Is Fabry disease an indication for a transcatheter aortic valve implantation? A case of successful surgical aortic valve replacement with an adverse postoperative course

Miha Antonič1,2

1University Medical Center Maribor, Division of Surgery, Department of Cardiac Surgery, Maribor, Slovenia; 2University of Maribor, Faculty of Medicine, Maribor, Slovenia

Abstract

Purpose: Fabry disease (FD) is an extremely rare X-linked lysosomal storage disorder caused by a deficiency of the enzyme α-galactosidase A, which results in intracellular accumulation of glycosphingolipids. In the heart, accumulating sphingolipids and accompanying fibrosis promote hypertrophy, conduction disturbances, thickening of the valves, and accelerated coronary artery disease resulting in substantial morbidity and mortality.

Case report: Here, we present a case of a 57-year old male with FD, severe aortic valve stenosis, and permanent atrial fibrillation who underwent successful surgical aortic valve replacement, but postoperatively developed severe complications of nearly all organ systems, which resulted in death.

Conclusion: Although the patient risk profile did not meet the criteria for transcatheter aortic valve implantation, this treatment option is...
Fabry disease (FD) is an extremely rare X-linked lysosomal storage disorder caused by a deficiency of the enzyme α-galactosidase A, which results in intracellular accumulation of glycosphingolipids. The skin, cornea, kidney, peripheral nerves, and heart are especially affected by FD, leading to progressive failure of these organs (1). In the heart, accumulating sphingolipids and accompanying fibrosis cause thickening of the ventricular walls and hypertrophy, resulting in impaired diastolic and systolic function (2). Other cardiac manifestations include conduction disturbances, thickening of the valves, and accelerated coronary artery disease. Cardiovascular involvement substantially contributes to morbidity and mortality of these patients. Males (hemizygous) are more severely affected and present symptoms earlier than females (heterozygous) (3). The severity of the disease is highly variable with an average life expectancy of about 50 years in men and 70 years in women when left untreated (4). Recently, enzyme replacement therapy (ERT) was introduced as a therapeutic option based on evidence of reduced glycosphingolipid accumulation. However, although ERT is a promising therapeutic option, its clinical effectiveness in cardiac disease remains to be clarified (5).

Here, we report a case of a 57-year old male with FD receiving ERT with severe aortic valve stenosis and permanent atrial fibrillation who underwent successful and uncomplicated surgical aortic valve replacement, but postoperatively developed severe complications of nearly all organ systems, resulting in death.

A 57-year-old male with severe symptomatic aortic valve stenosis was admitted for aortic valve replacement. He was diagnosed with FD 12 years before and has received ERT for the last 11 years. Preoperative echocardiography showed a heavily calcified and stenotic aortic valve (mean/peak pressure gradients, 48 and 80 mmHg, respectively; valve area, 0.5 cm²), severe left ventricular (LV) hypertrophy (indexed LV mass, 185 g/m²), normal LV ejection fraction (53%), and enlarged atria (left atrial diameter, 5.3 cm; right atrial diameter, 4.6 cm) (Figure 1).

The patient was diagnosed with atrial fibrillation 2 years before and stage 4 chronic renal failure. Laboratory tests revealed elevated serum creatinine (354 μmol/l), pro-BNP (B-type natriuretic peptide; 2683 pmol/l), and troponin I (0.76 μg/l). Spirometry revealed moderate restrictive as well as obstructive lung function impairment. Surgical risk evaluation was low (EuroSCORE II, 2.24%).

A standard aortic valve replacement was performed through a full sternotomy with antegrade and retrograde cold blood cardioplegia for cardiac protection. A heavily calcified aortic valve was encountered. After careful decalcification, a Trifecta® stented pericardial biological valve was implanted (size, 21; St. Jude Medical, Inc., St. Paul, MN, USA). Radiofrequency ablation of the pulmonary veins, connecting lesions, and left atrial appendage was also performed. The left atrial appendage was then closed. Weaning from cardiopulmonary bypass was characterized by hemodynamic instability and rhythm disturbances.

In the intensive care unit, the patient stabilized over the next 24 h and was extubated one day after surgery. However, due to acute renal failure, renal replacement therapy was necessary. Recurrent
pleural effusions required bilateral chest drainage. Extensive right-sided pneumonia further complicated the postoperative course. The patient received antibiotic treatment under the supervision of an infectologist. However, his condition worsened and severe respiratory failure developed, requiring reintubation and mechanical ventilation. Furthermore, despite preventive administration of proton pump inhibitors, massive gastrointestinal bleeding occurred due to an acute diffuse erosive hemorrhagic gastritis, requiring blood transfusion. Additionally, signs of evolving paralytic ileus emerged. The kidneys showed no signs of recovery; thus, dialysis was continued. The pneumonia and respiratory function continued to worsen with evident clinical signs of sepsis with fever, leukocytosis, high C-reactive protein levels, and need for vasopressors. No pathogen was isolated from blood cultures or bronchial aspirate. LV function worsened and the LV ejection fraction was <20%. Despite aggressive antibiotic and supportive treatment, the patient died due to sepsis and multiple organ failure on postoperative day 20.

