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INTERMEDIATE

CASE REPORT: CLINICAL CASE

The Many Lives of a Complex Marfan Syndrome Patient

Staged Therapeutic Decisions

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ABSTRACT

We present a complex Marfan case, with previous type A aortic dissection, subsequent progressing aortic arch aneurysm, type B chronic aortic dissection, and Barlow disease with severe mitral regurgitation, all expressions of the same phenotype, all needing staged complex surgical therapies. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:236–41) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

We present a case of staged therapeutic management of a 49-year-old man with Marfan syndrome (MS). The patient was referred to us in late 2019 for lower neck pulsatility and intermittent chest discomfort. Clinical examination revealed a marfanoid habitus (2.0 m [6 ft 7 inches] and 115 kg [254 lbs]), bilateral corrected ectopia lentis, normal audible metallic valve clicks in the aortic and in mitral positions, and left parasternal and apical systolic murmurs.

LEARNING OBJECTIVES

- To understand the cardiovascular pathological features and evolution of MS.
- To understand the importance of family screening in MS.
- To familiarize with the possibility of a communication between the LV and the RA, and its possible causes.

PAST MEDICAL HISTORY

The patient received a diagnosis of MS in 1996 at the age of 26 years, when he had a type II De Bakey aortic dissection. At that point, he underwent successful emergency surgery using the Cabrol technique consisting of total replacement of the proximal ascending aorta with a tube graft containing a prosthetic aortic valve and reimplantation of the coronary arteries by use of an intermediate tube graft (**Figures 1A and 1B**). After a 14-year symptom-free period, an asymptomatic type B aortic dissection was diagnosed and was treated conservatively (**Figures 2A and 2B**).

INVESTIGATIONS

In 2016, transthoracic echocardiography revealed severe mitral regurgitation secondary to prolapse of all scallops, also confirmed at transesophageal echocardiography (**Figures 3A to 3C**), with a mildly dilated left ventricle (LV) with preserved ejection fraction (55%)

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and a severely dilated left atrium. A left-to-right shunt between the LV and the right atrium (RA) was also discovered (**Figures 4A to 4C**). The ascending aortic aneurysm measured a maximum diameter of 52 mm on the computed tomography scan, with a steady increase from 48 mm the previous year and 42 mm 4 years earlier. The aortic arch also showed significant dilation of 59 mm (**Figure 5**). The type B dissection remained uncomplicated and stationary. The heart team decided on mitral valve surgery and LV-to-RA shunt closure, thus leaving the ascending aortic aneurysm to be resolved at a later date. Surgery was performed with an uneventful recovery.

MANAGEMENT

Four years later, the patient's yearly work-up showed progressive enlargement of the aortic arch from 52 mm (in 2016) to a maximum of 66 mm (in 2020). The patient underwent successful aortic arch replacement in a hybrid 1-stage procedure combining endovascular treatment with conventional surgery, known as the frozen elephant trunk technique (**Figure 6**). The dissected distal descending aorta was decided to be kept under close computed tomographic observation. An additional later endovascular procedure cannot be excluded.

The clinical diagnosis of MS was established on the basis of the revised Ghent nosology (1), with a systemic score of 11. In the setting of this genetic disorder, thorough examination of the patient's pedigree allowed early management of his siblings (**Figure 7**). His father and older brother had a marfanoid constitution and died suddenly at a young age without a positive diagnosis of connective tissue disease, and 2 of the 3 sisters were also subsequently diagnosed with MS and dilated ascending aortas. One of the 2 sisters underwent preventive surgery of the aortic root with preservation of the cusps (the Tyrone David procedure), whereas the other is being followed up in the Expert Center for Rare Genetic Cardiovascular Diseases at Prof. C. C. Iliescu Institute of Cardiovascular Disease Emergencies, Bucharest, Romania.

