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VALVULAR DISEASE

CASE REPORT: CLINICAL CASE

Transcatheter Edge-to-Edge Mitral Valve Repair in a Patient With Anderson-Fabry Disease

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ABSTRACT

Severe degenerative mitral regurgitation (DMR) is one cardiac manifestation of the multiorgan metabolic enzyme disorder Anderson-Fabry Disease (AFD). Although DMR is normally managed surgically, many patients with AFD are unsuitable for this. We present the first case of mitral transcatheter edge-to-edge repair in a patient with AFD. (J Am Coll Cardiol Case Rep 2024;29:102271) © 2024 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/).

HISTORY OF PRESENTATION

A 63-year-old man presented with a 3-month history of progressive shortness of breath, right elbow tenderness, and acute delirium. On examination, there were inspiratory crepitations and low oxygen saturations consistent with pulmonary edema. A pansystolic murmur was audible, consistent with significant mitral regurgitation. His right elbow was swollen and erythematous.

LEARNING OBJECTIVES

- To adopt a heart team approach when deciding the treatment modality for AFD patients with valvular disease.
- To emphasize favorable immediate outcomes and very abbreviated recovery times when using TEER to treat severe DMR associated with AFD, even in multimorbid patients.
- To achieve stable leaflet grasping, including with the use of multiple percutaneous edge-to-edge mitral valve repair devices, and preserve leaflet integrity after TEER for DMR associated with AFD.

PAST MEDICAL HISTORY

His past medical history was significant for Anderson-Fabry Disease (AFD) complicated by end-stage renal failure on hemodialysis, frontal lobe stroke, atrial fibrillation, and hypertension.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses included left ventricular failure, infective endocarditis, and degenerative mitral regurgitation (DMR).

INVESTIGATIONS

Blood tests were remarkable for raised inflammatory markers, and his blood cultures transiently grew methicillin-sensitive *Staphylococcus aureus*.

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ABBREVIATIONS AND ACRONYMS

AFD = Anderson-Fabry disease

DMR = degenerative mitral regurgitation

Gal A = galactosidase A

Gb3 = globotriaosylceramide

LVOT = left ventricular outflow tract

MV = mitral valve

SSM = surgical septal myectomy

TAVR = transcatheter aortic valve replacement

TEE = transesophageal echocardiography

TEER = transcatheter edge-to-edge repair

Computed tomography of his elbow revealed uncomplicated bursitis. Transthoracic echocardiography revealed severe DMR with preserved left ventricle function and mild right ventricle dysfunction. Transesophageal echocardiography (TEE) to further determine the etiology of his DMR revealed bileaflet mitral valve (MV) prolapse with marked leaflet thickening consistent with sphingolipid infiltration, resulting in severe MV regurgitation (Videos 1 and 2). No vegetations were seen.

MANAGEMENT

Right elbow bursitis was managed with intravenous cephazolin to good effect. Inflammatory markers settled, but his heart failure symptoms persisted. Given that MV surgery was indicated, his TEE findings were discussed at a heart team meeting. The consensus was to proceed with transcatheter edge-to-edge MV repair (TEER) rather than MV surgery in view of his comorbidities.

The TEER procedure was performed in the standard way under general anesthesia using TEE and fluoroscopic guidance from the right femoral vein. In brief, a transseptal puncture was performed and the left atrium was instrumented with a 20-F sheath. A MitraClip (Abbott Medical) percutaneous edge-to-edge MV repair system featuring a 6-mm-wide (NTW) clip was placed at the medial aspect of the A2 and P2 scallops of the MV, reducing the DMR from severe to moderate. A further percutaneous edge-to-edge MV repair system featuring a 4-mm-wide (NT) clip was deployed lateral to this, with only trivial residual mitral regurgitation, stable appearances, and no change to the MV gradient (Videos 3 to 5). He recovered uneventfully and was discharged the following day.

DISCUSSION

Anderson-Fabry disease is an inherited X-linked metabolic disorder caused by a mutation in the galactosidase alpha (*GLA*) gene, encoding lysosomal enzyme α-galactosidase A (Gal A). α-Gal A breaks down glycolipids such as globotriaosylceramide (Gb3). α-Gal A is absent/deficient in AFD, resulting in excessive accumulation of Gb3 in the cellular lysosomes, mainly in the heart, skin, kidneys, and central nervous system, leading to the constellation of symptoms seen in AFD.[1]

Cardiac manifestations include left ventricular hypertrophy with impaired diastolic function, left ventricle outflow tract (LVOT) obstruction, coronary insufficiency, arrhythmias, and valvular pathology. These manifestations are thought to be driven by Gb3 deposition in cardiomyocytes, conduction system cells, and valvular fibroblasts. Left ventricle systolic function as measured by ejection fraction is rarely decreased in AFD. Assessment with the use of strain-rate imaging, however, may demonstrate decreased contractility occurring earlier in the longitudinal than in the radial dimension. This explains why contractility impairment may be undetectable by the measurement of ejection fraction or fractional shortening. Diastolic dysfunction is quite common owing to marked fibrosis of the cardiomyocytes, resulting in a restrictive cardiomyopathy.[2]

Valvular pathologies arise from infiltrative changes within valvular fibroblasts, resulting in valvular thickening and deformation. Valvular changes are found almost exclusively in the left heart valves. Mitral and aortic regurgitation are the most prevalent pathologies; however, they are usually of a mild to moderate severity, asymptomatic, and seldom require any intervention.[2] Published studies pertaining to valvular interventions in AFD have therefore been very limited.

