Cardiac Amyloidosis

Carlos José Mota de Lima, Gustavo Ney de Morais Gouveia, Sandra Nívea dos Reis Saraiva Falcão, Benício Kerlly Barbosa Gonçalves, Cezário Antônio Martins Gomes

Hospital Dr. Carlos Alberto Studart Gomes (Hospital de Messejana), Fortaleza, CE - Brazil

Introduction

Amyloidosis includes a group of multietiological disorders due to extracellular deposition of insoluble betafibrilar proteins, which consist of amyloid deposits that cause structural damage to the tissue.[1] The term "amyloid" was adopted in 1954 by Virchow based on coloration of the tissue with iodine and sulfuric acid . All amyloid fibrils share an identical secondary structure, the β-pleated sheet conformation, and an identical non-fibrillar component, the pentraxin serum amyloid P.

This disease can be subdivided into both localized (when the material is deposited in a single organ) and systemic form (when it affects more than one organ). The isolated cardiac involvement, wherein the myocardium becomes firm and less flexible, is polymorphic and can be present in any type of systemic amyloidosis, with or without associated clinical manifestations, more common in the elderly.[1]

In clinical practice, it is classified as primary, secondary, hereditary amyloidosis, and is age-related. Primary amyloidosis appears without background or coexisting disease involving mesenchymal organs, such as the cardiovascular system, gastrointestinal tract and muscle tissue, with cardiac involvement being common. Secondary amyloidosis is associated with chronic diseases and has a tendency to be deposited in parenchymal organs such as the liver, spleen and kidneys, with rare cardiac involvement. Finally, hereditary amyloidosis is usually inherited in an autosomal dominant manner.[1,2]

The clinical forms of cardiac amyloidosis are varied: heart failure, arrhythmias, pulmonary embolism and even sudden death from ventricular fibrillation. The anatomical and pathological changes include the increase in ventricular wall thickness associated with abnormal myocardial texture, with possible involvement of heart valves by the amyloid, the mitral valve being the most affected (90%), followed by the tricuspid valve (70%).[3] Cardiac amyloidosis findings vary in severity and duration.

Electrocardiography (ECG) reveals low voltage in 50% of cases and may also shows varying degrees of atrioventricular and intraventricular blocks. Echocardiography (ECC) is an essential examination for suspected diagnosis, because it can show the infiltrative and restrictive involvement, factors suggestive of cardiac amyloidosis. The ECC can show an abnormal, diffusely bright, speckled myocardium.[4] In the early stages of the disease, abnormal texture is subtle and inflow patterns on Doppler echocardiography may suggest delayed relaxation rather than a restrictive pattern.[5] Moreover, the presence of pericardial effusion and atrial dilation can be noticed. [6]

Patients with amyloidosis and congestive heart failure have a worse prognosis.[7] In the literature, several authors describe prognostic markers that can guide the clinician. Myocardial thickness of the LV free wall assessed on the ECC is closely related to prognosis. The thicker the wall, the worse the evolution. [8] Patients with more than 1.2 cm and less than 1.5 cm have 1.3-year survival, and those with more than 1.5 have higher mortality rates.[9]

This study aimed to describe the case of a patient with late-onset isolated cardiac amyloidosis, with organic complications of the disease, in order to illustrate the pattern of cardiac involvement by the disease on the echocardiographic examination.

Case report

Five years ago, 81-year-old, black, male patient P.M.S. started to develop recurrent, progressive dyspnea on exertion and edema of the lower limbs and abdomen, which caused the patient to seek emergency medical care, be referred to hospital for admissions, showing clinical improvement after stabilization of the acute condition, but without definite diagnosis or outpatient disease control. In one of the admissions, a left ventricular hypertrophy was observed, the etiology of which was initially unknown. The patient has no arterial hypertension or other comorbidities. On his last visit to the emergency room, he had a clinical condition of biventricular heart failure with dry cough, dyspnea at rest and edema of the limbs. Physical examination revealed hypophonetic heart sounds, B3, fine teleinspiratory crackles in the lower two thirds of the lungs. ECG examination, used during investigation with complementary tests, showed low voltage in the peripheral leads (< 0.5 mV), absence of left ventricular hypertrophy, intraventricular conduction delay or arrhythmias (Figure 1). Laboratory tests showed elevation of nitrogenous compounds: urea: 74 mg/dL and creatinine: 1.29 mg / dL; Blood count revealed normocytic and normochromic anemia with leukocytes: 6,115/mm^3. Differential count revealed the presence of neutrophils (segmented): 48.6%; eosinophils: 0.4%; basophils: 1%; lymphocytes: 40%; and monocytes: 10%, with platelets: 192.500/mm^3. A transthoracic Doppler echocardiography

