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Case Report Open Access

A Typical Case of a Multiple Myeloma Revealed by Cardiac Amyloidosis

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Abstract

We report the case of a man of 72 years, without specific medical history, presenting congestive heart failure and multiple lymphadenopathies. Electrocardiogram and TTE were oriented towards diagnosing cardiac amyloidosis, showing pericardial effusion of great abundance and restrictive cardiomyopathy with a low voltage at the electrocardiogram. The cervical CT had objectified thrombosis of the internal jugular vein right. Lymph node biopsies had confirmed the diagnosis of multiple myeloma. The patient died before he started systemic chemotherapy. A cardiac screening in all patients with multiple myeloma should include at least an electrocardiogram and TTE. Conversely, all patients with cardiac amyloidosis, multiple myeloma should be sought for its poor prognosis.

Keywords: Cardiac amyloidosis; Multiple myeloma; Restrictive cardiomyopathy

Introduction

Amyloid cardiomyopathy is a rare disease characterized by the extracellular deposition of insoluble fibrils resistant to proteases. It may be secondary to chronic inflammatory conditions, hereditary diseases or to the production of a light chain of monoclonal immunoglobulin. This often leads to an infiltrative cardiomyopathy with a restrictive pathophysiology, conventionally associated with significant morbidity and poor prognosis: 30% survival at 2 years and a life expectancy of six months without treatment [1].

Some cases had described the association between cardiac amyloidosis and multiple myeloma. However, the interest of this observation is related to the rarity of this association, the diagnosis difficulty of cardiac amyloidosis and more to find its etiology.

Case Report

A 72-year-old man, without any particular medical history, was admitted to the hospital complaining of progressive dyspnea with minimal exertion and orthopnea over the preceding several weeks.

On physical examination, the patient was afebrile and in the supine position had blood pressure of 119/77 mm Hg and a regular heart rate of 110 beats per minute. When patient stood, orthostatic changes in blood pressure and heart rate were noted. He was breathing at a rate of 22 breaths per minute. Oxygen saturation on room air was 90%. The rest of the clinical examination had found Bilateral crackles on lung auscultation, bilateral lower extremity edema and jugular venous distension with bilateral cervical and axillary lymphadenopathy, the largest measured 8 cm.

Electrocardiogram revealed a normal sinus rhythm at a rate of 110 beats per minute and low voltage complexes (Figure 1).

At the first time, the trans-thoracic echocardiography (TTE) showed an abundant pericardial effusion with signs of compression, punctured with removal of one liter of sero-haematic liquid. After pericardiocentesis, the TTE demonstrated restrictive cardiomyopathy involving asymmetric hypertrophy of the left ventricle with abnormal myocardial texture, described as 'granular sparkling', a restrictive mitral profile with a moderate systolic dysfunction of the left ventricle (ejection fraction of 45%), bi-atrial enlargement and a small pericardial effusion persistent after the pericardiocentesis. The Pulmonary artery systolic pressure was Estimated Across the flow of tricuspid regurgitation at 50 mm Hg (Figure 2).

Chest X-ray showed cardiomegaly and pulmonary edema. Cervical and thoracic CT scan, done first to find the etiology of cervical lymphadenopathy and pericardial effusion, showed thrombosis of the right internal jugular vein without any significant abnormality at the thoracic CT. A complete blood cell count revealed mild normocytic anemia at 9 g/dl, an Erythrocyte Sedimentation Rate at 70 mm with a low serum albumin level to 29 g/l. The patient had moderate renal impairment with creatinine clearance to 35 ml / min / 1.73m^2, and a positive proteinuria 3700mg / 24h. Circulating N-terminal pro-brain natriuretic peptide (NT-proBNP) level increased to 6635 pg/ml (reference values 0–125 pg/ml). The electrophoresis of plasma showed a Gamma peak. The biopsy of the salivary glands, bone marrow aspiration and bone marrow biopsy were not contributory. Lymph

