An Unusual Heart Failure
Cardiac Amyloidosis Due to Light-Chain Myeloma

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A 53-year-old white woman presented to the emergency department with severe dyspnea. She reported progressively worsening dyspnea during the previous 3 months. The patient had no prior history of any cardiovascular disease or relevant family history. The chest radiograph showed a typical picture of congestive heart failure with cardiomegaly, vascular redistribution, and bilateral pleural effusions (Figure, A). The ECG (Figure, B) showed low-voltage QRS complexes in the limb leads and poor R-wave progression in the chest leads. Such characteristics were particularly evident when compared with a previous ECG executed 4 years before (Figure, C). Holter monitoring did not reveal any significant arrhythmias. Initial laboratory analysis detected a marked increase of natriuretic peptide levels (N-terminal pro-brain natriuretic peptide 4556 pg/mL, with normal levels ≈270 pg/mL) and mild hypogammaglobulinemia; the other parameters, including blood cell count, renal and liver function, and cardiac-specific troponin concentration, were normal.

Echocardiography (Figure, D and E, and Movies I through III in the online-only Data Supplement) revealed increased ventricular mass with thickening of the ventricular walls and granular sparkling pattern of the myocardium (black arrows). Remarkably, the discordance between the increase in ventricular wall thickness and the reduced voltages on ECG, as seen in this case, is strongly suggestive of an infiltrative cardiomyopathy, especially amyloidosis, and the granular sparkling refraction of myocardium is considered pathognomonic for such disease.1,2 Cardiac magnetic resonance imaging (Figure, F through I) confirmed wall thickness, estimated a mild reduction of left ventricular ejection fraction (48.6%), and showed diffuse late subendocardial tissue enhancement by gadolinium, especially at the posteriorlateral wall (white arrows), consistent with myocardial amyloid deposits.1 Late gadolinium enhancement is common in cardiac amyloidosis and detects interstitial expansion from amyloid deposition. Global transmural or subendocardial late gadolinium enhancement is most common, but focal patchy late gadolinium enhancement has also been observed.3

Although no serum monoclonal immunoglobulin band was detected, both Bence-Jones proteinuria (45 mg/L) and an excess of free λ chains (1067 mg/L) with an abnormal κ-λ ratio were observed, suggesting the presence of plasma-cell dyscrasia. Finally, Congo red–stained positive abdominal fat biopsy and bone marrow biopsy defined the diagnosis of light-chain smoldering myeloma with systemic acquired monoclonal immunoglobulin light-chain amyloidosis involving the heart. The patient was referred to a hematology institute and to a specialist amyloidosis center in Italy. Finally, she began therapy with bortezomib, melphalan, and dexamethasone for amyloidosis and the underlying myeloma.

Amyloidosis is caused by extracellular deposition of abnormal insoluble fibrils that are derived from misfolded proteins from various origins. Amyloidosis in turn is classified by the protein precursor as primary (due to immunoglobulin light chain), secondary-reactive (due to serum amyloid A), hereditary-familial (due to transthyretin, apolipoprotein AI, or apolipoprotein AII), acquired-senile (due to transthyretin), isolated atrial (due to atrial natriuretic peptide), and hemodialysis-associated (due to β2-microglobulin) amyloidosis (for a review, see References 1 and 2). Amyloid deposition can infiltrate multiple organs, leading to extremely variable clinical manifestations (eg, cardiac involvement → heart failure and arrhythmias; renal involvement → proteinuria and nephrotic syndrome; liver involvement → hepatomegaly; neurological involvement → peripheral neuropathy, autonomic dysfunction, and carpal tunnel syndrome; soft tissue involvement → macroglossia), so that the diagnosis of amyloidosis remains a challenge, as well as because of the relative rarity of this condition. On the other hand, as stated in a clinical aphorism, the heart of the matter is that amyloidosis often attacks the heart.4 However, although several types of amyloid infiltrate the heart, only primary, hereditary, and senile amyloidosis commonly cause clinically significant disease.3 Primary light-chain amyloidosis is the most frequent type, affecting 10 patients per million persons per year and including 10% to 15% of patients with myeloma or Waldenström macroglobulinemia.4 Moreover, in nearly 50% of cases, such amyloidosis is complicated by a serious cardiac involvement characterized by high clinical morbidity and a very poor prognosis.2

In summary, cardiac amyloidosis is a rare disorder in which the diagnosis requires specific clinical suspicion,
especially in the case of heart failure without history of traditional cardiovascular risk factors. Light-chain myeloma, with its characteristic hypogammaglobulinemia, absence of abnormal band on serum electrophoresis, and light-chain proteinuria, may be a cause of cardiac amyloidosis.

Disclosures

None.

References

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