Surgical aortic valve replacement is generally a safe procedure with low overall mortality and morbidity with a 10-year survival rate of about 70%, which is dependent on comorbidities and especially patient age (6). However, in a subset of patients with high or prohibitive surgical risk, transcatheter aortic valve implantation (TAVI) offers an excellent alternative treatment option. The current indications and recommendations for TAVI are specified in the current European (2012) and American (2014) guidelines (7,8). To sum up, TAVI can be performed in patients with severe aortic stenosis with no surgical option and as an alternative to high-risk surgery, when TAVI is favored by a multidisciplinary Heart Team. The surgical risk of these patients is usually evaluated using the EuroSCORE and STS (The Society of Thoracic Surgeons) scoring systems and classified as high when greater than 20% or 10%, respectively, or when the Heart Team considers that the patient has significant comorbidities or weakness/frailty not reflected in these scores (7,8). Current guidelines recommend TAVI only for inoperative or high-risk patients; however, there is also a strong worldwide trend of TAVI implementation for intermediate-risk patients (STS score 3%–8%) (9). Although the best results of TAVI are expected in lower-risk patients, there are two limitations that will determine wider approval: procedural safety and long-term durability of the valve itself.

In the presented case, the patient was considered low-risk (EuroSCORE II, 2.24%) and the Heart Team also classified him as low-risk and suitable for surgery. This decision was partly influenced by rare case reports in the literature describing successful open-heart surgery in patients with FD, although most were younger and/or female (10–12). Moreover, the patient was on enzyme therapy, in good
condition, and did not appear to be clinically fee-
ble. However, preoperative levels of troponin, the
presence of chronic renal failure, and spirometry
results all indicated progressive multiple organ da-
age. Furthermore, being 57 years old, he had alre-
ady reached the average life expectancy of male FD
patients. Taking all this into account, we now beli-
eve that the progress of FD and consequently the
surgical risk were underestimated. We also believe
that in this group of patients, standard risk profile
tests are not reliable, as they were not designed nor
clinically tested in this group of patients.

In conclusion, although lacking experience in FD
patients, we are now convinced that these patients
should be evaluated with caution and on individual
basis, and that the Heart Team should be required
to include a specialist with superior knowledge in
this field of medicine. Furthermore, in our opini-
on, especially in male patients aged >50 years with
aortic stenosis, the threshold for TAVI should be
low.

REFERENCES

Isogari Y. Fabry’s disease. Intern Med 1992; 31:
682-5.
2. Linhart A, Paleček T, Bultas J, Ferguson JJ, Hru-
dová J, Karetová D et al. New insight in cardiac
structural changes in patients with Fabry’s dis-
GO, Krawisz JE. Fabry cardiomyopathy in the fe-
male confirmed by endomyocardial biopsy. Mayo
4. Vujkovac B, Šabovič M, Verovnik F, Benko D, Co-
kan A, Špegel M et al. Recommendation for diag-
nosis and treatment of Fabry’s disease in Slove
5. Eng CM, Guffon N, Wilcox WR, Germain DP, Lee
P, Waldek S et al. Safety and efficiency of recom-
binant human alfa-galactosidase: a replacement
345: 9-16.
6. Desai ND, Christakis GT. Bioprosthetic aortic
valve replacement: stented pericardial and por-
cine valves. In: Cohn, LH ed. Cardiac Surgery in
860-94.
Barón-Esquivias G, Baumgartner H et al. Guide-
lines on the management of valvular heart disease
8. Nishimura RA, Otto CM, Bonow RO, Carabello
ACC Guideline for the Management of Patients
With Valvular Heart Disease: A Report of the
American College of Cardiology/American Heart
Association Task Force on Practice Guidelines. J
Am Coll Cardiol 2014;63:e57-185.
9. Cribier A, Durand E, Eltchaninoff H. Patient selec-
tion for TAVI in 2014: is it justified to treat low-
or intermediate-risk patients? The cardiologist’s
et al. Fabry disease with aortic regurgitation. Ann
11. Kunkala MR, Aubry MC, Ommen SR, Gersh BJ,
Schaff HV. Outcome of septal myectomy in pa-
12. Chimenti C, Morgante E, Critelli G, Russo MA,
Frustaci A. Coronary artery bypass grafting for
Fabry’s disease: veins more suitable than arteries?