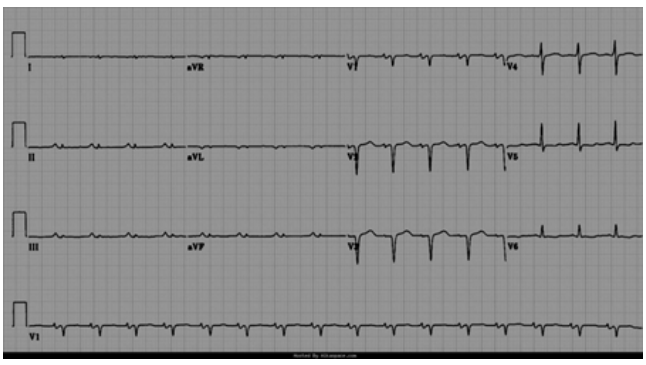

Figure 1: 12-lead ECG demonstrating low-voltage.

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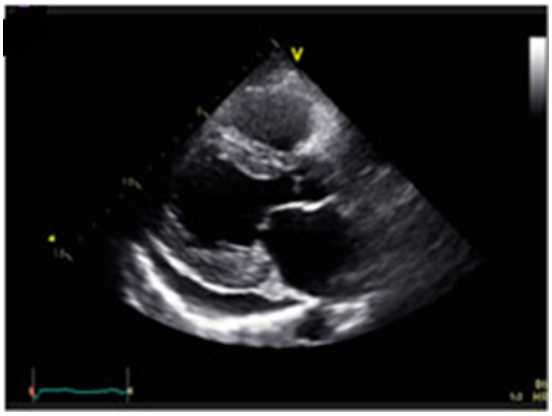

Figure 2: TTE showing a hypertrophied left ventricle and abnormal myocardial texture, described as 'granular sparkling' with low pericardial effusion.

node biopsies redone several times had found a soft tissue infiltration by amyloid deposits which were positive for Congo red stain, associated with the node location of a plasma cell proliferation with monotype Lambda composed exclusively of lambda (λ) light chains, explaining the negativity of bone marrow aspiration and bone marrow biopsy. Subsequent laboratory evaluation registered elevated, free λ light chains (88.1 mg/L (normal: 5.7– 26.3 mg/L)) and positive Bence-Jones protein (0.40 g/24 h) in the urine. Skeletal surveys or bone scans have not been carried out initially because the diagnosis of multiple myeloma was not suspected.

After we made the etiologic diagnosis, we no longer see the need to do a kidney biopsy and/or endomyocardial biopsy with the right heart catheterization.

The patient initially received standard therapy for heart failure—including diuretics and ACE inhibitors— with heparin curative dose, but the patient's condition continued to worsen, and renal function continued to deteriorate. After a few days, before starting systemic chemotherapy the patient died despite all resuscitative efforts.

Discussion

Amyloidosis is a systemic organ-limited disease in which insoluble homomeric amyloid fibrils that are composed of a variety of serum proteins gradually replace normal tissue in various body organs [2]. In the clinical setting, major forms of amyloidosis that affect the heart can be classified into 6 subtypes: (1) AL or primary amyloidosis ;(2) AA or secondary amyloidosis; (3) familial (hereditary) amyloidosis ;(4) senile systemic amyloidosis, also known as wild-type transthyretin; (5) isolated atrial amyloidosis; and (6) hemodialysis related amyloidosis resulting from accumulation of beta-2 microglobulin [3].

Clinical evidence of cardiac involvement occurs in up to 50% of patients with AL amyloidosis but only in 10% of individuals with AA amyloidosis and less than 5% with familial syndromes [4]. It is important to emphasize that although only 10% of the patients with multiple myeloma develop systemic light-chain amyloid disease, their prognosis is very poor, especially in the presence of cardiac amyloidosis [5,6].

The mean age of diagnosis of patients with AL amyloidosis is 64 years [7]. Amyloid depositions occur mainly in the interstitium of contractile myocardium but may also involve the pericardium, the endocardium and the conduction system [8]. Coronary angiography in patients with cardiac amyloidosis and angina is often normal because amyloid fibrils are deposited in the small intramural vessels sparing the epicardial arteries [9,10].

Few similar cases have been described, the first discovered in postmortem after rapidly progressive heart failure [5], the second revealed by a congestive heart failure associated with ventricular tachycardia, efficiently treated with Bortezomib [11], and the third discovered following an asymmetric hypertrophic cardiomyopathy and unexplained heart failure [12].