There have been a few reported cases of surgical interventions for various valvular and structural heart pathologies in AFD patients. In general, cardiac surgical interventions for this group of patients are associated with extremely poor outcomes. This may be a consequence of the multiorgan nature of the disease or as a result of the impact of AFD on cardiac function, which makes cardiopulmonary bypass higher risk. Furthermore, event-free survival in AFD patients over time is extremely poor, particularly in men with a typical AFD phenotype.[3]

Although there have been cases of patients with certain phenotypes of AFD undergoing cardiac surgery with favorable short-term outcomes, in most cases of conventional cardiac surgery requiring sternotomy and cardiopulmonary bypass, serious postoperative complications are common. Fernandez et al[4] reported favorable short-term outcomes in a patient with AFD after MV surgery; however, that was a minimally invasive procedure.

Surgical septal myectomy (SSM) to relieve LVOT obstruction in AFD patients has been reported. Meghji et al[5] presented a series of 7 AFD patients with LVOT obstruction undergoing SSM. The impact of SSM on patients' comorbidities and long-term prognoses, however, was not reported. Interestingly, 6 of those 7 patients were women, and it appears that men with the typical AFD phenotype have poorer outcomes.[3]

In most cases of conventional cardiac surgery, AFD patients are thought to have a high incidence of serious perioperative complications, including renal dysfunction,[6] cardiac arrhythmias, prolonged critical illness, and difficulties related to ongoing renal replacement therapy.[7]

Transcatheter procedures, such as mitral TEER, transcatheter aortic valve replacement (TAVR), and alcohol septal ablation, provide an attractive alternative option for patients with AFD and health care systems that cater to the AFD population for reducing recovery and hospitalization periods in those with significant valve disease. Successful TAVR procedures have been reported in AFD patients, mostly with favorable outcomes.[8,9] Furthermore Zemánek et al[10] presented a series of patients with LVOT obstruction undergoing alcohol septal ablation with good initial results and relatively few complications.

To our knowledge, this is the first recorded case of mitral TEER being used for a patient with AFD. In theory, this therapy may prove to be advantageous for patients with AFD, given the abbreviated time for recovery, next-day discharge, and impact on other organ diseases common in this patient group. This case also demonstrates that MV disease related to AFD can withstand instrumentation with multiple percutaneous edge-to-edge MV repair devices to substantially reduce the extent of MR and heart failure symptoms.

CONCLUSIONS

AFD is a rare lysosomal storage disease that can have cardiac manifestations. Surgical interventions are associated with prolonged recovery and numerous postoperative complications. This case report emphasizes the use of less-invasive procedures to manage valvular pathologies in high-risk AFD patients. It describes the first mitral TEER procedure in an AFD patient. The patient had excellent immediate outcomes, but long-term outcomes are yet to be determined.

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REFERENCES

1. Mehta A, Beck M, Sunder-Plassmann G, eds. *Fabry Disease: Perspectives from 5 Years of FOS*. Oxford PharmaGenesis; 2006.

2. Linhart A, Lubanda JC, Palecek T, et al. Cardiac manifestations in Fabry disease. *J Inherit Metab Dis*. 2001;24(Suppl 2):75-83 [discussion: 65].

3. El Sayed M, Hirsch A, Boekholdt M, et al. Influence of sex and phenotype on cardiac outcomes in patients with Fabry disease. *Heart*. 2021;107(23):1889-1897.

4. Fernandez J, Sigurdsson G, Farivar RS. Cardiac surgery in patients with Fabry's disease: review of literature. *J Card Surg*. 2012;27(4):478-480.

5. Meghji Z, Nguyen A, Miranda WR, et al. Surgical septal myectomy for relief of dynamic obstruction in Anderson-Fabry Disease. *Int J Cardiol*. 2019;292:91-94.

6. Vlachou A, Gogakos AS, Cheva A, Drossos G. Surgical treatment of severe aortic valve stenosis with concomitant Fabry disease. *Cardiovasc Med*. 2019;22:w02066.

7. Watanabe T, Tokunaga N, Tsujimoto K, et al. Case report: a surgical case of mitral valve replacement for a patient with Fabry disease complicated with hemodialysis. *Kawasaki Med J*. 2020;46:145-151.

8. Giustino G, Chieffo A, Montorfano M, et al. First case reported of transcatheter aortic valve implantation in a patient affected by Fabry's Disease and severe low-flow low-gradient aortic valve stenosis. *Case Rep Intern Med*. 2014;1(2):71-74.

9. Saccheri MC, Cianciulli TF, Blanco FL, Blanco RI. Rapidly progressive aortic stenosis treated with transcatheter aortic valve implantation in a patient with Fabry disease: a case report. *Eur Heart J Case Rep*. 2021;5(6):ytab124.

10. Zemánek D, Marek J, Dostálová G, et al. Usefulness of alcohol septal ablation in the left ventricular outflow tract obstruction in Fabry disease cardiomyopathy. *Am J Cardiol*. 2021;150:110-113.

KEY WORDS cardiomyocytes, heart failure, MitraClip, mitral regurgitation

APPENDIX For supplemental videos, please see the online version of this paper.