Case Reports

Interventricular Septal Rupture in a 62-Year-Old Man With Familial Amyloid Polyneuropathy

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Cardiac involvement in familial amyloid polyneuropathy consists of arrhythmias, conduction disturbances, and heart failure. To our knowledge, heart rupture has never been described in association with this condition.

We report the case of a 62-year-old man with a 6-year history of refractory familial amyloid polyneuropathy who underwent liver transplantation. The operation was complicated by severe hypotension because the neuropathy involved the autonomic system. Perioperatively, the patient had a myocardial infarction, and during the next 10 days, a complete interventricular septal rupture developed, resulting in a systemic-to-pulmonary shunt. Coronary angiographic findings were normal. However, the shunt caused unstable hemodynamics, resulting in cardiogenic shock. An attempt to close the rupture percutaneously failed. The patient underwent successful heart transplantation 50 days later.

Macroscopic examination of the explanted heart showed thickening of both ventricles, septal rupture, and a gray scar in the interventricular septum around the cavity. Histopathologic examination revealed intramural amyloid angiopathy.

Our case shows that heart rupture can occur in patients with familial amyloid polyneuropathy who have no history of obstructive coronary artery disease, perhaps as a result of tissue fragility caused by amyloid angiopathy. Therefore, autonomic disturbances should be regarded with concern and promptly treated in the perioperative period. ***(Tex Heart Inst J 2020;47(4):302-5)***

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Familial amyloid polyneuropathy (FAP), also called transthyretin (TTR)-related hereditary amyloidosis, is a form of systemic amyloidosis caused by mutant amyloidogenic TTR, a glycoprotein produced mainly by the liver. Misfolded monomers and dimers of normally tetrameric TTRs are deposited in the nervous system, heart, and other organs. According to the underlying mutation, the clinical phenotype can be predominantly neuropathic, cardiac, or mixed.[1]

Cardiac involvement in FAP generally consists of arrhythmias or conduction disturbances; heart failure in FAP is not a common finding.[1] Heart rupture, a rare life-threatening condition, has been described in a few patients with cardiac amyloid light-chain (AL) amyloidosis.[2,3] To our knowledge, however, no cases of heart rupture have been reported in patients with FAP until now, in one of our patients who underwent liver transplantation.

Case Report

A 62-year-old man with a 6-year history of symptomatic FAP underwent liver transplantation because of progressively worsening neuropathy (upper and lower limb neuropathy and orthostatic hypotension). His heart was also affected by the FAP, so he had undergone several cardiac evaluations before the operation. An electrocardiogram recorded low QRS voltage in the peripheral leads. A Doppler transthoracic echocardiogram (TTE) showed normal left ventricular (LV) volume and ejection fraction, but increased mass and concentric thickness (interventricular septum, 17 mm). Magnetic resonance images confirmed LV concentric thickening, in addition to a thickened right ventricular (RV) free wall and interatrial septum. Global subendocardial late gadolinium enhancement was observed in both ventricles; no myocardial perfusion defects were noted.

After anesthesia was induced, vasodilatory shock developed, necessitating high doses of norepinephrine and epinephrine. Continuous electrocardiographic monitoring showed no abnormalities in the QRS or ST segment, and intraoperative transesophageal echocardiograms showed preserved LV function with no wall-motion abnormalities.

Two hours after completion of the liver transplant procedure, an electrocardiogram showed a right bundle branch block and a left anterior fascicular block. An electrocardiogram 12 hours later showed narrowing with a QS wave in lead V_1 and a reduction of the R wave in the precordial leads without repolarization abnormalities. A TTE showed reduced biventricular systolic function (LV ejection fraction, 40%; RV fractional area change, 28%) caused by diffuse hypokinesia. Cardiac markers were elevated, peaking on day 1 (creatine kinase-MB, 401 ng/mL; troponin T, >10.0 ng/L). Cardiac catheterization showed normal epicardial coronary arteries.

On day 5, a new harsh holosystolic murmur developed. A TTE revealed a fissured interventricular septum with a new cavity that opened into the LV (Fig. 1); blood flowed back and forth between the two, as shown on Doppler TTEs. A residual thin wall separated the RV from the cavity. The patient was hemodynamically stable, so we opted to continue closely monitoring him.

