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Case Report

Medium-term outcome of transcatheter aortic valve replacement in mucopolysaccharidosis type I-HS (Hurler-Scheie syndrome)

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ABSTRACT

Mucopolysaccharidoses (MPSs) are inherited metabolic diseases characterized by the deficiency of lysosomal enzymes and the accumulation of glycosaminoglycans in various organs, including the heart. In particular, aortic valve disease causes high morbidity and mortality rates, and sometimes requires surgical aortic valve replacement (SAVR) at a young age. Although transcatheter aortic valve replacement (TAVR) for severe aortic stenosis (AS) in surgical high-risk patients is a well-established treatment, there are few reports of TAVR in MPS and medium- and long-term outcomes are not known. We present a case of severe AS in a MPS patient with high risk for SAVR who was successfully treated with TAVR and has shown a fine medium-term result. A 40-year-old woman with MPS type I-HS (Hurler-Scheie syndrome) receiving enzyme replacement therapy as a systemic treatment had complained of syncope and worsening dyspnea, and she was diagnosed with severe AS. The patient had a history of temporary tracheotomy because of the difficulty of endotracheal intubation. Considering risk for general anesthesia, TAVR was performed under local anesthesia. She has improved symptoms for one-and-a-half years. TAVR for severe AS in MPS would be an alternative option for surgical high-risk patients and can demonstrate preferable medium-term outcomes combined with systemic therapies.

Learning objective: Mucopolysaccharidoses (MPSs) are metabolic diseases affecting various organs. The MPS patients requiring surgical aortic valve replacement (SAVR) for severe aortic stenosis (AS) often have a high surgical risk. However, in MPS, transcatheter aortic valve replacement (TAVR) could be an alternative procedure to SAVR. We report a MPS patient treated with TAVR showing a preferable medium-term outcome. We suggest that TAVR for severe AS in MPS is an acceptable treatment option.

Introduction

Mucopolysaccharidoses (MPSs) are a group of rare inherited lysosomal storage disorders caused by a deficiency of essential enzymes for the degradation of glycosaminoglycans (GAGs). The accumulation of GAGs causes damage to various organs, including the heart. The most common cardiac manifestations are mitral and aortic valve diseases (regurgitation and/or stenosis), and the prevalence of aortic stenosis (AS) is 3–36 % [1,2]. In MPS, while surgical aortic valve replacement (SAVR) has been reported for severe AS [2], patients with inoperable status because of multisystem disorders are common. However, reports of transcatheter aortic valve replacement (TAVR) are scarce, and its medium- and long-term outcome are not clear. In our case, a young patient suffering from MPS type I-HS (Hurler-Scheie syndrome) underwent TAVR for severe AS due to her high risk for SAVR and has shown an uncomplicated medium-term outcome.

Case report

A 40-year-old woman with MPS type I-HS (Hurler-Scheie syndrome) suffered from heart failure [New York Heart Association (NYHA) functional class III] caused by severe AS. MPS type I-HS was diagnosed at 3 years old. The patient has received intravenous enzyme replacement therapy (ERT) with recombinant human laronidase once a week for 19 years and intrathecal ERT concurrently every three months for 3 years.

She underwent tonsillectomy and has been treated with continuous positive airway pressure due to upper airway constriction and obstructive sleep apnea syndrome. Her past medical history also included spinal canal stenosis treated with C1–3 laminectomy, atrioventricular

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nodal reentry tachycardia treated with catheter ablation, mental retardation, and recurrent pneumonia.

Moderate AS (mean aortic gradient of 27 mmHg) was found 4 years previously. She was referred to our hospital for syncope and worsening dyspnea. Her height was 134 cm and her weight was 35 kg. On auscultation, Levine IV/VI systolic murmur was heard in the aortic area. No leg edema was noted. Routine laboratory values and electrocardiogram were normal.

Transthoracic echocardiogram (TTE) showed good left ventricular function and thickened aortic valve leaflets with severe stenosis: left ventricle ejection fraction (LVEF) of 65 %, peak aortic velocity of 4.0 m/s, mean aortic gradient of 32 mmHg, aortic valve area of 0.5 cm^2, and aortic valve area index of 0.4 cm^2/m^2 (Fig. 1A, B, and Online Video 1). Multidetector computed tomography (CT) demonstrated a tricuspid aortic valve with leaflet thickening and negligible calcification (Fig. 1C). Aortic annulus area was 311.3 mm^2 (Fig. 1D), and aortic root was not dilated (Fig. 1E and F). Coronary CT angiography showed no significant stenosis, and cardiac magnetic resonance imaging revealed no findings of cardiomyopathy.

At first, SAVR was contemplated because of her age and the non-calcific aortic valve. However, it was considered that the risk of surgery with general anesthesia was high because of difficulty with endotracheal intubation. Furthermore, she had undergone an emergency tracheotomy during her previous surgery. After multidisciplinary meetings and the careful discussion with the patient and her family, our heart team decided to perform TAVR under local anesthesia.

