

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Abstract

Our aim is to report a severe case of Infantile Marfan syndrome, which presented to the Emergency Department for shortness of breath, intense pallor and loss of appetite. Her particular physiognomy made us immediately think of Marfan syndrome. Marfan syndrome in infancy is a rare condition usually associated with poor prognosis. The child was admitted in the ICU for polypnea, failure to thrive and signs of heart failure. She was clinically evaluated, we performed lab tests, cardiology examination and AngioCT. The patient was referred to a surgical center because of a gigantic left atrium due to a severe mitral regurgitation. Unfortunately, she had a cardiac arrest during sleep. The genetic test confirmed Marfan syndrome. Clinical features for infantile Marfan syndrome have to be detected early after birth and genetically tested. Cardiac evaluation is mandatory. These patients have to be directed to an expert pediatric cardiovascular surgery center, because the heart involvement of the mitral valve is severe and hard to treat at this age.

Keywords: infantile Marfan syndrome, giant atrial dilatation, severe mitral regurgitation, dysplastic mitral valve.

Introduction

Marfan syndrome (MFS) is a hereditary disease involving chromosome 15, which affects connective tissue. The disease can cause a wide variety of issues. The main symptom of patients with Marfan syndrome is the excessive height, long arms and legs, flexible joints, which are more noticeable in adulthood. However, Marfan syndrome can be a de novo mutation, and in this situation, symptoms develop early in life, as early as infancy. Infantile Marfan syndrome is a rare phenotype of the disease and is the most severe form. Literature states that the majority of patients with infantile Marfan syndrome develop severe cardiac pathology with poor prognosis [1, 2, 3].

Case report

A 6 months old girl, presented into our Emergency Department for dyspnea, loss of appetite and intense pallor. Upon inquiry, we found out that the patient had prior admittances, after birth, being a premature baby with respiratory distress and another one at 3 months after birth, also for respiratory distress. We also found out that the child's aunt is with hyper stature (198 cm) and that her father has arachnodactyly and dilated cardiomyopathy.

At the first admittance, due to the particular physiognomy: excessive length, arachnodactyly, dolichostenomelia, muscle hypotonia, mix thoracic malformation with superior pectus carinatum and inferior pectus excavatum, lack of fatty tissue, the doctors in the neonatal department demanded a cardiology and genetic consult. From the cardiology point of view, the patient had a slight aortic bulb ectasia, but nothing else pathological and from the genetic point of view she was proposed to be tested for Marfan syndrome. Family did not respect the follow up program proposed by the cardiology doctor after the evaluation.

At the last admission, the general status was altered, the child's stature exceeded the 99th CDC percentile for age, and she had arachnodactyly and overlapping toe (Fig.1. A, B, C) that was impressive. She was also severely underweight, she had 5100 grams at 6 months of age. All physiological traits described above were present in the clinical evaluation. Furthermore, she presented polypnea and dyspnea, without pulmonary rales, hepatomegaly, severe hypotonia and loss of appetite.

At the cardiology clinical examination, the patient presented tachycardia 166 b/min, Oxygen saturation was low and grade IV-V/6 systolic cardiac murmur was detected in the apex, irradiating all over the precordium, with palpatory thrill.

The ECG showed sinus tachycardia, right axis deviation, mitral P wave and ischemia, with negative T waves almost to V6 (Fig.2.). The cardiac biomarkers value were extremely high, with an NTpro BNP of 26.964 pg/ml (normal value for age is 37-1000 pg/ml), which translates the fact that the myocardium is severely afflicted, with severe heart failure; Troponina T - 32, 83 pg/ml (normal value for age is 14 pg/ml) that confirms the myocardial ischemia. We did a chest X-ray (Fig.3.), which showed severe left cardiomegaly.

