

Isolated Tricuspid Regurgitation: Initial Manifestation of Cardiac Amyloidosis

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Amyloid deposits in the heart are not exceptional in systemic amyloidosis. The clinical manifestations of cardiac amyloidosis may include restrictive cardiomyopathy, characterized by progressive diastolic and eventually systolic bi-ventricular dysfunction; arrhythmia; and conduction defects. To the best of our knowledge, no previous cases of isolated tricuspid regurgitation as the initial manifestation of cardiac amyloidosis have been reported. We describe a rare case of cardiac amyloidosis that initially presented with severe tricuspid regurgitation in a 42-year-old woman who was successfully treated with tricuspid valve replacement. Unusual surgical findings prompted additional evaluation that established a diagnosis of plasma cell myeloma.

Key words: 1. Tricuspid valve
2. Amyloidosis

CASE REPORT

A 42-year-old woman was referred to Samsung Medical Center with a year-long history of gradually progressive lower-extremity swelling caused by tricuspid regurgitation refractory to medical therapy, including diuretics. Upon clinical evaluation, she was found to have a blood pressure of 120/80 mmHg and a sinus rhythm of 90 beats per minute. Transthoracic echocardiograms showed severe tricuspid valve regurgitation with coaptation failure (Fig. 1A), right atrial (RA) enlargement (42.2 mm in the apical four-chamber view) and normal systolic function of both ventricles. We decided to perform cardiac surgery, and the preoperative evaluation included computed tomographic (CT) coronary angiography and cardiac magnetic resonance imaging (MRI). CT coronary angiography did not demonstrate any abnormal findings in the coronary vessels, but revealed pulmonary edema, ascites,

and RA enlargement. Cardiac MRI showed that the systolic function of both ventricles was normal, as were wall thickness and cavity size. The only abnormal finding was mildly increased septal wall thickness.

We performed tricuspid valve surgery under cardiopulmonary bypass support. The tricuspid valve leaflets were thickened and were yellowish in color (Fig. 2A). Tricuspid valve annular dilatation was observed, and the saline test revealed a central leak caused by inadequate leaflet coaptation. We attempted to repair the tricuspid valve via ring annuloplasty, but this attempt failed due to the stiff tricuspid valve annulus, which was not sufficiently reduced (Fig. 2B). The saline test showed a large amount of residual central leakage. We decided that tricuspid valve replacement was inevitable. After tricuspid valve replacement, the patient recovered without any postoperative complications and her symptoms improved substantially. Thirty days postoperatively, transthoracic echocar-

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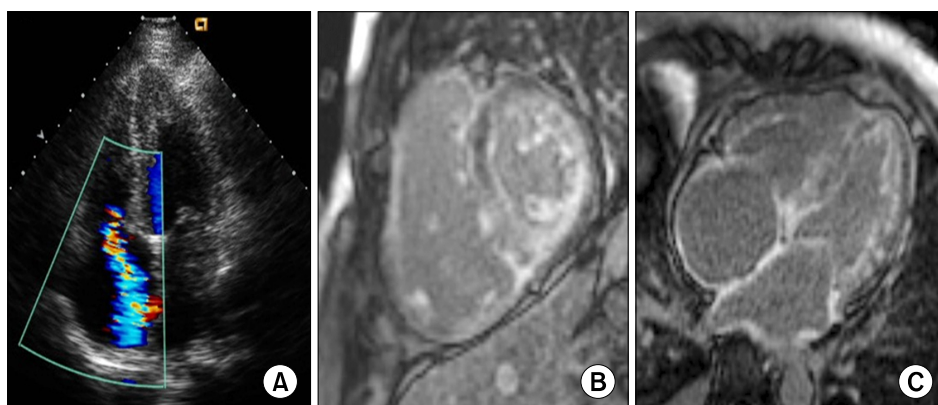


Fig. 1. (A) Preoperative echocardiography showed tricuspid regurgitation with coaptation failure. (B, C) Preoperative cardiovascular magnetic resonance imaging; the (B) short-axis and (C) transverse views showed mildly increased septal wall thickness and diffuse subendocardial enhancement of the bilateral ventricles and atria.