On day 12, cardiogenic shock developed. Doppler TTEs showed a complete rupture of the septum between the cavity and the RV, which caused a systemic-to-pulmonary shunt. During cardiac catheterization, a fluoroscopic left ventriculogram showed normal epicardial coronary arteries and indicated that the shunt was clinically significant (Qp/Qs, 2.4) (Fig. 2). A 25-mm fenestrated Amplatzer septal occluder was placed through the opening between the LV and the cavity. However, one hour later, the device became dislodged and was trapped inside the cavity, with no further embolization.

The patient remained dependent on inotropic agents. Myocardial fragility made surgical repair of the defect impractical. Heart transplantation was advised and was performed successfully on day 62.

The explanted heart weighed 500 g and showed LV and RV thickening, an intraseptal cavity (20 × 5 mm) communicating with both ventricles, and a gray scar in the interventricular septum around the cavity (Fig. 3).

Histopathologic examination of the myocardium showed areas of fibrosis with hemosiderin deposits, suggesting postischemic changes (Fig. 4). Congo red staining revealed large amyloid deposits in the myocardium (Fig. 5), epicardium (both in adipose tissue and vessel walls), and intramyocardial vessels. Immunostaining for TTR was widely positive for amyloid deposits (Fig. 6).

At the patient's most recent follow-up, 2 years after the index event, his condition was satisfactory after steady improvement.

Discussion

A few cases of heart rupture have been reported in patients with AL amyloidosis and obstructed epicardial coronary arteries.[2,3] Myocardial ischemia due to intramural vessel amyloid deposits has also been described.[4] Amyloid angiopathy can also cause spontaneous bleeding or spontaneous hematoma when FAP or AL amyloidosis is present,[5] although only one case of atrial intramural hematoma and 3 cases of pericardial hematoma have been reported.[6,7] There appear to be no reports of heart rupture in individuals with FAP.

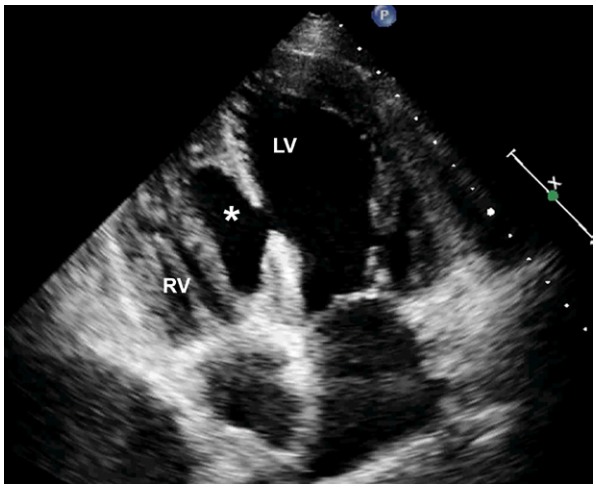

Fig. 1 *Transthoracic echocardiogram (B-mode, 4-chamber view) shows the intraseptal cavity (asterisk) and the opening into the left ventricle (LV).*

RV = right ventricle

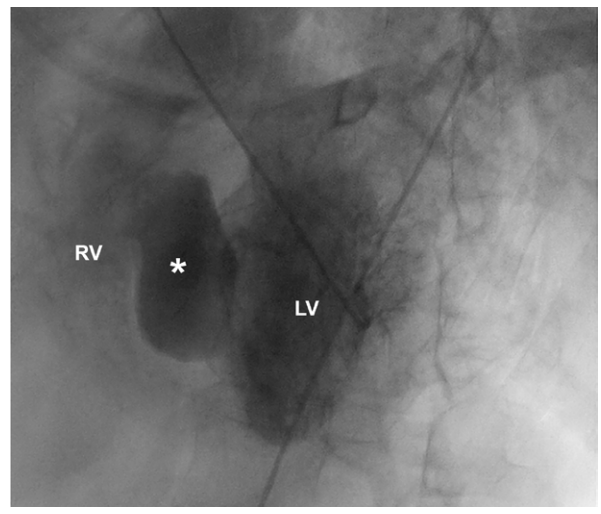

Fig. 2 *Fluoroscopic left ventriculogram shows the intraseptal cavity (asterisk) and the left-to-right shunt.*

LV = left ventricle; RV = right ventricle

Supplemental motion image is available for Figure 2.