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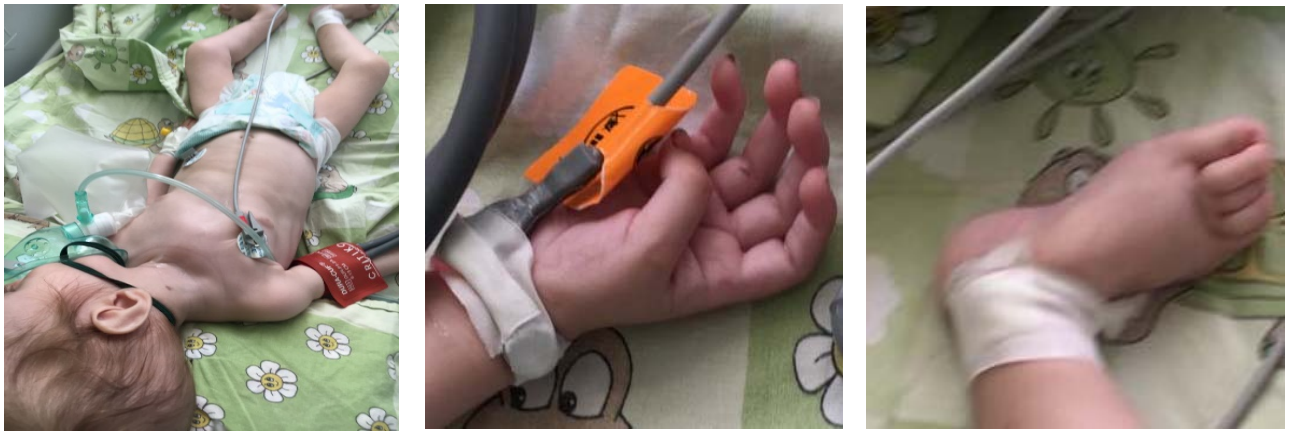

A **B** **C**

Fig.1. A: 6 months old infant girl with clear hyper stature. B: The patient's hand with arachnodactyly. C: The patient's foot with arachnodactyly and overlapping toes.

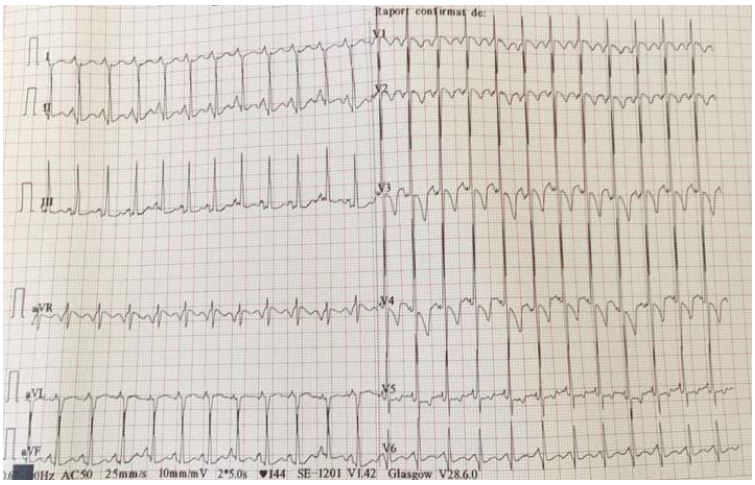

Fig.2. ECG with right axis deviation, mitral P wave and negative T waves in almost all precordial leads

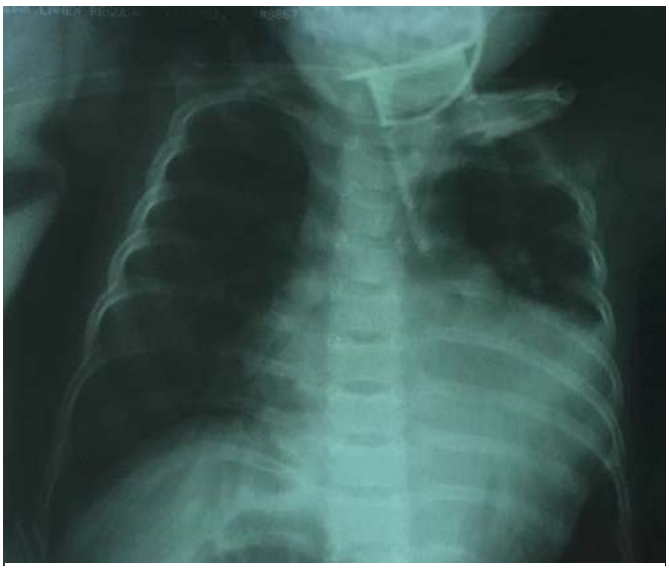

Fig.3. Chest X ray showing severe left cardiomegaly.