ABBREVIATIONS AND ACRONYMS

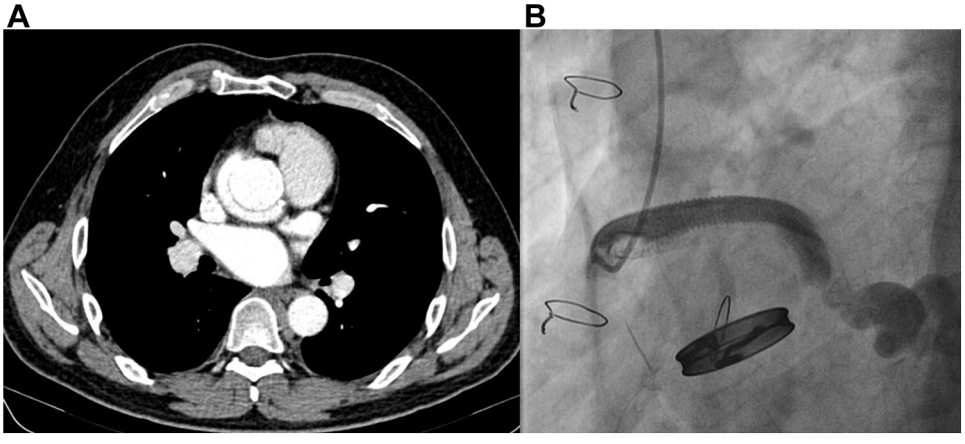
LV = left ventricle
MS = Marfan syndrome
RA = right atrium

DISCUSSION

This is a complex MS case, with previous De Bakey type II aortic dissection, subsequently progressing aneurysm of the aortic arch, and developing type III chronic aortic dissection, as well as Barlow disease of the mitral valve leading to severe regurgitation, all expressions of the same phenotype (**Figure 8**). An apparently unrelated finding was that of an LV-to-RA shunt, also known as Gerbode ventricular septal defect.

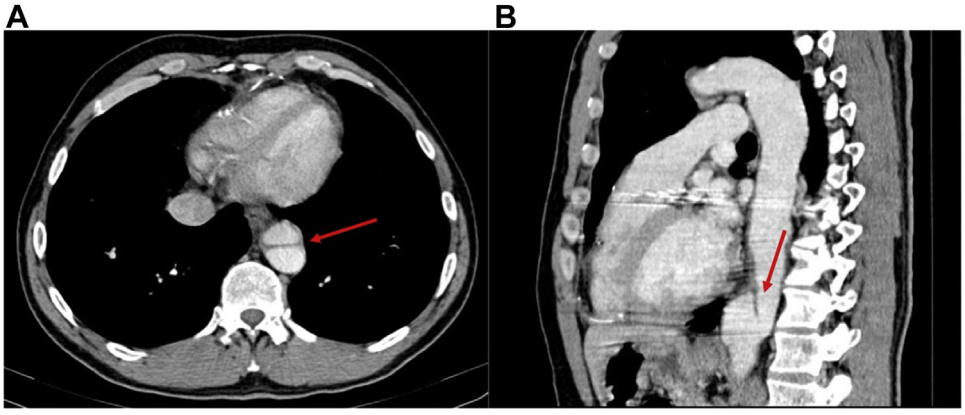
This case reflects the severe and complex cardiovascular pathological features of MS, with its 2 most important cardiovascular manifestations: aortic dilatation or dissection and mitral valve regurgitation through prolapse (2–4). The risk that these disorders will develop or worsen progressively increases with age, thereby prompting the need for constant and

FIGURE 1 Cabrol Conduit



(A) Computed tomography angiography transverse view of the aortic root with a circumferential Cabrol conduit. **(B)** Angiographic left anterior oblique view of the Cabrol conduit and origin of the left coronary artery.

FIGURE 2 Aortic Dissection



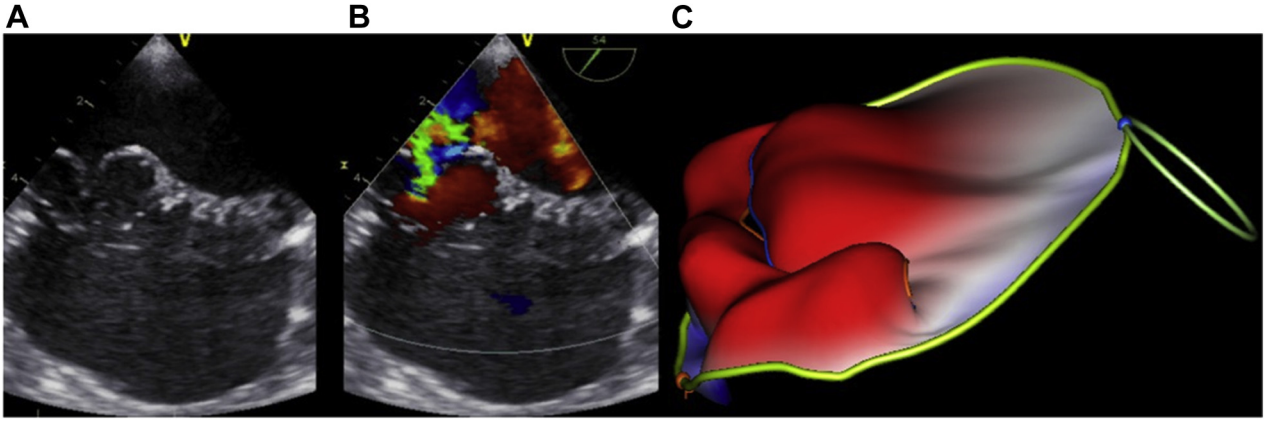
(A) Transverse and **(B)** sagittal images of chronic type B aortic dissection **(red arrows).**

regular follow-up. This was clearly shown in our patient's case whose aortic diameter and mitral regurgitation have increased through the years.

