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Cardiac surgery of aortic valve and ascending aorta (Bentall procedure) in a patient with Fabry disease without enzyme replacement therapy: an overview of aortic and aortic valve surgical tips

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ABSTRACT

Introduction: Fabry disease (FD) is a rare disease in which cardiovascular events are one of its manifestations. Aortic and mitral valve involvement are among its manifestations, but due to the concern of suture failure without enzyme replacement therapy (ERT), the desire for its surgery has been very low, and its reported cases have been few. After the introduction of ERT, cardiovascular surgery for such patients has been gradually reported from different places, but due to the high cost of ERT, it is not practically available to patients in the third world and the backward countries. Reports of the experiences of patients with FD who underwent cardiac surgery without ERT can help improve cardiac surgery in these patients.

Case Report: A 34-year-old man diagnosed with FD due to chronic renal failure and underwent dialysis 3 times a week for 1.5 years became a candidate for kidney transplant. In pre-transplant examinations, dilatation of aortic root and aortic valve insufficiency were diagnosed, and the patient's kidney transplant surgery was postponed until after cardiac surgery. The patient underwent cardiac surgery, aortic valve replacement, and ascending aortic replacement, as well as re-implantation of both right and left coronary buttons on the ascending aorta (Bentall procedure). The post-surgery period passed without any special event. The patient's dialysis continued; after 4 months, he underwent kidney transplant surgery, and the one-year follow-up period also was good.

Conclusion: Although there is very little evidence of cardiovascular surgery in patients with FD without ERT, and surgeons have always been worried about suture failure and complications of cardiac surgery, due to the high cost of ERT, this treatment is not available to everyone. The introduced patient underwent cardiac surgery by Bentall procedure without receiving ERT and was discharged without any special complications. By reporting and collecting similar cases, guidance may be provided for patients with FD for whom ERT is not available.

Case Report

Implication for health policy/practice/research/medical education:
Cardiac, kidney, and brain disorders are commonly seen in patients with FD. Although ERT is recommended in such patients, due to its high cost, it is not available in all countries and for everyone. Cardiac and aortic surgery can be performed for these patients due to the fibrosis of the intima layer of the created vessels. Patients with FD who are not under treatment with ERT should not be deprived of the benefits of surgery if having indication.

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Introduction

Fabry disease (FD) is an x-linked glycosphingolipid, caused by a defect in α-galactosidase activity and leads to the accumulation of globotriaosylceramide (Gb3) in all tissues of the body, especially skin, cornea, kidney, and heart (1). Vascular changes in patients with FD are usually seen when they reach less than 1% and are more common in men (2). The causes of early death in patients usually include renal insufficiency, cardiovascular events, and cerebrovascular complications (3).

Aortic involvement is seen in 25.5% to 47% of patients with FD (1,4). Aortic regurgitation is not much, and usually mitral valve disorders are more common than aortic disorders (1).

In 1988, Owens et al reported a 46-year-old man with FD who had aortic regurgitation with III/IV and complete atrioventricular (AV) block. They did not replace the aortic valve due to the concern of suture failure (5). Since 2001, enzyme replacement therapy (ERT) became available and recommended for FD. Renal, cardiac, and cerebral complications were clearly reduced (5). The first case of improvement of morphological changes following ERT was reported by Owens et al (5), the first case of aortic valve replacement in FD patients under treatment with ERT was reported by Choi in 2008 (1), and the first case of ascending aortic remodeling after long-term ERT was reported in 2017 by Monney et al (6).

Although ERT is now recommended in patients with FD, it is not available in all countries due to its high cost (7), and not all people can benefit from it.

Due to the concern of suture failure, aortic valve or ascending aortic replacement in patients who are not able to undergo ERT has been reported very little, and patients who require both aortic valve and ascending aortic replacement have been reported very rarely. The introduced patient in this article did not undergo ERT due to the lack of access to ERT and also its high cost, and because he was a kidney transplant candidate, he must have undergone aortic valve and ascending aortic replacement simultaneously (Bentall procedure).