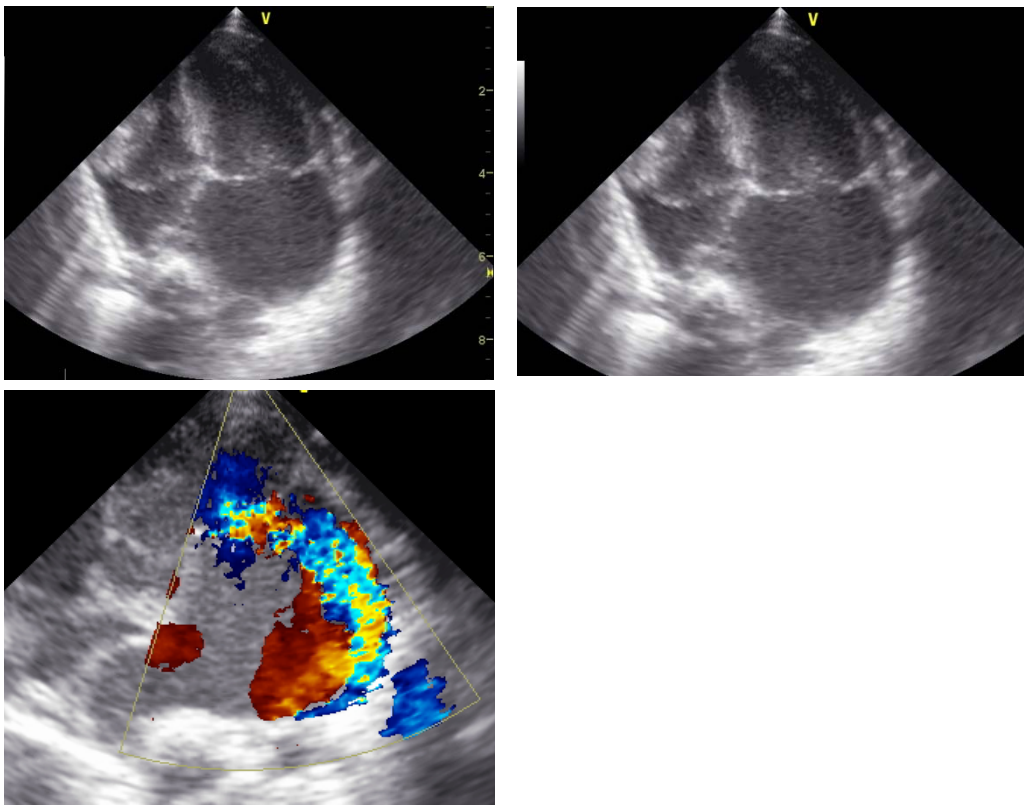

Fig.4. A: Echocardiography 4 chamber view showing severely dilated left atrium; B: Echocardiography modified 4 chamber view depicting a dysplastic mitral valve; C: Echocardiography color Doppler severe mitral regurgitation with Coanda effecT

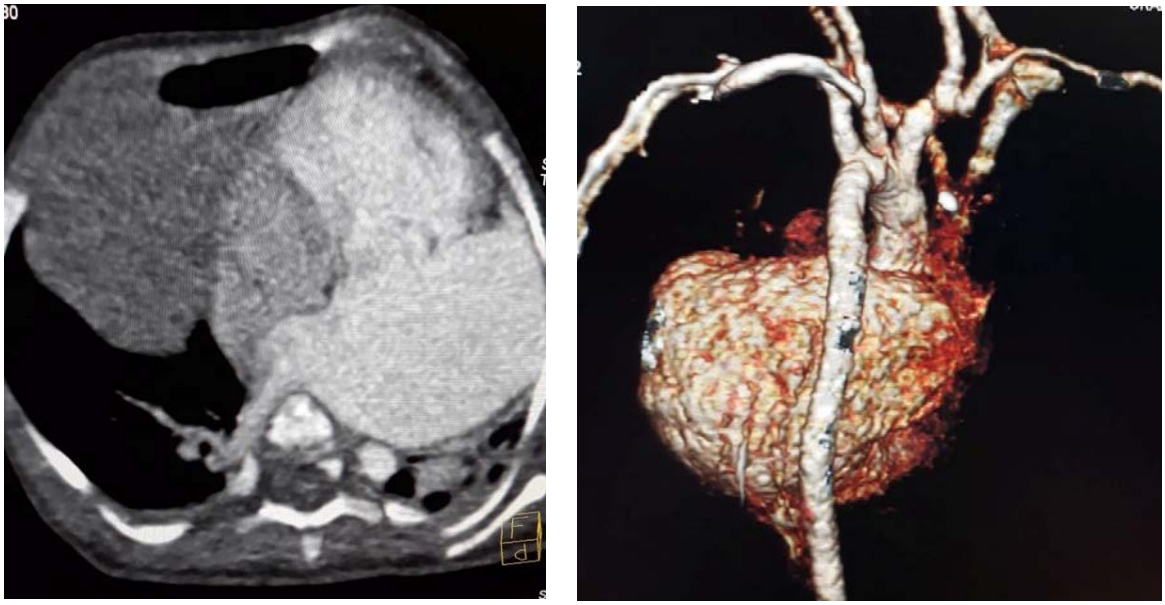

Fig.5. A: AngioCT showing enlarged left atrium; B: 3D reconstruction of the gigantic left atrium