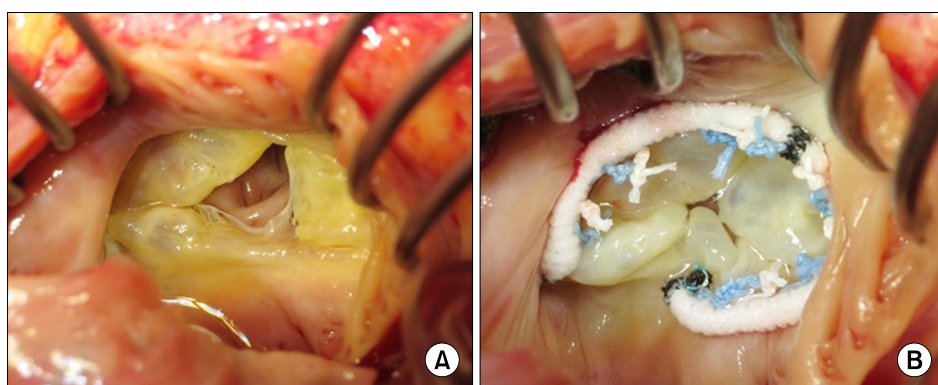


Fig. 2. (A) The tricuspid valve leaflets were observed to have thickened and had developed a yellowish color. (B) After tricuspid ring annuloplasty, the stiff tricuspid valve annulus was not reduced sufficiently.

diagrams showed a well-functioning prosthetic tricuspid valve (mean pressure gradient, 1.86 mmHg), RA enlargement (41 mm in the apical four-chamber view), and normal systolic function in both ventricles.

Due to the unusual surgical findings, we retrospectively reviewed her medical records, laboratory findings, and imaging studies. Her preoperative electrocardiogram (ECG) showed low voltage in the frontal leads. We re-evaluated the cardiac MRI and found diffuse subendocardial enhancement of the ventricles and atria bilaterally, suggesting amyloidosis (Fig. 1B). In light of the MRI findings, an investigation for amyloidosis was conducted. A free light chain (FLC) assay and a cardiac muscle biopsy were performed. The FLC assay indicated an increase in free kappa and lambda light chains and a substantial decrease in the kappa-to-lambda ratio. A hematoxylin and eosin stain of the cardiac muscle revealed interstitial and perimycytic amyloid deposits (Fig. 3A). The Congo red stain showed apple-green birefringence under polarized light, which is a characteristic finding associated with

amyloid deposits. Immunohistochemical stains were positive for primary amyloidosis (Fig. 3B–D). Bone marrow aspiration and biopsy were then performed. Eventually, the patient was diagnosed with plasma cell myeloma. She was discharged from the hospital in stable condition and her plasma cell myeloma was treated with chemotherapeutic agents.

DISCUSSION

Amyloidosis is a clinical disorder caused by the deposition of insoluble abnormal amyloid fibrils in the extracellular and/or intracellular space [1]. Amyloid deposits in the heart are not rare in systemic amyloidosis [2]. Cardiac amyloidosis usually presents as diastolic heart failure, restrictive cardiomyopathy, arrhythmias, and conduction defects. Prominent valvular amyloid deposits causing severe valve regurgitation are uncommon. A few reports have described heart valvular surgery in patients diagnosed with cardiac amyloidosis [3]. To the best of our knowledge, no previous cases have been re-