Keywords

Amyloidosis; Heart Failure; Cardiac Arrhythmias; Atrial Fibrillation; Echocardiography/methods.

Mailing address: Carlos José Mota de Lima •
Rua Jonas Sampaio, 551, Casa 14. Postal Code 60830-465, Jose de Alencar, Fortaleza, CE - Brazil
E-mail: carlos_mota_lima@yahoo.com.br
Manuscript received March 1st, 2016; revised April 24, 2016; accepted August 28, 2016.

DOI: 10.5935/2318-8219.20160034

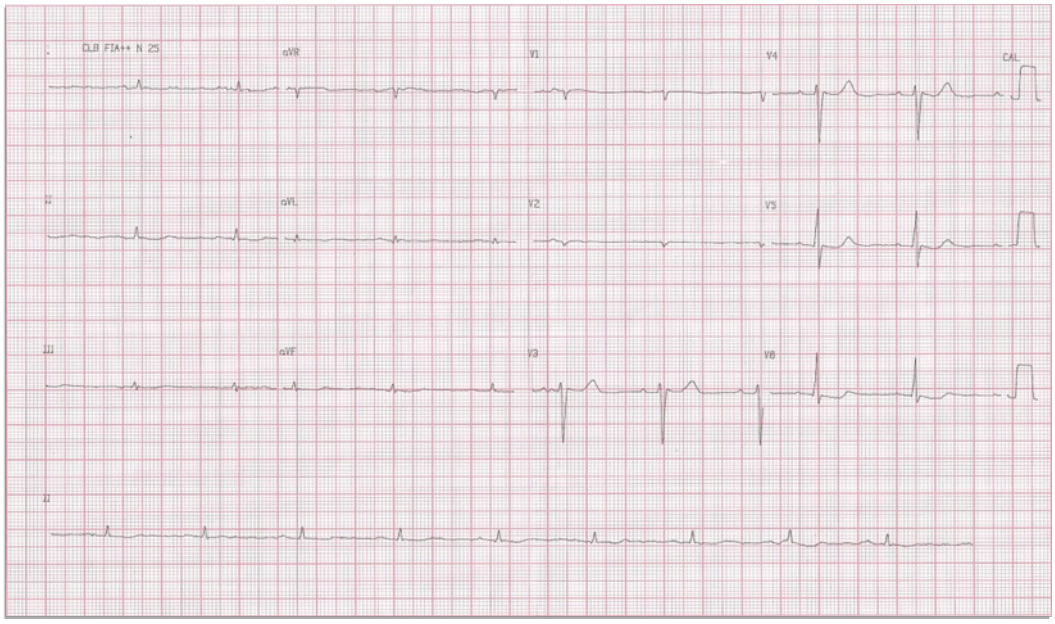

Figure 1 – *Patient ECG shows low voltage associated with slow progression where R in the anterior wall.*

was performed, of which findings were consistent with a restrictive infiltrative cardiomyopathy, with thickening of the septal wall and left ventricle, shimmering granulations at the left ventricular myocardium level (Figure 2), associated with biatrial enlargement (Figure 3), showing a restrictive filling pattern on Doppler, suggestive of cardiac amyloidosis.

The diagnosis was, therefore, confirmed using histopathological examination of abdominal fat after biopsy. The patient authorized the use of his medical record by means of an Informed Consent.

