CASE REPORT

Type B aortic dissection triggered by heart transplantation in a patient with Marfan syndrome

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SUMMARY

Heart transplantation in patients with Marfan syndrome is challenging and raises concerns with regards to the haemodynamic and immunosuppressive-induced effects on the inherently fragile aorta. Most aortic events following transplantation reported so far in the literature occurred in patients with pre-existent distal aortic dissection. We report a case of successful orthotopic heart transplantation in a patient with Marfan syndrome that was complicated by late-onset type B dissection in pre-existing mild and stable distal aortic dilation. Serial aortic imaging revealed progressive growth at the level of the descending thoracic aorta. An open thoracoabdominal aortic repair procedure was successfully performed 6 months after the transplantation.

BACKGROUND

End-stage heart failure in patients with Marfan syndrome (MFS) is uncommon, though the incidence may increase with better survival rates due to improved management of aortic root disease. Indeed, long-term follow-up series in patients with MFS having previously undergone aortic root surgery indicate that heart failure and arrhythmias rank at the top of the list of causes of death, along with dissection or rupture of the residual aorta.^{1 2}

Heart transplantation in patients with MFS is challenging and major concerns arise with regard to the effects—both haemodynamic and immunosuppressive-induced—imposed on the distal aorta. Most aortic events reported so far in the literature have occurred in patients with pre-existent distal aortic dissection.

We report a case of successful orthotopic heart transplantation in a patient with MFS with end-stage heart failure that was complicated by late-onset type B dissection in pre-existing mild and stable distal aortic dilation. We aim to emphasise the importance of careful medical follow-up, including aggressive blood-pressure management, in these fragile patients.

CASE PRESENTATION

In 2010, a 36-year-old man with Marfan syndrome presented at our outpatient clinic, for cardiac follow-up. He already had an extended cardiovascular history including a Bentall procedure combined with mitral valve annuloplasty and closure of a type II atrial septum defect at the age of 13 years. In the years following this procedure, he developed progressive left atrial and ventricular dysfunction with dilation (LVEDD 68 mm at the age of

24 years), complicated by atrial fibrillation and ventricular arrhythmias. He also presented progressive mitral valve and tricuspid valve regurgitation eventually necessitating a second intervention with mitral valve replacement and tricuspid valve repair combined with cardiac resynchronisation therapy-defibrillator implantation at the age of 33 years. At the time of presentation at our centre, he presented significant left ventricular dilation with severe dysfunction (LVEDD 80 mm, ejection fraction 20%), but with an acceptable functional status (New York Heart Association (NYHA) class II). In the subsequent years, however, he gradually developed progressive heart failure with malignant arrhythmias and recurrent hospitalisations despite optimal heart failure treatment, consisting of ACE-inhibitors and diuretics titrated to renal function, and the lowest tolerated blood pressure (systolic 100 mm Hg). He was listed on the heart transplant waiting list in February 2013. CT imaging of the aorta at that time revealed mild fusiform dilation at the thoracoabdominal level (maximal diameter 40 mm—unchanged for at least 10 years) (figure 1). After 1 year, in February 2014, he was hospitalised with end-stage heart failure necessitating listing on the high-urgency transplant list. Ten days later, he underwent successful orthotopic heart transplantation. His recovery was uncomplicated. Blood pressure medication after transplantation consisted of a calcium channel blocker combined with an angiotensin receptor blocker and low-dose diuretics, and was titrated to achieve systolic blood pressures <125 mm Hg. He received standardised immunosuppression therapy according to protocol, consisting of mycophenolate mofetil, tacrolimus and prednisolone, tapered as dictated by the clinical status.