Case Report

A 34-year-old man with diagnosed FD, who suffered from end-stage renal disease following chronic renal failure since 1.5 years ago undergoing dialysis three times a week, became a candidate for kidney transplantation. The following findings were reported in echocardiographic examinations:

Dilatation of aortic root, dilatation of sinotubular junction, mild to moderate aortic insufficiency, mild left ventricular (LV) dilatation, mildly impaired LV systolic function, ejection fraction (EF): 45%, moderate LV hypertrophy (LVH). Therefore, he became a candidate for aortic root replacement surgery.

In the operating room, after anesthesia, the patient underwent prep and drep, and mid-sternotomy was performed. The pericardium was opened, the heart was larger than normal, and LVH was present. After heparin injection, cannulation of aorta and right atrium was placed, and cardiopulmonary bypass (CPB) was established. The aorta was clamped, and the patient was cooled to 32°C. During the injection of cardioplegia, the heart was distended, and after opening the aorta, it was observed that the aortic valve insufficiency was more severe than the cases reported in the echo. Therefore, it was decided to perform the Bentall operation (the aortic valve and ascending aortic replacement simultaneously). Due to the lack of a suitable conduit graft, the aortic STM regent mechanical heart valve St. Jude No. 25 valve on the edge of a No. 28 tube graft was continuously sewn with 0-4 Prolene thread (we created a hand-made Conduit graft). Then, the aortic valve was resected. Buttons of both right and left coronaries were separated; the ascending aorta was resected and removed; Bentall operation was performed (valve and tube graft were sewn to the aortic ring with 0-4 Prolene thread semi-continuously). Then, the left and then the right buttons were sewn to the tube graft with 0-5 Prolene thread separately, and the distal tube graft was anastomosed with 0-2 Prolene thread continuously in one layer to the beginning of the aortic arch. Then, the patient was rewarmed gradually. After de-airing, the aortic cross-clamp was opened, the patient was gradually weaned from CPB, and the surgery was completed. The intensive care unit (ICU) and the post-op period of the patient passed without any incident and the patient was discharged from the hospital. The patient's dialysis continued 3 times a week.

In echocardiography one month after surgery, the patient's EF had increased to 60%. The ascending aortic wall pathology answer was reported as: Aortic wall with foci of myxoid degeneration and no significant in Flammarion. The aortic valve resection pathology answer was reported as; cardiac valvular tissue with fibrosis and myxoid degeneration.

One month after the surgery, the patient developed flutter 2:1 tachycardia, was hospitalized, and was given intravenous amiodarone protocol. The heart rate was then controlled, and he was discharged with oral amiodarone. Four months later, he underwent a kidney transplant, and during the one-year follow-up, he had no special heart or kidney problems.

Discussion

Since FD is a false disease and its clinical phenol type is heterogeneous, the affected patient is normally misdiagnosed, and the diagnosis is usually delayed until complications appear (8). In general, it is predicted that the prevalence of FD is between 1 in 40 000 to 117 000 live male births in the world (7). Although the screening of newborn male infants showed that this disease was more common than thought and about 1 in 3200, its appearance is later, and its incidence is varied (9) and since about 1000

α-galactosidase A mutations can cause it, then its clinical symptoms and manifestations are a spectrum (10). The patients are usually men, and it is seen in women relatively less and at older ages (11), just like what had been introduced in the patient. FD is usually multi-disorder (8,12) and its manifestations are as follows (1,6,12,13).

- Gastrointestinal tract (diarrhea, abdominal pain)
- Skin (angiokeratomas)
- Sensory organs (hearing loss, tinnitus, cornea, vermiculate)
- Lung (obstructive and restrictive respiratory diseases)
- Heart (heart failure, cardiac arrhythmia, left ventricular hypertrophy)
- Central nervous system (stroke)
- Peripheral nervous system (neuropathic pain)
- Kidney (renal insufficiency)

Its symptoms can be early onset of stroke, life threatening arrhythmia, myocardial infarction, cardiac failure, or renal failure (7,8).

In recent years, ERT has become the standard treatment for patients with FD (1), which is recombinant galactoside enzyme replacement. Desnick et al have suggested that therapeutic interventions should be performed as soon as possible to prevent disease manifestations (14). ERT can reverse microvascular changes and lead to improvement of heart function by lipid deposit catabolism (4).

Wilcox et al pointed out that ERT should be started before the occurrence of kidney damages, and it was irreversible if changes in glomeruli occurred (15).