Considering future coronary access and possibility of valve-in-valve TAVR, we selected a balloon-expandable valve. TAVR was performed with the transfemoral approach. We inserted a 14 Fr expandable sheath (eSheath, Edwards Lifesciences, Irvine, CA, USA) into the right common femoral artery. A 20 mm SAPIEN 3 Ultra (Edwards Lifesciences) was positioned ensuring the central balloon marker was at the annular plane, and it was directly deployed at the proper position under rapid pacing (Fig. 2A and B). We used center marker-guided implantation, not radiolucent line-guided implantation to avoid distal migration or embolization of the valve and to ensure future coronary access. Post-procedure TTE showed moderate residual aortic pressure gradient (peak aortic velocity of 2.3 m/s, mean aortic gradient of 12 mmHg) and mild paravalvular leak. There were no perioperative complications. She was discharged to home on day 2.

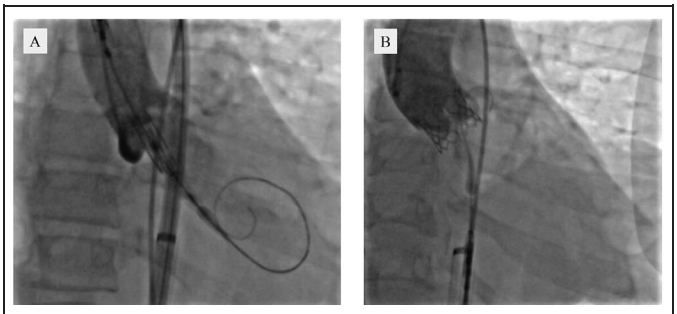

Fig. 2. Transcatheter aortic valve replacement angiography. (A) Aortic root angiography during deployment of 20 mm SAPIEN 3 Ultra. (B) Aortic root angiography after valve deployment showing proper position of device.

Intravenous and intrathecal ERT has been continued. The patient started to take aspirin and clopidogrel after TAVR. Clopidogrel was continued for 3 months. Aspirin has been continued. At one-and-a-half year follow-up, she reported the improvement of symptoms (NYHA functional class I). TTE revealed normal LVEF (65 %) with peak aortic velocity of 2.8 m/s, mean aortic gradient of 18 mmHg, and no paravalvular leak. There is no sign of leaflet deterioration.

Discussion

We report a case of a young patient with MPS type I-HS (Hurler-Scheie syndrome) who received TAVR for severe AS and has demonstrated a good medium-term outcome. This case highlighted two important issues. First, TAVR for severe AS in inoperable MPS patients would be an alternative option to SAVR. Second, TAVR for severe AS in MPS can show a preferable medium-term outcome combined with systemic therapies.

MPSs are a family of rare hereditary diseases characterized by multisystem disorders, such as circulatory, respiratory, musculoskeletal, and central nerve systems [1]. MPSs are classified into seven types

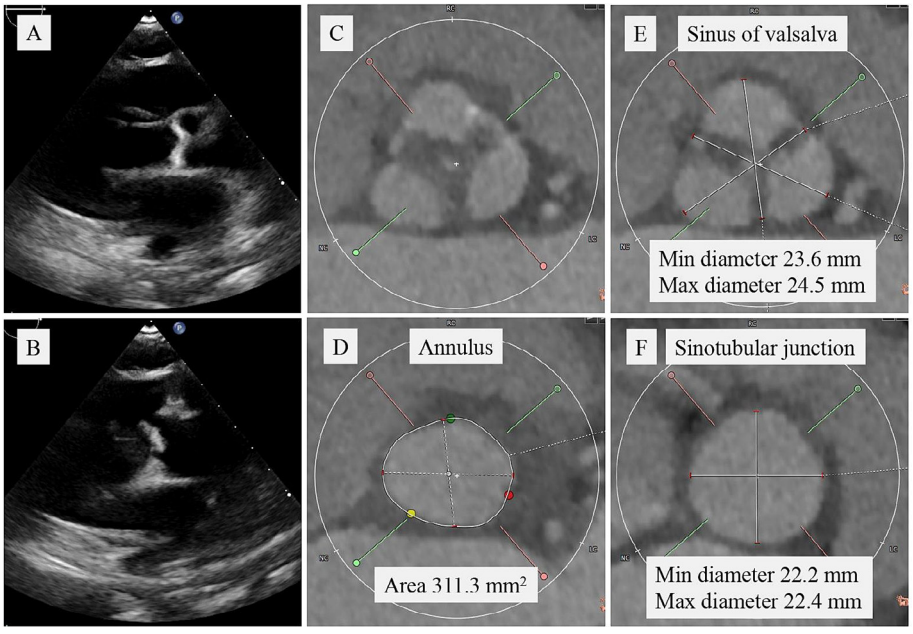

Fig. 1. Pre-procedural transthoracic echocardiogram (TTE) and multidetector computed tomography (MDCT) of the aortic complex. (A) (B) TTE in parasternal long-axis view in diastolic frame (A) and systolic frame (B) showing thickened aortic valve leaflets. (C) MDCT showing thickening of all leaflets. (D) The measurement of aortic annulus area with MDCT. (E) MDCT showing no dilatation of sinus of Valsalva. (F) MDCT showing no dilatation of sinotubular junction.