Six weeks after transplantation, the patient presented with back pain and pain in the left leg. Blood pressure (right brachial artery) at that time was 126/65 mm Hg. CT scanning revealed a type B aortic dissection with an entry tear 14 cm distally from the left subclavian artery and a dissection flap extending to the proximal right iliac artery with spontaneous recanalisation (figure 2). While the right renal artery, coeliac trunk and inferior mesenteric artery were perfused from the true lumen, the left renal artery, superior mesenteric artery and left common iliac artery were perfused from the false lumen. According to the guidelines, optimal medical treatment was initiated with strict tension control and close follow-up. The dose of the angiotensin receptor blocker was increased to a maximum daily dose of 100 mg losartan. The

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Figure 1 CT image before heart transplantation. Cardiomegaly (A). Fusiform thoracoabdominal aortic dilation—maximal diameter 40 mm (B).

calcium channel blocker was stopped. Serial aortic imaging in the following months revealed progressive growth at the level of the descending thoracic aorta (+3 mm over a 3-month period), despite adequate blood pressure control (systolic <120 mm Hg). Since increased growth in a recently dissected aorta does not always immediately necessitate surgery, our initial decision after multidisciplinary team discussion was to continue close follow-up with strict blood-pressure control. This proposed strategy, however, was not well taken by the patient, who experienced major anxiety requiring repeated admissions at the emergency department. Finally, and in full agreement with the patient, we decided to refer him for open surgical repair of the aneurysmatic thoracoabdominal aorta. A type III thoracoabdominal aortic repair procedure was performed with reimplantation of the abdominal vessels (figure 3). The native distal ascending aorta and aortic arch were left in place. The postoperative

Figure 2 CT image of aortic dissection after heart transplantation. Entry tear (arrow). False lumen (C). True lumen (D).

course was complicated by transient renal failure requiring haemodialysis. The patient was discharged after 1 month. Blood pressure was adequately controlled with a combination of an angiotensin receptor blocker and low dose diuretics.

OUTCOME AND FOLLOW-UP

At present, 14 months after heart transplantation and 6 months after thoracoabdominal aortic repair, the patient is doing well, with perfect cardiac allograft function and good functional capacity (NYHA class I).

DISCUSSION

MFS is an inheritable connective tissue disorder caused by mutations in the *fibrillin1* gene (*FBN1*).³ Aortic root aneurysm at the level of the sinus of Valsalva with its inherent risk for type A aortic dissection is the principal cardiovascular manifestation in MFS and the main determinant of life expectancy.^{4 5} Other acknowledged cardiovascular features include mitral valve prolapse, pulmonary artery dilation, and distal aortic aneurysms and dissections. Left ventricular dysfunction, though

Figure 3 CT image 1 month after thoracoabdominal aortic repair procedure. No intravenous contrast was used because of impaired renal function. Aortic prosthesis, proximal part (arrows). A residual temporary haematoma is indicated by an asterisk.

uncommon, should be considered as part of the cardiovascular phenotype in MFS, especially since survival rates have significantly increased with improved treatment strategies for aortic root disease. Left ventricular dysfunction may clinically present as heart failure but may also be a major determinant of arrhythmias in patients with MFS, as has been recently acknowledged.⁶ Large series on long-term survival after aortic root surgery indicate that heart failure and arrhythmias constitute major causes of late mortality.^{1 2} Underlying causes of left ventricular

dysfunction in MFS may be the result of significant valvular heart disease in some cases but it is likely that concomitant intrinsic ventricular dysfunction also plays an important role. This has been demonstrated in several independent human studies,^{7–9} and recent data in mouse models have confirmed the existence of Marfan cardiomyopathy, which probably results from a combination of impaired elastic fibre quality, altered TGF β signalling and altered mechanosignalling caused by the underlying *FBN1* mutation.^{10 11}

No data are available regarding optimal treatment of Marfan cardiomyopathy and these patients are managed according to the conventional guidelines for heart failure, including heart transplantation at end-stage. Although the initial experience was not encouraging,¹² more recent reports show hopeful long-term results.¹³ The major concern relates to complications occurring in the distal aorta. Indeed, the presence of a strong new donor heart along with the collagen weakening effect of immunosuppression may have detrimental effects on the inherently weakened aorta. This concern is also supported by the observation of an increased incidence and a more aggressive course of abdominal aortic aneurysms in transplant recipients (both heart and abdominal organ transplantations).^{14 15} There are no evidence-based guidelines for adequate preventive treatment of the weakened aorta in this specific case but it has been demonstrated that the need for reintervention in the distal aorta of patients with MFS with previous aortic root surgery is significantly increased in patients with previous hypertension as compared to those without hypertension.¹⁶ This implies that blood pressure control is of utmost importance. In the same study, no differences were noted with regards to various drug treatment regimens (β -blocker, calcium channel blockers, ACE inhibitors or angiotensin receptor blockers).