The LV-to-RA shunt was an unexpected discovery, which can be congenital or acquired. The congenital defect (also called Gerbode defect) is rare and can be caused by a structural abnormality of the central fibrous body in combination with arrested maturation of the membranous ventricular septum (5,6). The acquired defect is generally attributed to previous cardiac surgery (particularly aortic and mitral valve replacement) or infective endocarditis. Interestingly, in most cases the acquired shunt is not identified immediately following the cardiac surgery, but rather months or years later, as was the case in our patient (7). In this case the most likely cause of the defect was the initial aortic root surgery. The presence of the shunt did not influence management because it did not appear to have any hemodynamic impact, without right chamber remodeling.

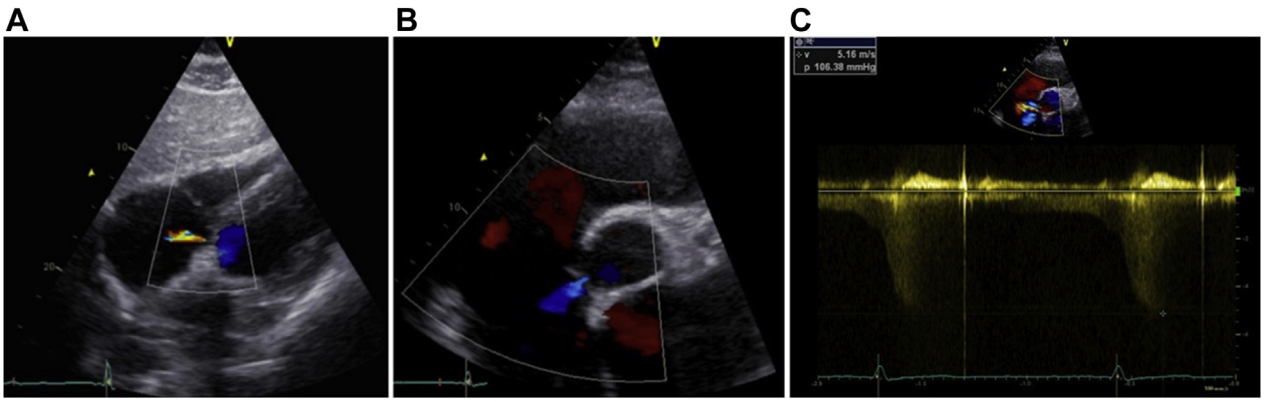
The present case also raises the issue of staged management, which can be particularly complex in

FIGURE 3 Mitral Valve Prolapse



(A) Transesophageal 2-chamber view showing prolapse of both mitral leaflets. **(B)** Transesophageal 2-chamber view showing severe mitral regurgitation Doppler color flow. **(C)** Mitral valve 3-dimensional model reconstruction using transesophageal echocardiography and showing billowing of both leaflets and prolapse of all 6 scallops.

FIGURE 4 Left Ventricle-to-Right Atrium Shunt



Transthoracic echocardiographic **(A)** subcostal 4-chamber and **(B and C)** parasternal short-axis views of the left ventricle-to-right atrium shunt.

MS. Thus, given the continuously evolving nature of the disease, patients may require more than 1 cardiac intervention, which increases the risk of complications and also makes it challenging to decide on the most appropriate timing for intervention. In the case presented, both the aortic aneurysm and the mitral regurgitation had a clear indication for intervention. The European Society of Cardiology guidelines recommend surgery for patients with MS for severe symptomatic mitral regurgitation, as well as for ascending aortic aneurysm ≥45 mm (3,4), and they favor surgery over endovascular aortic repair in the case of patients with MS (3). Our institution's heart team decided that attempting to resolve both mitral regurgitation and an aortic arch aneurysm would pose too great of a risk for the patient and that initially only the mitral valve would be replaced, thus postponing the aneurysm repair for a later date. All the procedures undergone by the patient spanned over 24 years and remarkably prolonged his life in the presence of such a severe phenotype.