Discussion

Cardiac amyloidosis is characterized by extracellular deposition of insoluble betafibrilar proteins (amyloid deposits) in the heart. This may be part of a systemic disease, which is more common, or a local phenomenon.[8]

Cardiac involvement in amyloidosis usually manifests in the primary form of amyloidosis and often progresses with repeated hospital admissions for heart failure associated with a worse prognosis. A presumptive diagnosis of cardiac amyloidosis is made when observing heart failure associated with low voltage on electrocardiography and echocardiographic abnormalities suggestive of infiltration.

The low voltages in all leads shown on ECG, combined with increased wall thickness on echocardiography, has sensitivity (72%) and specificity (91%). Amyloidosis is a systemic disease whose clinical manifestations are evident only after considerable tissue infiltration, so that the presence of changes in the ECC is suggestive of advanced disease.[7]

The ECC of the patient in question revealed increased thickness of the left ventricle walls, diffuse hyper-refractive granular twinkles, myocardial hyperechogenicity, slightly diffuse hypokinesia, interatrial septum thickening, showing a restrictive filling pattern on Doppler. Thus, the ECC during investigation was fundamental to characterize the disease, as the examination established the suspected diagnosis of amyloidosis.[5]

The thickening of the upper interventricular septum by 1.98 cm associated with low voltages in the ECG (Figure 1) is highly suggestive of cardiac amyloidosis, with 72% sensitivity and 91% specificity.[9] Moreover, the presence of granular twinkles on ECC has high sensitivity (87%) and specificity (81%), and may achieve 100% sensitivity when are present with atrial enlargement. Although the diagnosis of cardiac amyloidosis is only confirmed after the tissue biopsy, ECG and ECC are the most common examinations used in clinical practice to assess the progression of cardiac involvement.

Although there is no specific echocardiographic finding for the diagnosis of amyloidosis, there are common echocardiographic features that, once associated with the clinical context, confirm the diagnosis of amyloidosis, even in the absence of biopsy. Thus, the combination of several of these findings may be feasible for diagnosis.[6,9]

New diagnostic techniques such as tissue Doppler, strain and strain rate enable earlier diagnosis of the disease, even in the absence of systolic dysfunction. The tissue Doppler of mitral annulus has proven to be the most accurate method in the early detection of diastolic dysfunction in patients with cardiac amyloidosis.[10]

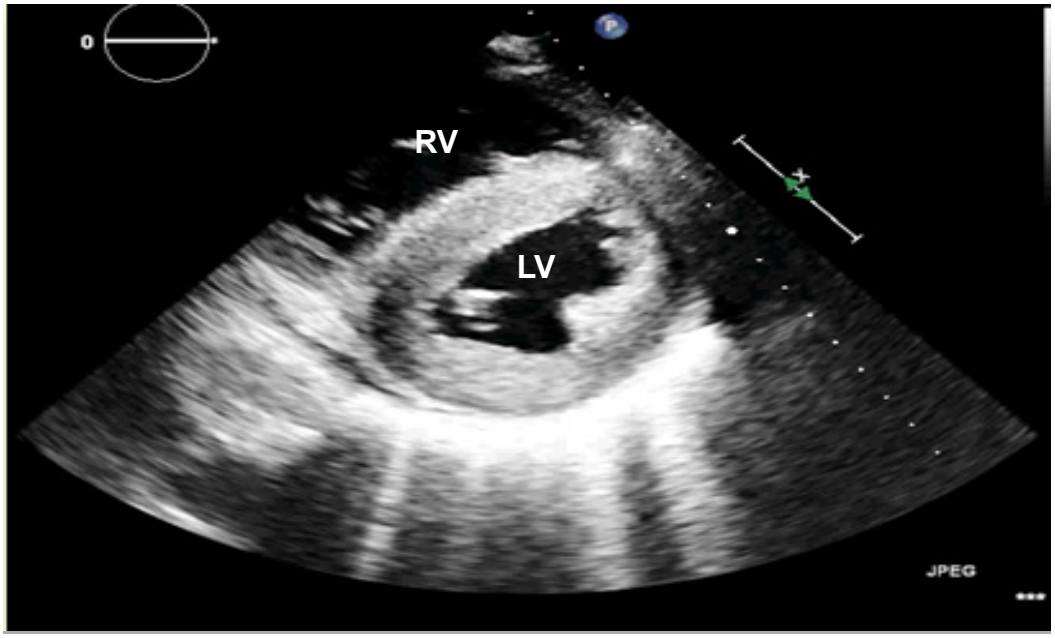

Figure 2 – *Echocardiogram cross parasternal projection demonstrating increased thickness and appearance in sparkling granular myocardial the left ventricle. LV: left ventricle; RV: right ventricle.*