Table 1
Transcatheter aortic valve replacement in patients with mucopolysaccharidosis.

Case	Age/Sex	Type	Device	Outcome	Follow-up after discharge
Felice (2014) [7]	30/M	I-S	SAPIEN XT 26 mm	Improvement of dyspnea	None
Nakazato (2020) [8]	52/F	Undescribed	SAPIEN XT 20 mm	Undescribed	Severe AS due to SVD two-and-a-half years later
Gorla (2021) [9]	64/F	IV	ACURATE TA size S	Improvement of dyspnea, MPG 11 (mmHg)	MPG 5 (mmHg) 60-day later
Mori (2021) [10]	50/M	II	Evolut PRO 26 mm	Improvement of dyspnea	None

AS, aortic stenosis; SVD, structural valve deterioration; MPG, mean pressure gradient.

biochemically according to associated lysosomal enzymes and GAGs. In addition, MPS type I patients are also differentiated into three subtypes clinically by the degree of severity. MPS type I-HS (Hurler-Scheie syndrome) is the intermediate form, whose median age of diagnosis is 4 years and pre-treatment life expectancy is 21.6 years. In MPS, cardiac involvements are common: cardiac valvular disease (mitral regurgitation, mitral stenosis, aortic regurgitation, and aortic stenosis), cardiomyopathy, coronary artery disease, and aortic root dilatation. Cardiac valvular disease, which is most common and causes high mortality rates, was observed in 59 % of MPS type I-HS patients in a previous report. It has been reported that hematopoietic stem cell transplantation (HSCT) and ERT as systemic MPS therapies cannot improve progressed cardiac valvular disease; therefore, SAVR has been performed for severe AS [2]. However, MPS patients are sometimes considered inoperable because of airway obstruction, abnormal cervical vertebrae, and mixed pulmonary disease making general anesthesia and perioperative airway management difficult [3]. According to a previous report, 11 out of 24 MPS patients who received surgical valve replacement had difficulty with endotracheal intubations, and 5 of those required emergency tracheotomy [4]. In our case, it was predicted that endotracheal intubation and perioperative airway management were difficult; hence TAVR was performed under local anesthesia. Non-calcific aortic stenosis is risk of transcatheter heart valve (THV) migration or embolization because anchoring of the THV could be impaired. However, a previous report about TAVR shows that 30-day and one-year mortality rates, complication rates, and six-month echocardiographic outcome were similar between non-calcific and calcific aortic stenosis. In this case, there were no perioperative complications and the patient recovered without sequelae.

Mechanical valves are generally recommended for SAVR in young patients in terms of valve durability. Moreover, bioprosthetic valves can be affected by accumulation of GAGs resulting in lower durability in MPS patients. Therefore, mechanical valves were implanted in most of the reports of SAVR in MPS. According to a previous report, none of the patients whose echocardiographic follow-up data were obtained showed mechanical valve failure ($n = 8$, follow-up range of 5–36 months) [2]. On the other hand, bioprosthetic valves might be considered for female patients of childbearing age and patients with intolerance to anticoagulation due to comorbidities. Indeed, there is a report of SAVR with bioprosthesis for a MPS patient, and this shows a fine result three years after the surgery [5]. While ERT and HSCT cannot improve the progressed valve disease, it has been reported that ERT may prevent the development of cardiac valvular disease if introduced before the onset of significant symptoms [6]. Therefore, the medium- and long-term durability of THV might also be achieved with concurrent ERT administration.

Until now, 4 reports of TAVR for MPS patients have been published (Table 1) [7–10]. However, there are no reports about medium- and long-term results of TAVR for MPS patients. As shown in Table 1, two have no follow-up data after discharge [7,10], and one has short-term follow-up [9]. The other received surgical explantation of transcatheter aortic valve bioprosthesis and SAVR two-and-a-half years after TAVR [8]. Although the authors concluded that the explantation was required for severe AS resulting from structural valve deterioration associated with deposition of GAGs, they did not mention type of MPS, systemic MPS treatments, TTE outcome of post-TAVR, and pathological findings of explant THV. In our case, the risk of structural valve deterioration was considered low in terms of the native aortic valve feature because non-calcific valve does not prevent the expansion of THV and leads to lower risk of structural valve deterioration. Regarding the device type, the most important difference from these previous reports is using SAPIEN 3 Ultra, which is the latest generation balloon-expandable valve. This valve shows lower rates of paravalvular leak than older-generation balloon-expandable valves by improving the outer skirt. This might also be one of the factors that leads to a good medium-term outcome.

In conclusion, TAVR for severe AS in MPS is an alternative option for patients with high risk for SAVR. TAVR for MPS patients can also demonstrate a preferable medium-term outcome combined with systemic treatments. Owing to the advances in systemic therapies, the life expectancy of MPS patients has improved. Therefore, the number of MPS patients who require valve replacement will increase, and valve durability in MPS will become much more important. Because THV durability in MPS is still unclear, frequent echocardiographic follow-up might be necessary. Further reports should be accumulated to show the medium- and long-term durability of THV for MPS patients.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jccase.2022.12.015.

Declaration of competing interest

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