Finally, the importance of family screening cannot be understated. MS is transmitted as an autosomal dominant disease, associated with mutations in the *FBN1* gene that encodes fibrillin-1, an important component of connective tissue (8). If a parent has the gene mutation, the theoretical chance of each child to inherit it is 50%; in the case of our patient's family, 4 of the 5 siblings had features of MS, with severe manifestations at an early age in the 2 brothers. In addition, the disease has an important

FIGURE 5 Evolution of Terminal Ascending Aorta Aneurysm Diameter as Measured Using Computed Tomography Angiography

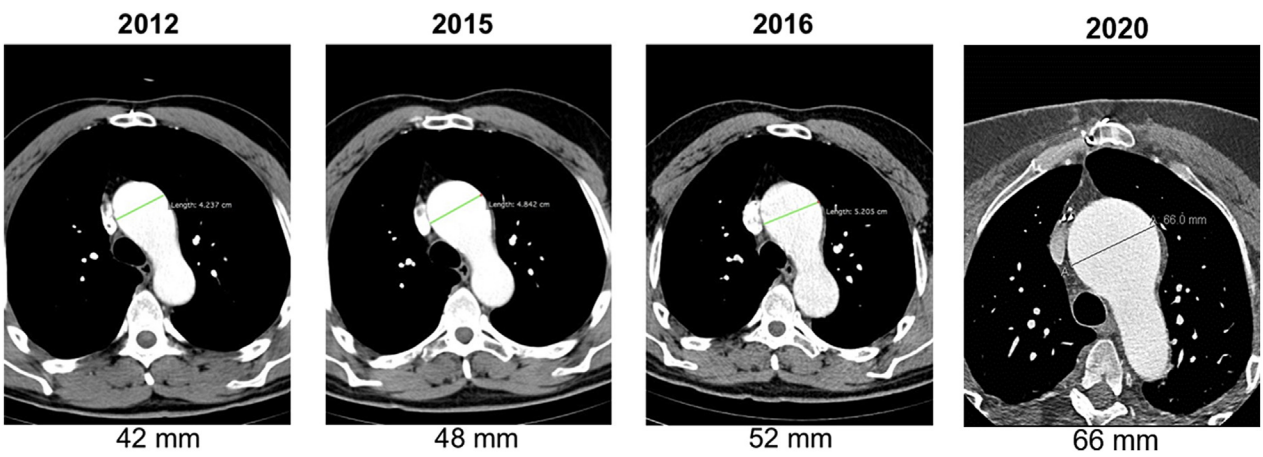
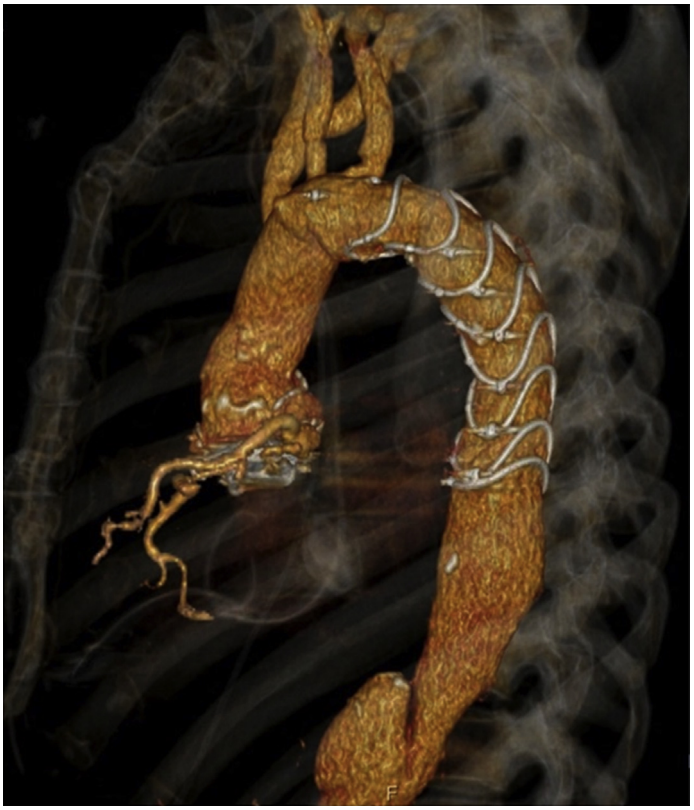


FIGURE 6 3-Dimensional Reconstruction of Contrast-Enhanced Computed Tomography Angiography of the Thoracic Aorta



The Thoraflex (Terumo, Tokyo, Japan) hybrid stent graft is visible making the connection between the aortic arch and the descending aorta.

