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Case Report

Aortic Valve Replacement in a Patient with Multiple Myeloma and Cardiac Amyloidosis

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ABSTRACT: Patients suffering from malignant hematological disorders may be at an increased risk when undergoing cardiac surgery. A case of a 67-year-old man with multiple myeloma and cardiac amyloidosis, who underwent aortic valve replacement for severe aortic stenosis, is reported. The patient's postoperative course was uneventful, and he was discharged 16 days after surgery. Currently, two years after surgery, he continues to visit the hospital for dialysis and maintenance therapy without recurrence or exacerbation of multiple myeloma.

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KEYWORDS: multiple myeloma, aortic stenosis, cardiac amyloidosis, aortic valve replacement, cardiac surgery

Background

Multiple myeloma (MM) is a malignant neoplasm of plasma cells that accumulate in bone marrow. MM has a poor prognosis and is unfortunately not considered curable with current approaches. Malignant hematological disorders may increase the patient's risks of coagulation defects, changes in blood viscosity, immunosuppression, and bone marrow insufficiency when undergoing cardiac surgery.[1)] Therefore, indications for cardiovascular surgery in such cases are controversial and must be carefully considered. A case of cardiac surgery in a patient with MM and cardiac amyloidosis is reported.

Case presentation

The patient was a 67-year-old man who had been diagnosed with MM [Internal Staging System: ISS Stage III[2)]], renal amyloidosis, and gastrointestinal amyloidosis while being evaluated for renal failure at another hospital two years earlier. Hemodialysis was then started for the first time, and it has continued to date. The MM was confirmed to show a complete response (CR) by immunofixation electrophoresis after six months of chemotherapy. He then visited our hospital for dialysis, but his blood pressure decreased gradually during dialysis. Electrocardiography demonstrated normal sinus rhythm. Transthoracic echocardiography demonstrated severe aortic stenosis with left ventricular hypertrophy, and the myocardial texture

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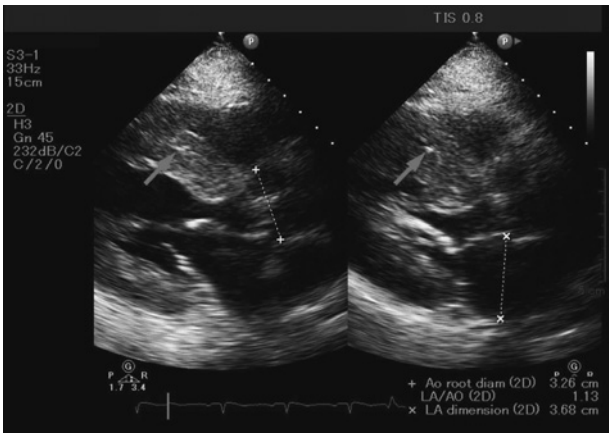

Fig. 1 Transthoracic echocardiography showing thickening and calcification of aortic cusps and "granular sparkling (arrowheads)" in the intraventricular muscle.

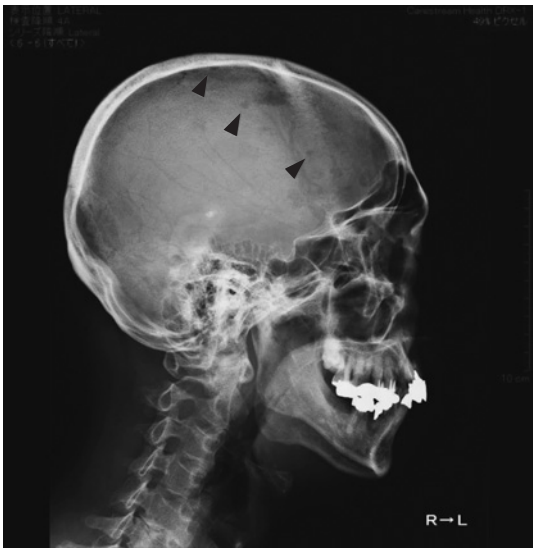

Fig. 2 Skull X-ray showing punched-out lesions (arrowheads).

was described as granular sparkling, which suggested cardiac amyloidosis (Fig. 1). The ejection fraction of the left ventricle was normal. On cardiac catheterization, the mean aortic valve pressure gradient was 60.4 mmHg, and the aortic valve area was 0.84 cm^2. The coronary arteries were intact. Laboratory data included brain natriuretic peptide (BNP) of 254.7 pg/ml. The blood coagulation system and immunoglobulins were normal, with no cytopenia. Punched-out lesions were observed on skull X-ray (Fig. 2).

