Cardiac Amyloidosis

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Abstract

Amyloidosis is a multisystem disorder. Cardiac involvement causes restrictive cardiomyopathy. A 65-year-old gentleman presented with worsening shortness of breath. Investigations including echo and cardiac MRI showed cardiomyopathy consistent with amyloidosis. Cardiac involvement is related to poor prognosis and increased mortality.

Keywords: Cardiac Amyloidosis

Case Report

A 65-year-old gentleman was admitted with worsening SOB and ongoing chest discomfort for the last 1 year. He presented with a 2-week history of worsening chest tightness on minimal exertion and had a recent episode of SOB at rest. There were associated pressure-like symptoms for weeks in the chest, which radiated to the right arm. Exercise tolerance was reduced to around 50 yards.

A coronary angiogram performed 2 years ago for similar symptoms showed 50% stenosis RCA and was managed medically.

Past medical history included hypercholesterolemia and ischaemic heart disease. He was an ex-smoker with a 10 pack year smoking history. He drank alcohol occasionally. The examination was unremarkable. Trop I was mildly raised 232 and 257. Electrocardiography showed normal sinus rhythm and left bundle branch block, low voltage QRS complexes, and old posterior Q waves. Echocardiography was performed which showed mild left ventricular hypertrophy, significant diastolic dysfunction and trivial regurgitation of all valves.

A repeat coronary angiogram showed moderate ostial disease in small vessels, and mild mid-vessel disease with muscle bridging in mid to distal segment.

He subsequently had a cardiac MRI, which showed significant left and right ventricular wall thickening (up to 17 and 19mm respectively) with moderate to severe systolic dysfunction on both sides. The delayed images following the administration of gadolinium were consistent with cardiomyopathy.

For protein electrophoresis, Lambda-free light chain bands were present in the serum and the urine. Urinary protein concentration was high with a value of 0.12(0.01g/l). Lambda was high to 1020(5.70-26.30 mg/l). Skeletal survey was negative and ultrasound abdomen showed no visceromegaly.

Discussion

Amyloidosis refers to a collection of conditions in which abnormal protein folding results in insoluble fibril deposition in tissues. The different types of amyloidosis include light-chain, senile systemic (wild-type transthyretin), hereditary (mutant transthyretin), and secondary (AA) diseases.

Cardiac involvement is most common and most severe in AL amyloidosis but can occur in all types of systemic amyloidosis (5). Cardiac amyloidosis presents as a restrictive cardiomyopathy characterized by progressive diastolic and subsequently systolic biventricular dysfunction and arrhythmia (6). Myocardial ischemia can result from amyloid deposits within the microvasculature (7-8).

Syncope is common and a poor prognostic sign (9). It is typically exertional or postprandial as part of restrictive cardiomyopathy, sensitivity to intravascular fluid depletion from loop diuretics combined with autonomic neuropathy, or conduction tissue involvement (atrioventricular or Sinoatrial nodes) or ventricular arrhythmia (10-12). Other symptoms are fatigue, dizziness, dyspnoea, angina, pulmonary oedema, cardiac tamponade, pulmonary hypertension and death.

Laboratory investigations include NT-proBNP, serum and urine protein electrophoresis, serum and urine immunofixation, urine for proteinuria, Transthyretin protein (TTR) and genetic studies.

Echocardiogram shows increased muscle wall thickness, biventricular dysfunction and granular or sparkling appearance of the myocardium. A low voltage on the electrocardiography and increased septal and posterior left ventricle wall thickness on the echocardiogram are highly specific for cardiac amyloidosis in the setting of biopsy-proven systemic amyloidosis. Other electrocardiography features include conduction defects and arrhythmias. Atrial fibrillation and flutter are most common arrhythmias
Late gadolinium-enhanced (LGE) cardiovascular magnetic resonance imaging (CMRI) is useful in the evaluation of cardiac amyloidosis. Amyloid infiltration leads to the expansion of extracellular space that retains gadolinium, resulting in a signal enhancement in comparison with normal myocardium, which can be detected in the late washout phase during delayed enhanced imaging. Global subendocardial enhancement is the most common pattern (13-17).

Endomyocardial biopsy has been considered to be the gold standard for demonstrating cardiac amyloid deposition(18). Amyloid deposits show characteristic apple-green birefringence under polarized light when stained with Congo red. It also differentiates with other infiltrative causes (19-21).

Treatment is generally supportive with diuretics, beta-blockers and ACE inhibitors. Calcium channel blockers and digoxin are avoided due to risk of toxicity (22-24).

Pacemakers or implantable cardioverter defibrillators may not prevent sudden cardiac death due to electromechanical dissociation (25). Biventricular pacing may be beneficial as a pacing option to avoid decompensation of the stiffened ventricle as a result of induced dyssynchrony from right ventricular pacing (26).

Chemotherapy has been used in AL amyloidosis with a response rate of 60 per cent. Cardiac transplantation is not a good choice in patients with cardiac involvement because of increased mortality (27-33).

A 2016 Mayo Clinic study showed a median overall survival of 3.5 years in 23 patients (median age, 53 years) with AL who received orthotopic heart transplantation (34).

Seven patients who achieved a complete hematologic response to either chemotherapy or autologous stem cell transplantation had a median survival of 10.8 years (34).

Conclusion

In summary, AL amyloidosis is a multisystem heterogeneous disorder with multiorgan involvement. Cardiac involvement is related to poor outcomes. Early intervention with symptomatic treatment and chemotherapy can be beneficial. A cardiac transplant is not a good choice due to increased mortality.

Disclosure:
The authors report no conflicts of interest in this work

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