In the series on heart transplantation in patients with MFS reported by Knosalla,¹³ there was a 30% incidence of post-operative thoracic aortic events while this is extremely rare outside the setting of MFS, varying from 1% to 2%.¹⁷ Importantly, only one new onset aortic dissection was reported in this currently most extensive series and most case reports in the literature confirm an adverse outcome limited to those cases with pre-existent aortic dissection.^{18–20} Similar to our case, Botta *et al*²¹ reported a case of type B aortic dissection 30 days after heart transplantation, despite prior normal aortic diameters. Their patient developed rapid growth of the dissected aorta after 2 years, necessitating intervention. In contrast to our case, the patient underwent endovascular stent-graft treatment. Although endovascular procedures are less invasive and hence seem a more attractive solution for patients with important comorbidity, caution is warranted in patients with underlying connective tissue disorders such as MFS. Several cases of reintervention after initial endovascular procedures have been reported.^{22 23} Furthermore, success rates of conventional thoracoabdominal surgery in patients with MFS are encouraging.²⁴

As shown in our case, open surgery of the thoracoabdominal aorta, even in a setting after heart transplantation, is a high-risk but feasible strategy.^{18 20}

Contributors TA collected the data and wrote the case presentation. MDP managed the medical transplant aspects of the case and critically revised the manuscript. KF managed the surgical aspects of the case and critically revised the manuscript. JDB managed the pretransplant aspects of the case, identified the case, wrote the discussion section, revised the paper and is responsible for the overall content.

Patient's perspective

- ▶ From very early on after the heart transplant, I felt invincible. I had never felt so energetic and in such good shape in my life. Realising that I was given a new chance to get on with my life is hard to put in words.
- ▶ Unfortunately, this euphoria was short lived when, after a few weeks, I learned that the pain I felt in my stomach, back and legs appeared to be caused by a dissection of the aorta. The disappointment could not have been greater. It was as if I hit the wall with a hard blow. From then on, I was constantly focused on avoiding pressure rises in my blood vessels. The result was a growing concern that was very present in everything I did or felt. The prospect of having to live with a dissected vessel for an indeterminate time was very frightening and made me slightly desperate.
- ▶ Ideally, I wanted to have surgery as soon as possible, which I thought would allow me to continue rebuilding the life that I had tasted here. The doctors carefully considered the wishes and feelings of me and my wife. I certainly did not underestimate the surgery and was aware of all the risks. Yet I had, also by the positive attitude of the doctors concerned, a lot of confidence in a good outcome.
- ▶ The impact of the aortic surgery on my body was many times greater than the previous heart operations through the sternum. In the weeks prior to the surgery I was in contact with two people with Marfan syndrome who had undergone similar surgery. They told me how heavy the operation was and how difficult the recovery afterwards. You cannot possibly look forward to something like this, but I decided to just let it all come at me. It makes no sense to worry too much in advance. I never did. I feared chronic pain due to the incision as both patients had mentioned. The recovery was indeed very difficult, but after a few months, all the pain completely disappeared.
- ▶ Now, after half a year, I feel invincible again. And this time even without the incentive effect of the cortisone... I am grateful to the people of Ghent University Hospital who have fought so hard for my life. I am now a very happy person, though I am aware that Marfan syndrome will never go away. I will always continue following the rules of life.

Learning points

- ▶ Heart failure is an established cardiovascular feature of Marfan syndrome and may require cardiac transplantation in rare cases.
- ▶ Aortic complications are frequent after heart transplantation in patients with Marfan syndrome.
- ▶ Not only rapid progressive dilation of (chronic) aortic dissection but also new-onset aortic dissection may be encountered after heart transplantation in patients with Marfan syndrome, despite adequate blood-pressure control.
- ▶ Open surgical repair for thoracoabdominal aortic dissection after heart transplantation is a feasible strategy.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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