As suggested by electrocardiographic, laboratory, angiographic, and pathologic findings, our patient had a perioperative septal myocardial infarction caused by severe hypotension, despite having no obstructive coronary artery disease. We hypothesize that septal rupture resulted from an intraventricular dissecting hematoma (IDH), from complications of myocardial infarction, or both. These 2 conditions are associated: IDH is caused mainly by myocardial infarction.[8]

The underlying mechanisms of heart rupture in both IDH and myocardial infarction are considered to be rupture of injured microvasculature into the interstitium, embrittlement of the infarcted myocardium, and increased coronary capillary perfusion pressure due to microvascular obstruction.[9,10] Increased vascular fragility in amyloidosis is presumed to be secondary to vascular infiltration with amyloid.

We surmise that severe perioperative hypotension caused the myocardial ischemia in our patient, as previously described in patients with AL amyloidosis.[3] Circulatory instability with severe hypotension related to autonomic neuropathy frequently causes complications and increases the risk of perioperative death after liver transplantation in patients with FAP and increases perioperative mortality risk.[11] These patients are sensitive to decreases in preload induced by common anesthetics and surgical factors. Safety during anesthesia can be ensured by strictly monitoring arterial pressures and promptly infusing a vasopressor to support circulation in case of severe hypotension. Nonetheless, cases of intractable hypotension despite early circulatory support have been described.[12]

In conclusion, heart rupture can occur in patients who have FAP—even in the absence of obstructive epicardial

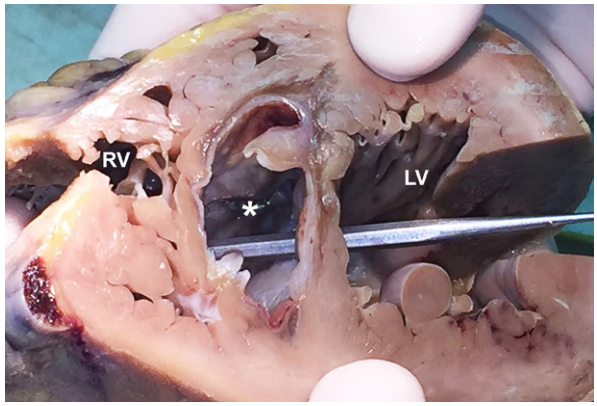

Fig. 3 *Gross examination of the explanted heart shows complete septal rupture, confirmed by inserting a probe through the openings on the RV and LV sides of the intraseptal cavity (asterisk).*

LV = left ventricle; RV = right ventricle

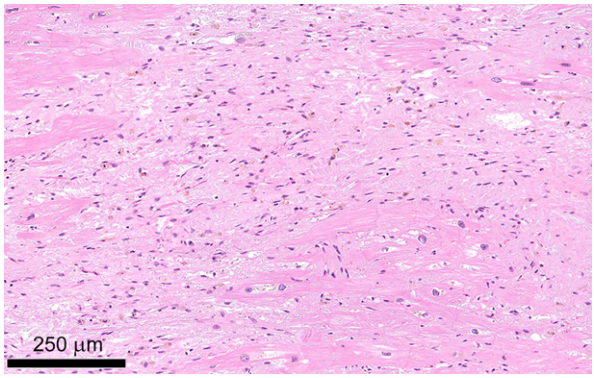

Fig. 4 *Photomicrograph of a myocardial specimen shows fibrosis and hemosiderin deposits, suggesting postischemic changes (H & E, orig. ×100).*

Fig. 5 *Photomicrograph of a myocardial specimen shows green birefringence in amyloid deposits within the myocardium (Congo red stain, orig. ×200).*

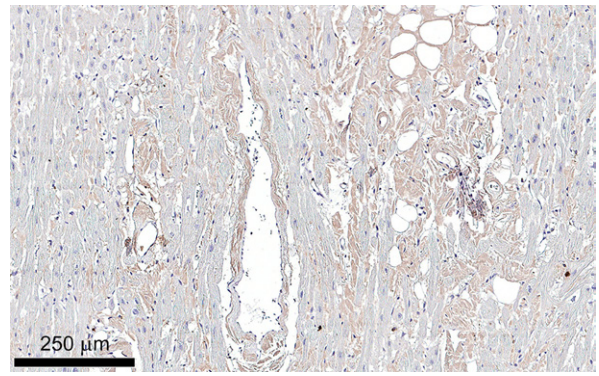

Fig. 6 *Photomicrograph of a vessel wall specimen immunostained for transthyretin (antibodies provided by amYmed) shows widespread amyloid deposits (orig. ×100).*

coronary artery disease. Amyloid angiopathy can cause fragility in affected tissues, thus increasing their vulnerability to injury. Autonomic disturbances during anesthesia in patients with FAP are life-threatening and should be promptly treated in the perioperative period.

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