FIGURE 7 Patient's Family Marfan Disease Pedigree

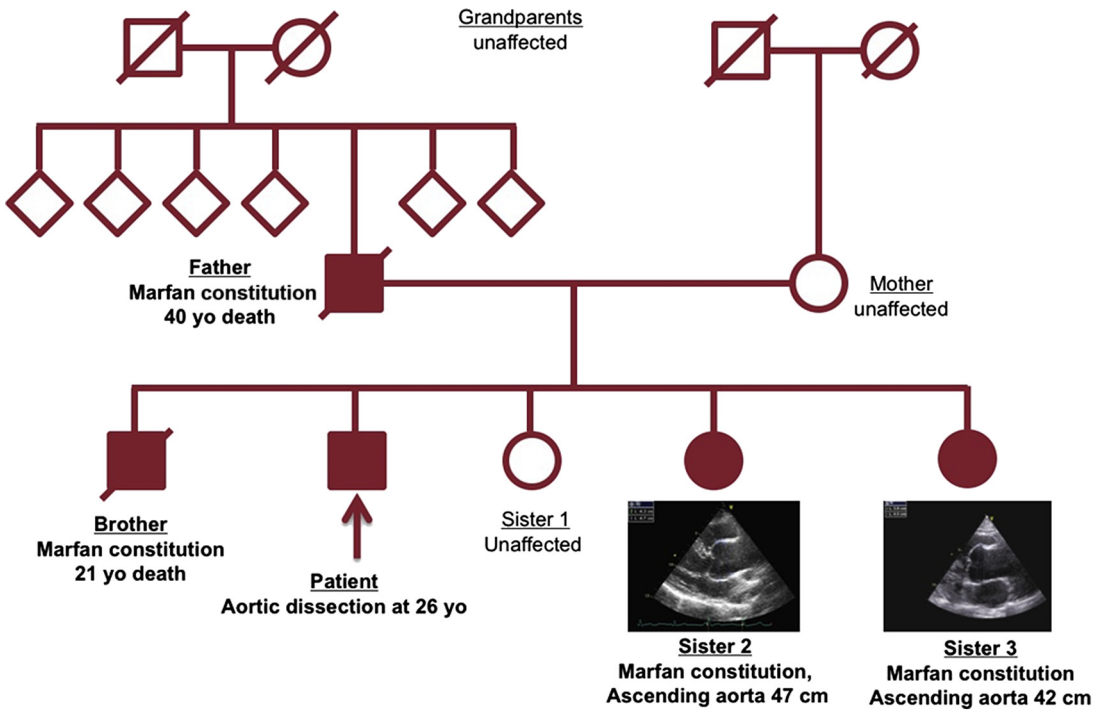
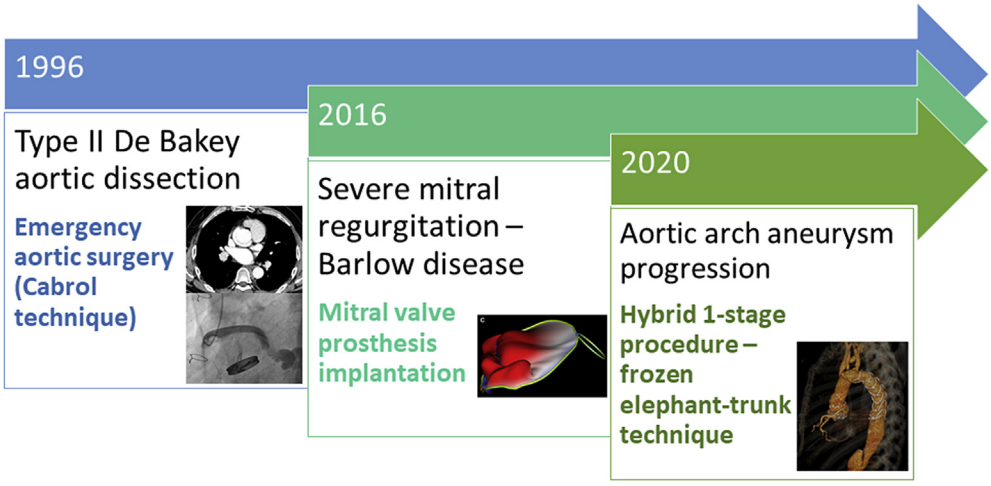


FIGURE 8 Timeline of Patient's Surgical History



phenotypic heterogeneity, as evident from our patient's family history.

CONCLUSIONS

This case gave us the opportunity to observe and manage the full typical and very complex MS cardiovascular phenotype with staged development of cardiovascular complications and the difficult management decisions that come along with it.

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