Plasma levels of B-natriuretic peptide are also elevated, likely the result of elevated ventricular filling pressures and possibly the result of direct damage to myocytes caused by amyloid deposition [13]. Accumulation of electrically inert amyloid protein in the extracellular matrix of the myocardium leads to an increase in ventricular wall thickness and a false impression of ventricular hypertrophy on sonography. On the electrocardiogram, however, there are no signs of LV hypertrophy and the recorded voltage is low. The ventricular myocardium in amyloidosis may have a "snowstorm" or "sparkling" appearance on sonographic images [14]. A thickened interatrial septum, which is rarely present even in the later stages of the disease process, has been shown to have 100% specificity [15].

The diagnosis of cardiac amyloidosis can be ascertained by either (1) a positive biopsy from a noncardiac tissue in addition to sonographic evidence of amyloidosis, which includes a mean LV wall thickness of greater than 12 mm in the absence of other causes of LV hypertrophy, or (2) an endomyocardial biopsy illustrating amyloid deposition in addition to laboratory and clinical evidence of organ involvement. Biopsy specimen from the involved organ, such as the heart or from the abdominal fat pad, exhibits a red or pink color under light microscopy after chemical staining with Congo red and a dramatic apple-green birefringence under polarized light [16].

The primary manifestation of amyloid cardiomyopathy is congestive heart failure with preserved systolic and abnormal diastolic function. Classically, amyloidosis was described as a form of restrictive cardiomyopathy based on the so called restrictive mitral inflow pattern on spectral Doppler imaging. However, this severe form of LV diastolic dysfunction occurs only in the late stage of the disease. Early in the process, diastolic dysfunction is only mild and is characterized by the Doppler pattern of abnormal relaxation. On cardiac magnetic resonance imaging diffuse myocardial amyloid deposits lead to decreased tissue signal intensity along with a specific pattern of global late subendocardial tissue enhancement [5].

Cardiac MRI in patients with cardiac amyloidosis usually demonstrates global and subendocardial late gadolinium enhancement of the myocardium. However, gadolinium-based MRI should be used with extreme caution and preferably avoided in patients with moderate to severe renal disease, due to the risk of nephrogenic systemic fibrosis [17].

Aside from the treatment of the underlying cause of amyloid deposition, the treatment of symptomatic cardiac amyloidosis is primarily supportive. Preload and afterload reduction using diuretics alone or in combination with vasodilators, or long-acting nitroglycerin preparations, may be helpful. Digital glycosides may reduce the symptoms of congestive failure, but dysrhythmia and sudden death have been reported following their use [5].

Untreated patients with AL amyloidosis and heart failure have a median survival of 6–9 months [1]. For patients who are not candidates

for haematopoietic stem cell transplantation, the preferred regimen is melphalan plus dexamethasone [18] or cyclophosphamide plus thalidomide and dexamethasone [19], which prevents further amyloid deposition, gradual amyloid regression and marked improvement in New York Heart Association (NYHA) class [20]. Sustained improvement in cardiac function with persistent amyloid deposition is provided in a patient with multiple myeloma-associated cardiac amyloidosis treated with Bortezomib [11].

Cardiac transplantation may be a lifesaving measure for those patients with preserved extracardiac organ function who are also fit to undergo subsequent chemotherapy. Successful post-transplantation chemotherapy for 12 months has been shown to greatly improve the longevity of the patient, possibly leading to a survival of up to 10 years [21].

In summary, a cardiac screening in all patients with multiple myeloma should include at least an electrocardiogram and complete cardiac sonography. Conversely, all patients with cardiac amyloidosis, multiple myeloma should be sought for its poor prognosis. Even though there is no single noninvasive test that can accurately diagnose cardiac amyloidosis, the consolation of heart failure symptoms, sonographic findings, and low-voltage complexes at the electrocardiogram are highly suggestive of disease.