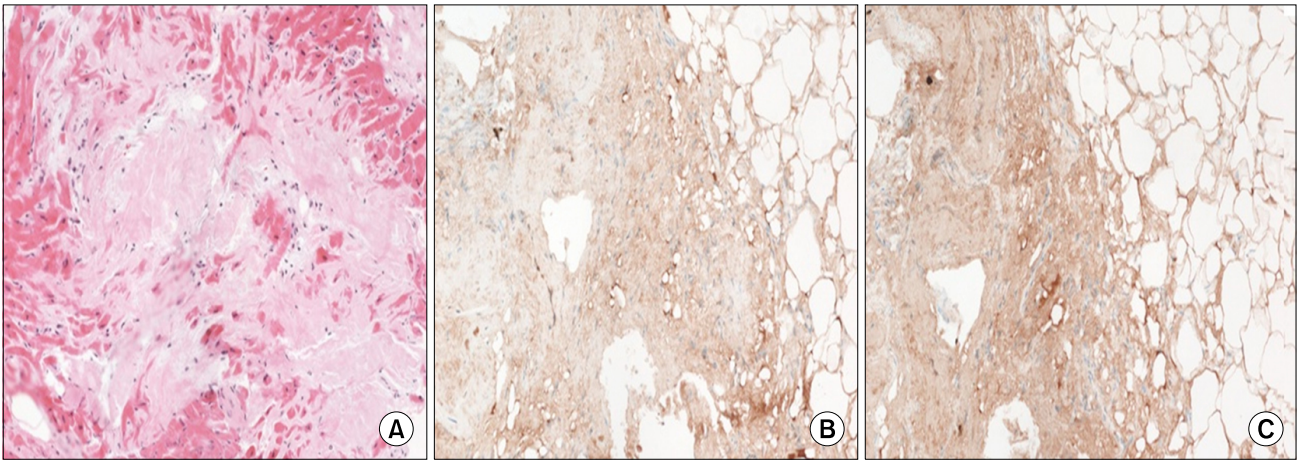


Fig. 3. (A) Myocardial biopsy specimen stained with hematoxylin and eosin. The amyloid stains light pinkish red ($\times 400$). (B) A kappa light chain immunohistochemical stain shows a weakly positive result ($\times 400$). (C) A lambda light chain immunohistochemical stain shows a positive result ($\times 400$).

ported in which the initial manifestation of cardiac amyloidosis was severe tricuspid regurgitation, which was treated with tricuspid valve replacement.

Amyloidosis is classified based on the type of fibril protein, including amyloid light-chain (AL) amyloidosis (involving amyloid fibrils that are produced from clonal light chains), amyloid A (AA) amyloidosis (involving amyloid fibrils that are produced from serum AA), transthyretin amyloidosis, and other subtypes. AL amyloidosis usually involves more than one organ and commonly involves the heart. Untreated patients with cardiac involvement tend to have a rapid progression of the disease. Since AL amyloidosis is a life-threatening disease, it is very important to diagnosis AL cardiac amyloidosis as early as possible [4].

Amyloidosis is a disease with considerable clinical heterogeneity and non-specific clinical manifestations. Therefore, clinicians might be misled or completely misdiagnose a patient without a high level of clinical suspicion [5]. In order to avoid delayed diagnoses, medical histories, symptoms, laboratory tests, and ECG data should be reviewed conscientiously. The most common symptoms include dyspnea, swelling, and chest discomfort. Patients may have systemic symptoms including tingling and numbness, carpal tunnel syndrome, dizziness on standing, and foamy urine [6]. In a significant number of patients, low-voltage QRS findings occur on the ECGs. These findings are non-specific, but are key elements that

may trigger diagnostic suspicion of cardiac amyloidosis [2]. In this case, the patient's initial symptoms were progressive lower extremity swelling and an ECG that showed low voltage in the frontal leads.

Echocardiography plays an important role in the diagnosis of cardiac amyloidosis. The echocardiographic features of cardiac amyloidosis are thickening of the left ventricular wall, interatrial septum, and valves; a speckled or granular myocardial appearance; enlargement of both atria; and diastolic dysfunction. However, it is important to recognize that these characteristic features are often present only in the later stages of the course of the disease [6]. Recently, cardiovascular MRI with a late gadolinium enhancement sequence has begun to play a role in the diagnosis of cardiac amyloidosis. Cardiovascular MRI provides not only functional and morphological information, but also detailed tissue characterization. Myocardial nulling (an inversion recovery pulse sequence) and diffuse enhancement in the delayed enhancement sequence are observed [7]. As in our case, cardiac MRI may assist in the early diagnosis of cardiac amyloidosis.

Cardiac involvement is a major determinant of treatment options and the prognosis. Approximately half of patients with AL amyloidosis expire due to cardiac involvement. However, cardiac amyloidosis patients who already have suffered heart failure have very poor prognoses [4] because the only therapeutic surgical option is heart transplantation [3].

Therefore, the early detection of cardiac amyloidosis and proper treatment of the underlying cause of amyloidosis are critical to ensure an optimal outcome.

Cardiac amyloidosis is a rare entity, especially in cases presenting with isolated tricuspid regurgitation, and requires a high level of diagnostic suspicion. Therefore, we contribute this case report to the growing literature on cardiac amyloidosis, with the goal of sharing our experience in the successful management of cardiac amyloidosis through tricuspid valve replacement and the subsequent use of chemotherapeutic agents to treat underlying plasma cell myeloma.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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