SCIENTIFIC LETTER

Vitorino Modesto dos Santos [1]
Gabriel Luan Queiroz Alves da Cunha [2]
Matheus Luan Queiroz Alves da Cunha [3]
Marisa Carla de Matos Queiroz [4]
Renan Lins Queiroz Alves da Cunha [4]

Marfan syndrome - management of complication during pregnancy: case study

1 Professor-adjunct of Internal Medicine of Armed Forces Hospital, and Catholic University of Brasília. Brasília-DF, Brazil.
2 Medical Resident of Internal Medicine of Armed Forces Hospital. Brasília-DF, Brazil.
3 Medical Student of Integrated Colleges of Education Union of the Central Plateau, Brasília-DF, Brazil.
4 Cardiologist of Saint Helena Hospital, Brasília-DF, Brazil.

Correspondence: Dr. Vitorino Modesto dos Santos
E-mail: vitorinomodesto@gmail.com

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Introduction

Marfan syndrome (MFS) is an autosomal dominant disorder, due to mutations on the gene that encodes fibrillin-1 (FBN1), which is a major component of extracellular microfibrils of the connective tissue [1, 2]. The incidence of MFS is about 2 to 3 per 10,000 individuals, with no difference in gender prevalence and, in approximately 75% of cases, the mutation is inherited from an affected parent, and the other cases can be due to de novo mutations [1].

The syndrome usually affects the skeletal, cardiovascular and optical systems, among others, and the accurate diagnosis is based on family history, clinical signs, and Ghent criteria [1–6]. Cardiovascular manifestations of MFS, in special aorta ecstasy and/or dissection, are related to poor outcomes, involving the most severe complications and the majority of deaths in this population. Therefore, additional care is recommended for patients intending to get pregnant [1, 2, 5].

Case report

An asymptomatic 34-year-old Brazilian female with a family history of MS, had the diagnosis of this condition in her childhood and was regularly followed in our service during seven years. Although completely advised about possible complications during pregnancy, and the risk of genetic transmission of the mutant gene to descendants, she maintained her intention to be pregnant. Her physical examination disclosed arachnodactyly and classical signs of articular hypermobility (**figure 1**), dolichocephalus, high stature and scoliosis, in addition to severe myopia. There were no abnormalities in her laboratory evaluations, and genetic evaluation was not done due to high cost.

Routine aortic images obtained before pregnancy showed an aortic root with 38 mm and slight prolapse of the mitral valve. Transthoracic echocardiograms revealed a persistent mitral valve prolapse and an ectasy of the aortic root ranging from 31 mm in 2006 to 38 mm in 2013 (**Table 1**). The patient was also evaluated by other imaging screenings, which disclosed a small liver hemangioma (at segment VII), in addition to colloid cyst and three nodes on the right thyroid lobe.

During the fifteenth week of pregnancy, she came to the emergency service complaining of intense abdominal pain and nausea, but abdominal ultrasonography study showed no abnormalities. With diagnosis of acute abdominal syndrome, the patient was surgically approached. During the open surgery, the retrocecal ruptured appendicitis was removed. An empiric schedule with cephalothin was initially used, and changed by gentamicin due to positive culture for *P. mirabilis*.

She persisted under medical control in gestation period, and a cesarean procedure was performed at forty weeks of pregnancy, when prophylactic propranolol 40 mg/ day was prescribed. Aortic root caliper and hemodynamic parameters as cardiac rate and blood pressure were

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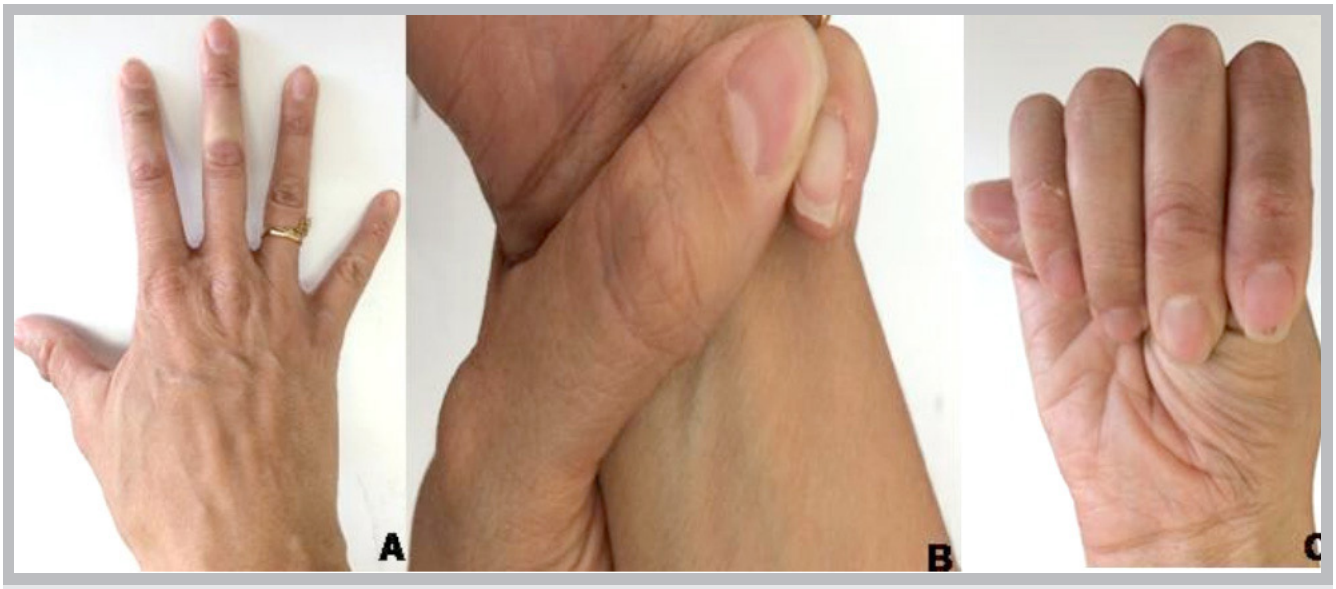

