Cardiac Amyloidosis – Two Case Reports with Variable Presentation

Bishav Mohan, Shibba Takkar Chhabra, Rohit Tandon, Naveen K Gupta, Naved Aslam, Naresh K Sood, Gurpreet S Wander

Abstract

Many cases of progressive heart failure due to cardiac amyloidosis remain undiagnosed due to the rarity and lack of suspicion on part of physician. Treatment options are limited and patients are also poor responders in later stages. Hence, early diagnosis by recognition of syndromic presentation and diagnostic modalities is helpful in retarding the disease process.

Introduction

Amyloidosis is a heterogeneous group of systemic disorders, which result due to extracellular deposition of an insoluble, amorphous, eosinophilic, substance known as amyloid. Due to the rarity and lack of suspicion on part of physician many cases of progressive heart failure due to cardiac amyloidosis remain undiagnosed. Treatment options are limited and patients are also poor responders in later stages. Hence, early diagnosis by recognition of syndromic presentation and diagnostic modalities is helpful in retarding the disease process. Here in we present two cases of cardiac amyloidosis with variable presentation.

Case 1

The patient, 60 years old male, presented with progressively worsening dyspnoea and easy fatigability for the last six weeks. On examination, the patient was in congestive cardiac failure with raised Jugular venous pressure (prominent X, Y descent) and prominent LV S4. He had periorbital ecchymosis and macular patches (Figures 1 and 2). The haemogram was normal and ESR was 25 mm/hr. He had mild renal insufficiency with blood urea of 55 mg/dl, Creatinine 1.6 mg/dl, Sodium 139 mmol/L, Potassium 3.9 mmol/L. The ANA was negative and thyroid profile was normal. Urine routine examination showed no proteinuria and RBC’s.

The working diagnosis was hence a case of congestive cardiac failure with underlying restrictive cardiomyopathy. Abdominal fat aspiration was negative for congo red stain. Endoscopic duodenal biopsy showed deposition of acellular eosinophilic material in vessel wall of submucosal blood vessels positive for congo red and methyl violet stain which was consistent with amyloidosis.

Patient was discharged on oral thalidomide. After 4 weeks patient developed slurring of speech and was readmitted with acute left MCA territory infarct. The antiplatelets and anticoagulants were started and later withheld due to upper GI bleed. Patient improved with conservative treatment and was discharged without any neurological deficit.

Case 2

The patient, 36 yrs female on ATT for four months presented with low grade fever, significant loss of appetite and weight and proximal muscle weakness for the last six months. On examination she was an undernourished female with peri-orbital macular spots and thick tongue with reduced opening of oral cavity. She had tachycardia and raised JVP with prominent V waves. Cardiac examination revealed grade II parasternal heave and LV S4. Bilateral basal crepits were present. Haemogram, renal functions, thyroid profile and anti-nuclear antigen (ANA) were normal.
Electrocardiogram revealed low voltage limb leads with Q waves in lead V1-V4. The transthoracic echocardiography demonstrated gross bi-ventricular hypertrophy, bi-atrial enlargement, inter atrial septum hypertrophy (Figure 5) and moderate MR with grade III/IV TR (PASP= 55 mm Hg). Pulse and tissue Doppler confirmed the restrictive pattern of filling (Figure 6). Rectal biopsy was positive for amyloidosis.

**Discussion**

Cardiac amyloidosis describes clinically significant involvement of the heart by amyloid deposition, which may or may not be associated with involvement of other organs. Different forms of cardiac amyloidosis are recognized (Table 1). Clinical evaluation of suspected cardiac AL amyloid includes screening for syncope, dizziness, postural hypotension, easy bruising, painful sensory polyneuropathy (10% to 20% of patients) and carpal tunnel syndrome (20%), as well as major visceral involvement of the liver and kidneys. The presence of both peri-orbital purpura and macroGLOSSIA has low sensitivity (10 – 20%) but is highly specific for the presence of disease as described above3-5. Our first case had prominent periorbital ecchymosis and macular patches and 2nd case had peri-orbital macular spots and thick tongue with reduced opening of oral cavity.
Although no single non-invasive test or abnormality is pathognomonic of cardiac amyloid, case control studies indicate that echocardiographic evidence of left ventricular wall thickening, increased echogenicity and biastral enlargement, in conjunction with reduced electrocardiographic voltage (presence of low QRS voltage amplitude 0.5 mV in all precordial leads) is strongly suggestive of cardiac amyloidosis; sensitivity (72% to 79%) and specificity (91% to 100%) have been reported for this combination. A thickened interatrial septum for amyloid in the later stages of the disease, has 100% specificity. The most common echocardiographic feature is thickening of the LV wall, particularly in the absence of hypertension. This is often referred to incorrectly as “hypertrophy” because the pathological process is infiltration, not myocyte hypertrophy. This combination is quite useful in guiding the physician for early tissue biopsy in such cases. Both our patients had characteristic ECG and echocardiographic features.