In patients with FD who have not undergone ERT, ascending aortic dilatation is observed in 50% of male patients and 20% of female patients after the age of 40 (2).

Today, patients with FD who have aortic regurgitation are recommended to undergo ERT (1). Patients with FD who have aggressive aortic regurgitation should undergo aortic valve replacement, whether they are under treatment with ERT or not (1).

The Monney and colleagues' study, conducted for 15 years (2000 to 2015) on 15 patients with FD who had undergone ERT for a long-time and had a minimum five-year follow-up, showed that long-term ERT was effective on aortic remodeling and was recommended (6). ERT is usually expensive (approximately €250000/year) (7).

Accordingly Kampmann and colleagues' study on 50 patients with FD reported the prevalence of heart valve diseases as follows (16):

- Aortic valve thickening (25.5%)
- Mitral thickening with mild insufficiency (25.5%)
- Mitral valve prolapse (10.9%)

Recent studies have shown that structural changes, such as increased valve thickness and prolapse, are more in mitral valve than in the aorta (16).

In a study on 30 patients with FD, Linhart et al reported the prevalence of mitral abnormalities in 57% of patients and aortic valve abnormalities in 47% of patients (17). If the risk factors of aortic dilatation, such as bicuspid aortic valve or hypertension, are diagnosed along with FD, in addition to the treatment of the risk factor, prophylactic treatment with beta blocker is also recommended (18). If no risk factor is detected for aortic dissection, surgical treatment of ascending aorta is recommended in 55 mm ≤ (9,18). In the limited research conducted, performing ERT at younger ages and before the development of aortic dilatation has been recommended (6). In the ascending aorta diameter above 45 mm, the possibility of ascending aortic dissection increases significantly (19) if dilatation of the ascending aorta is detected.

Patients with FD should be examined every 1-2 years by echocardiography and every 2-4 years by cardiac magnetic resonance imaging (CMRI) (18). Cardiac examinations in FD are performed by echocardiography and CMRI (13). In the normal population, the rate of increase in the diameter of ascending aorta during 10 years is between 0.9 mm (20) and 1.2 mm (21).

In patients with FD who have not undergone ERT, this rate is 2-3 times higher than in the aortic population (6). However, there is not still sufficient information to know how much ERT is effective in improving remodeling in the long-term. Some studies have reported this effectiveness to be low (22), and especially if fibrosis has occurred in the heart, kidney, or central nervous system, the effectiveness of ERT is reduced (23). Even in male patients who have undergone long-term ERT, annual expansion rate of the proximal ascending aorta is still twice that of the normal population (21). Asymptomatic proximal dilatation of ascending aortic aneurysm in patients with FD at younger ages is more than the rate of aneurysm and aortic dilatation in them, but the rate of dissection has been less reported in these patients, which can be due to two reasons. First, these patients are regularly subjected to echocardiography and annual cardiac examinations, especially in people over 60 years of age, and secondly, the resulting fibrosis in the vascular intima of these patients can itself have a protective effect (6,19) because the major structural changes in the main vessels of patients with FD who have normal blood pressure is an increase in intimal media thickness (25).

In the presented patient, aortic valve and ascending aortic replacement surgery was performed without ERT, which passed without any special complications, and the patient did not suffer from suture failure, which was probably due to fibrosis in the main vessels.

Conclusion

The introduced patient suffering from FD needed aortic valve and ascending aortic surgery and kidney transplant. The candidate for surgery was staged, and due to the unavailability of ERT, the patient did not receive any enzyme therapy. Ascending aortic and aortic valve surgery (Bentall procedure) was performed, and the patient was discharged without any special complications.

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Authors' contribution
Conceptualization: MH.
Methodology: HG.
Validation: ZAA.
Formal analysis: SAM.
Investigation: RT.
Resources: RT.
Data curation: SAM.
Writing—original draft preparation: HG.
Writing—review and editing: ZAA.
Visualization: MH.
Supervision: AA.
Project administration: HG.
Funding acquisition: MH.

Conflicts of interest
The authors declare that they have no competing interests.

Ethical issues
This case report was conducted in accord with the World Medical Association Declaration of Helsinki. The patient has given us a written informed consent for publication as a case report. The authors have observed ethical issues, including no plagiarism, no data fabrication, and no double publication.

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