Figure 1. Classical features of the Marfan syndrome.
A. arachnodactyly - the hand fingers are very long and slender in comparison to the palm of the hand.
B. sign of Walker-Murdoch - overlap of the distal phalanges of the thumb and fifth finger when encircling the opposite wrist.
C. sign of Steinberg - the thumb projects well beyond the limit of the hand if it is held across the same palm.

normal. Actually, she is asymptomatic and has been followed at outpatient Cardiology service.

Table 1. Comparative findings of transthoracic echocardiograms.

Data	Aortic diameter
October 23, 2006	38 mm
March 31, 2008	35 mm
January 26, 2010	31 mm
August 16, 2011	33 mm
December 07, 2011	38 mm
June 13, 2012	35 mm
August 03, 2012	36 mm
October 05, 2012	35 mm
November 28, 2012	35 mm
January 29, 2013	38 mm

Discussion

The patient herein reported with MFS was followed by clinical and echocardiographic assessment and did not have cardiovascular complications during pregnancy and puerperium. Worthy of note, periodic measurements of ascending aorta showed diameters <40 mm [1, 4–7]. Cardiovascular complications are expected to occur in patients with MS, and special care should be taken to accurately follow pregnant patients. Management of aortic complications, including aneurysmatic dilatation and/or dissection can be accomplished by the assessment of the aortic volume, usually by sequential echocardiograms during the period of pregnancy [1, 4–9]. Aortic angiotomography and angioressonance may be used to measure aortic parameters, but should be restricted to cases with dubious findings of transthoracic echocardiograms during pregnancy [3, 5].

Women with MFS must be recommended to avoid pregnancy, which poses hormonal end metabolic changes and increases the probability of aortic aneurism enlargement or dissection [4–7]. Perinatal prevalence of aortic dissection in MFS range from 3.9% to 12%, and complications as premature rupture of membranes or cervical incompetence may occur in up to 40% of cases [1, 3–5]. Pyeritz reported 20 pregnant women with MFS and acute aortic dissection and 16 (80%) died [8]. Moreover, according to recent guidelines aortic dissections during pregnancy more often occur with aortic root diameter >40 mm before pregnancy. Therefore, prophylactic replacement of the ascending aortic can be done prior the conception in this group of females [4–7].

Transesophagic echocardiogram is considered the gold pattern tool to evaluate patients with MS; although with less accuracy, the aortic changes of the patient herein reported were followed by transthoracic echocardiogram, which is easier to perform in developing countries [2]. The other systems that may be compromised by the syndrome are not likely to cause severe risk to the patients, but should be monitored as well (in special the oral hygiene, because oral

infection by diverse kinds of microorganisms may origin infective endocarditis [5, 8], which can play a significant role on poor outcomes, and often affect the quality of life of this group of patients.

Initial recommended cardiovascular management includes the use of beta-blockers, because they reduce the heart rate and the inotropism, lowering the risk of aortic dissection or aneurysm [9]. Ocular involvement occurs in up to 80% of cases and ectopia of lentis is the most common change. Ophthalmic treatment includes the use of glasses, and diverse local surgery procedures [9]. Counselling for patients should highlight the risk of high intensity exercises and physical jobs [6].

The patient herein reported had arachnodactyly, dolichocephalus, high stature, scoliosis, ectopia lentis, thumb and wrist signs, dilatation of the ascending aorta, and mitral valve prolapse [1, 2, 6]. New diagnostic criteria involve genetic analysis of mutations in the FBN1 gene [9, 10], with high cost [3]. Indeed, about 1000 variants have been reported in association with MFS [10]. People of high income can easily perform complete genetic evaluation to clear the origin of MFS, but the exact pathogenicity of the syndrome was not determined in our patient because of the cost [3].

In conclusion, despite of elevated risk of Marfan syndrome-related complications during pregnancy, which play a role in poor outcomes, the patient had uneventful evolution except for acute appendicitis. Early diagnosis and administration of beta-blockers in the setting of primary care attention constitute a useful tool, which can improve the quality of life and provides better outcomes in MFS. Physical features of MFS are easy to detect, if health workers pay the due attention about them. Case studies may increase the awareness of young physicians about less usual clinical conditions.

Conflicts of interest

The authors have no conflict of interest to disclose.

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Author contributions

The authors have the same contribution in the manuscript preparation.

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