Because there was a possibility that dialysis would become difficult with severe aortic stenosis, and the MM had fortunately maintained CR, surgery was chosen two years after the diagnosis of MM. Aortic valve replacement (AVR) was performed using a 22-mm Advancing The Standard valve (ATS Medical Inc., Minneapolis, MN) through a median sternotomy with cardiopulmonary bypass. Meticulous hemostasis was done. Additionally, immunoglobulin was administered for 3 days after surgery. Pathological analysis showed amyloid deposition in the myocardium of the left ventricular outflow tract and the cusps of the aortic valve; cardiac amyloidosis was therefore diagnosed (Fig. 3). The patient's postoperative course was uneventful, and he was discharged 16 days after surgery. Currently, two years after surgery, he continues to visit the hospital for dialysis and maintenance therapy without recurrence or exacerbation of multiple myeloma.

Discussion

MM is a bone marrow-based, multifocal plasma cell neoplasm associated with an M-protein in the serum and/or urine.[3] Its incidence in the Japanese population is approximately 3 per 100,000 individuals, with an annual mortality of around 4,000 individuals in Japan. This disease accounts for approximately 1% of all malignancies and approximately 10% of all hematopoietic malignancies, and these figures, along with the incidence and mortality, have been increasing over the years.[4] The International Staging System (ISS) is used to classify the disease in order to estimate prognosis in patients who have symptomatic myeloma with organ disorders such as renal failure, bone lesions, or amyloidosis. The median survival is 62 months in Stage I, 44 months in Stage II, and 29 months in Stage III.[2] Although symptomatic myeloma is not currently considered curable, recent progress in treatment modalities has led to the potential for long-term survival, with the goal of therapy being to prolong survival while maintaining quality of life (QOL).[4] The achievement of CR through chemotherapy with the concomitant use of novel drugs can lead to long-term progression-free survival.[5] When diagnosed, this patient was in Stage III, with gastrointestinal amyloidosis, renal amyloidosis, and renal failure, but CR was achieved approximately 6 months after the start of chemotherapy. The patient was then subsequently diagnosed with severe aortic stenosis at our hospital approximately 2 years after the diagnosis of MM. Comorbid cardiac amyloidosis was suspected on the basis of echocardiography findings, but the MM was in abeyance and remained in remission without any recurrence or relapse. Because the pro-

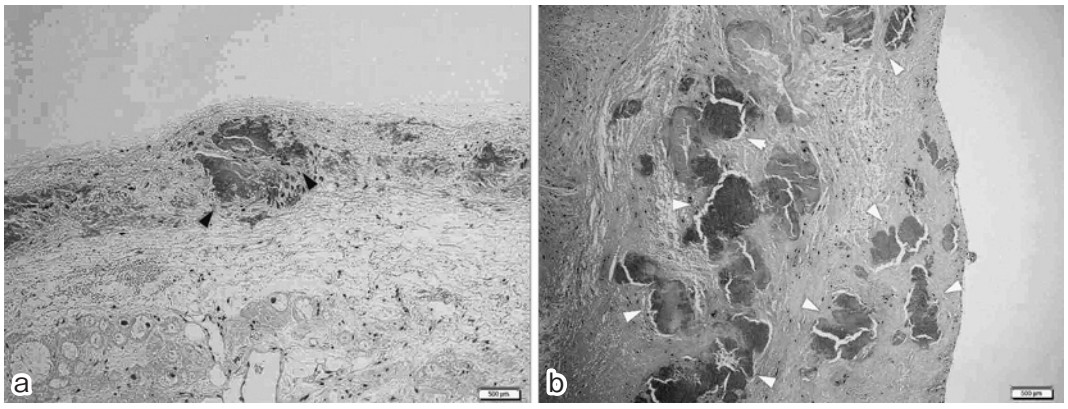

Fig. 3 Pathological findings. Direct fast scarlet (DFS) stain
Amyloid deposition (arrowheads) is seen in the myocardium of the left ventricular outflow tract (×200) [a] and the cusps of the aortic valve (×100) [b].

gressive severe aortic stenosis was compromising QOL and was highly likely to affect the prognosis, a surgical solution was needed.