Despite a plethora of information derived from non invasive tests, tissue biopsy remains definitive. Tissue diagnosis with abdominal fat, rectum, gingival, bone marrow, liver & kidney biopsy is 70-80% sensitive and with endomyocardial biopsy is 100% sensitive. Endoscopic duodenal and rectal biopsy were confirmatory in our case reports.

In AL amyloidosis, chemotherapy may reverse the disease with stabilization and improvement of symptoms. Thus early diagnosis is critical because patients with advanced disease are usually too ill for intensive chemotherapy. Chemotherapy with alkylating agents in combination with allogeneic bone marrow transplantation gives 70-80% cure rates. In selected patients cardiac transplantation is advocated.

Management of heart failure is challenging as these patients are poor responders due to various factors. This includes therapy for cardiac symptoms which involves decongestion of heart by judicious of diuretics, though with modified and cautious doses as risk of orthostatic hypotension is high. Usually larger doses of diuretics are required but optimal fluid balance is difficult to achieve as these patients are preload dependent. There is no data on the effectiveness of β-blockade on survival in amyloidosis, but the use of β-blockers may be limited because of refractory heart failure or disease-related hypotension.

Calcium channel blockers are contraindicated with reports suggestive of clinical deterioration more because of their negative inotropic effect. Digoxin is also of limited value as it binds to amyloid fibrils and toxicity tends to be enhanced due to its elevated levels. Increased incidence of sudden deaths have been reported post digoxin therapy in these patients. Angiotensin converting enzyme inhibitors too have limited role and have to be used cautiously in associated renal disease.

The value of routine anticoagulation in patients with severe heart failure of any cause is uncertain. However, unless major contraindications exist, the presence of atrial fibrillation in AL amyloidosis is a very strong indication for warfarin anticoagulation because of a very high rate of thromboembolic events. In severe cardiac amyloidosis, the atrium is infiltrated, and dysfunctional and atrial thrombi may be present even during sinus rhythm. It is therefore prudent to anticoagulate patients with AL amyloidosis even if they are in sinus rhythm (as in our first case) if there is a small transmitral A wave seen on transthoracic echocardiography (<20 cm/s).

### Table 1: Different forms of cardiac amyloidosis

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Precursor of amyloid fibril</th>
<th>Organ involvement</th>
<th>Treatment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>Ig light chain</td>
<td>Renal, cardiac, liver, GIT, autonomic nervous system</td>
<td>Chemotherapy</td>
<td>Related to plasma dyscrasias, predominantly multiple myeloma</td>
</tr>
<tr>
<td>ATTR(familial)</td>
<td>Mutant transthyretin</td>
<td>Heart, peripheral/autonomic nervous system</td>
<td>Liver transplantation</td>
<td>-</td>
</tr>
<tr>
<td>Senile cardiac amyloidosis</td>
<td>Wild type transthyretin</td>
<td>Heart</td>
<td>Supportive</td>
<td>Almost exclusively seen in elderly males</td>
</tr>
<tr>
<td>AA</td>
<td>Serum amyloid A</td>
<td>Kidney, liver, heart very rare</td>
<td>Treatment of underlying inflammatory condition</td>
<td>-</td>
</tr>
<tr>
<td>AANP</td>
<td>Atrial natriuretic peptide</td>
<td>Localized to atrium</td>
<td>None required</td>
<td>Common, may increase risk of atrial fibrillation</td>
</tr>
</tbody>
</table>

In summary, cardiac amyloidosis, although uncommon, is characterized by a typical appearance on echocardiography, the recognition of which should alert the astute clinician to the probable diagnosis. It is critical to recognize that several forms of amyloidosis may cause cardiomyopathy and that treatment and prognosis of these individual cardiomyopathies differ greatly from each other.

In AL amyloidosis, chemotherapy may arrest or possibly reverse the disease, with resultant stabilization or improvement of symptoms. Thus, early diagnosis is critical because patients with advanced disease are usually too ill for intensive chemotherapy. Recognition of non-AL cardiac amyloidosis is important to avoid unnecessary chemotherapy, to screen family members, and in the near future, to provide new medications that will stabilize the amyloidogenic substance in the blood and prevent the onset of progression of this important and under diagnosed condition.

### References