References

1. Kyle RA, Gertz MA (1995) Primary systemic amyloidosis: clinical and laboratory features in 474 cases. Semin Hematol 32: 45-59.
2. Merlini G, Bellotti V (2003) Molecular mechanisms of amyloidosis. N Engl J Med 349: 583-596.
3. Westermark P, Benson MD, Buxbaum JN, Cohen AS, Frangione B, et al. (2005) Amyloid: toward terminology clarification. Report from the Nomenclature Committee of the International Society of Amyloidosis. Amyloid 12: 1-4.
4. Kyle RA (1995) Amyloidosis. Circulation 91: 1269-1271.
5. Sedaghat D, Zakir RM, Choe J, Klapholz M, Saric M (2009) Cardiac amyloidosis in a patient with multiple myeloma: a case report and review of literature. J Clin Ultrasound 37: 179-184.
6. Dispenzieri A, Kyle RA, Gertz MA, Therneau TM, Miller WL, et al. (2003) Survival in patients with primary systemic amyloidosis and raised serum cardiac troponins. Lancet 361: 1787-1789.
7. Kyle RA, Gertz MA (1995) Primary systemic amyloidosis: clinical and laboratory features in 474 cases. Semin Hematol 32: 45-59.
8. Mathew V, Olson LJ, Gertz MA, Hayes DL (1997) Symptomatic conduction system disease in cardiac amyloidosis. Am J Cardiol 80: 1491-1492.
9. Al Suwaidi J, Velianou JL, Gertz MA, Cannon RO 3rd, Higano ST, et al. (1999) Systemic amyloidosis presenting with angina pectoris. Ann Intern Med 131: 838-841.
10. Mueller PS, Edwards WD, Gertz MA (2000) Symptomatic ischemic heart disease resulting from obstructive intramural coronary amyloidosis. Am J Med 109: 181-188.
11. Hiroya Tamaki (2010) Sustained improvement in cardiac function with persistent amyloid deposition in a patient with multiple myeloma-associated cardiac amyloidosis treated with bortezomib. Int J Hematol 92: 655-658.
12. Basha HI, Raj E, Bachuwa G (2013) Cardiac amyloidosis masquerading as biventricular hypertrophy in a patient with multiple myeloma. BMJ Case Rep 2013.
13. Nordlinger M, Magnani B, Skinner M, Falk RH (2005) Is elevated plasma B-natriuretic peptide in amyloidosis simply a function of the presence of heart failure? Am J Cardiol 96: 982-984.
14. Dubrey SW, Cha K, Skinner M, et al. (1997) Familial and primary (AL) cardiac amyloidosis: echo cardiographically similar diseases with distinctly different clinical outcomes. Heart 78: 74-82.
15. Falk RH, Plehn JF, Deering T, Schick EC Jr, Boinay P, et al. (1987) Sensitivity and specificity of the echocardiographic features of cardiac amyloidosis. Am J Cardiol 59: 418-422.
16. Gertz MA, Comenzo R, Falk RH, et al. (2004) Definition of organ involvement and treatment response in immunoglobulin light chain amyloidosis (AL): a consensus opinion from the 10th International Symposium on Amyloid and Amyloidosis, Tours, France Am J Hem Aug 79: 319-328.
17. Floros GV, Karatzis EN, Andreou J, Danias PG (2010) Typical cardiac magnetic resonance imaging findings of cardiac amyloidosis. Hellenic J Cardiol 51: 463-466.
18. Palladini G, Perfetti V, Obici L, Caccialanza R, Semino A, et al. (2004) Association of melphalan and high-dose dexamethasone is effective and well tolerated in patients with AL (primary) amyloidosis who are ineligible for stem cell transplantation. Blood 103: 2936-2938.
19. Wechalekar AD, Goodman HJ, Lachmann HJ, Offer M, Hawkins PN, et al. (2007) Safety and efficacy of risk-adapted cyclophosphamide, thalidomide, and dexamethasone in systemic AL amyloidosis. Blood 109: 457-464.
20. Skinner M, Sanchorawala V, Seldin DC, Dember LM, Falk RH, et al. (2004) High-dose melphalan and autologous stem-cell transplantation in patients with AL amyloidosis: an 8-year study. Ann Intern Med 140: 85-93.
21. Kpodonu J, Massad MG, Caines A, Geha AS (2005) Outcome of heart transplantation in patients with amyloid cardiomyopathy. J Heart Lung Transplant 24: 1763-1765.