Heart surgery in patients with comorbid MM has occasionally been reported.[1, 6, 7] Differences in myeloma stage, comorbidities, remission status, and the heart disease for which surgery is performed preclude across-the-board comparison, but cases of a difficult clinical course have also been reported, and the decision as to whether to actually embark on a surgical course requires extensive assessment on a case by case basis. In this case, the patient had achieved CR as a result of chemotherapy following the diagnosis of MM and was on maintenance dialysis for renal amyloidosis-induced renal failure, yet he remained in good general condition.

Cardiac amyloidosis is enigmatic, mimicking typical ischemic heart disease and congestive heart failure. It is believed that the amyloid deposition within the ventricles restricts normal ventricular function and causes abnormal conduction, with up to half of patients developing rapidly progressive congestive heart failure or fatal arrhythmias.[8] Typical echocardiography findings include concentric left ventricular hypertrophy without ventricular dilatation causing left ventricular diastolic dysfunction and a myocardial texture described as granular sparkling.[9, 10] Cardiac magnetic resonance imaging can demonstrate typical circular subendocardial late gadolinium enhancement of the left ventricle, and endomyocardial biopsy is the definitive diagnostic modality.[9, 11] There has also been a report of a case of open-heart surgery in which preoperative undiagnosed cardiac amyloidosis was not found until autopsy following sudden postoperative death,[6] and it appears that cardiac amyloidosis in itself may significantly affect perioperative risk. In this case, cardiac amyloidosis was suspected on the basis of preoperative echocardiography findings, but no myocardial biopsy was performed, and a pathological diagnosis was made on the basis of specimens collected during surgery. Fortunately, the patient's postoperative course was typical of AVR for aortic stenosis, and the patient was allowed to return home on Day 16.

In general, malignant hematological disorders may increase the patient's risk for coagulation defects, changes in blood viscosity, immunosuppression, and bone marrow insufficiency when undergoing cardiac surgery.[1] While their review was not limited to MM, Fecher et al. reported 24 cases of cardiac operations with hematologic malignancies in their institution. In-hospital death was seen in 4.1% of cases, and minor or major complications occurred in 50% of cases. Bleeding and infectious complications were observed most frequently. The 3-year actuarial survival was 83%.[7] Christiansen et al. suggested that it might be better to choose a bioprosthesis for a patient who requires valve replacement to avoid lifelong phenprocoumon therapy, because bleeding complications may occur despite adequate anticoagulation management.[1] In the present case, a mechanical valve was selected, with preference given to avoiding the risk of the degeneration of a bioprosthetic valve rather than the risk of hemorrhagic complications associated with anticoagulant therapy. No perioperative hemorrhagic complications occurred, but careful follow-up will still be required. Although dialysis patients are currently excluded from transcatheter aortic valve implanta-

tion (TAVI) in Japan, it may be an alternative procedure in this kind of case if TAVI for a dialysis patient is approved in the future.

Conclusion

AVR was performed for a patient with severe aortic stenosis, MM, and cardiac amyloidosis. The patient's postoperative course was uneventful for two years.

Because MM generally has a poor prognosis and is unfortunately not considered curable with current approaches, the indications for cardiovascular surgery in myeloma patients are limited. However, in a successfully treated case such as one that has achieved CR, aggressive surgery to maintain organ function may contribute to the improvement of performance status and QOL. Moreover, it could increase the therapeutic options with recurrence or relapse of MM.

Conflicts of interest: The authors have no conflicts of interest to disclose.

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