Echocardiography revealed a severe left atrium dilatation (left atrium of 3.5 cm, maximum value admitted for age and weight is 1.6 cm), due to a severe mitral regurgitation (Coanda effect on color Doppler flow and vena contract of 8 mm) secondary to dysplastic mitral leaflets. Despite that, the cardiac function was within normal ranges (ejection fraction was 64%) (Fig.4. A, B, C). Aortic root was ectatic with Z score over 2. Pulmonary hypertension was also detected.

After echocardiography, Angio CT was performed which confirmed the severe left atrium dilatation, the left atrium occupied 50% of the left hemithorax (Fig. 5. A, B). Treatment with diuretics: Furosemide and Spironolactone, Captopril and cardiotonics: (Dobutamine) was initiated. Oxygen therapy was needed due to O2Sat of 88%, also we started the correction of electrolytes and IV supplement with amino acids.

After the complete evaluation, imagistic explorations, lab investigation and treatment initiation, the patient was immediately referred to an intensive care cardiovascular pediatric unit with pediatric cardiovascular surgery department. Unfortunately, the intervention was postponed due to the clinical status of the patient that could not be improved. The evolution was not favorable, she had a cardiac arrest during sleep

The Marfan syndrome was confirmed by the genetic test

Discussion

Marfan syndrome is an autosomal dominant disease, which is why a careful anamnesis and data collection is important in the diagnosis of early onset MFS [1, 3]. The diagnosis is mainly clinical, but genetic confirmation is mandatory. The main characteristics one must pay attention to are comprehensively summarized in the revised Ghent nosology for Marfan syndrome [4]. Unfortunately, infantile MFS is a different entity and the most severe form in the spectrum of Marfan, therefore the Ghent nosology is not applicable. The severity of infantile MFS is caused by cardiac and pulmonary afflictions with rapid and unforeseeable evolution [2, 3].

Although the most frequent cardiac modification is aortic root dilatation, a wide variety of diseases can appear, as we saw in our patient [5, 6, 7, 8].

When discussing the case of our patient, a timely diagnosis was attained, however the evolution was almost fulminant, as with most cases with infant MFS, literature states that 95% of patients with infant MFS die within the first year of life.

There was a slight aortic root ectasia in the neonatal department, which is why there was a follow up plan established with the mother, unfortunately it was not respected. Months later, an upper tract infection brought our patient to the hospital. A cardiological examination was not performed, but iv Furosemide was necessary for the treatment. Her health progressively worse, she refused alimentation, she lost weight, when signs of dyspnea appeared she was referred into our service. The cardiological examination showed that the left atrium was 50% of the left hemithorax because of severe mitral regurgitation due to a dysmorphic and incompetent mitral valve. Even with inotrope medicine and diuretics, and Captopril, her general state did not improve, so that Sildenafil and surgery was mandatory. Surgery was not timely performed due to the altered state of the patient, who unfortunately suddenly died in her sleep.

Infants with Marfan syndrome are the most severe group in this genetic disease, due to the cardiac abnormalities that are very difficult to be managed at this age. Even in most developed countries the management of the mitral valve involvement in these patients represent a challenge. The mitral valve surgery is very difficult and postoperative complications remain a great risk at all-time [3, 9].

Conclusions

In patients with infancy Marfan syndrome it is essential to establish a close monitoring system in order to prevent severe and irreparable complications. It is very important that the family understands the gravity of this disease and the patient should be monitored by a multidisciplinary team, including: neonatologist, pediatrician, geneticist, cardiologist, intensive care doctors and nurse team and cardiothoracic surgeons. Sometimes invasive cardiac surgery is in the benefit of the patient, but sometimes it is not. This complex team has to decide together with the family what is the best treatment of choice in the interest of the infant caring the gene of Marfan syndrome that expressed so early in life.

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