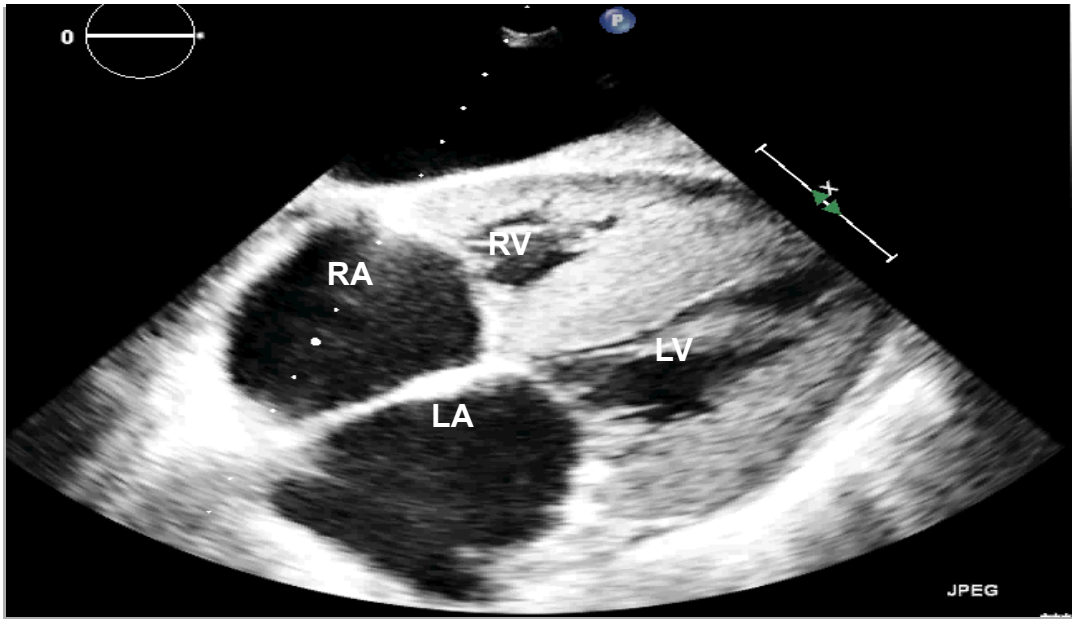

Figure 3 – *Echocardiography in subcostal projection shows increased thickness of the interatrial septum and biatrial enlargement. LV: left ventricle; RV: right ventricle. RA: right atrium; LA: left atrium.*

Biopsy is the method that really confirms the diagnosis, allowing histological characterization of amyloid substance. Diagnostic sensitivity to abdominal aspirate is 85%, while the endocardial biopsy sensitivity is close to 100%. Specific staining with Congo red or immunohistochemistry staining under the microscope with polarized light identifies its various types.[6]

Treatment is based on the detection of the underlying disorder and control of symptoms. Heart transplantation does not show good results in advanced cases because of the frequent recurrence of the disease in a short period of time, rarely indicated due to progression of amyloid in other organs and the possibility of occurring amyloid deposition in the heart of the donor.[7]

The cardiac amyloidosis remains a challenge for clinical medicine. The awareness and understanding of amyloidosis are relevant for cardiologists and clinicians, since early diagnosis is related to increased patient survival.

Conclusion

This case study illustrates the characteristic of a patient with amyloidosis concomitant with cardiac involvement. In the course of comorbidity, it is possible to see the fundamental role of the ECC and new techniques with greater sensitivity, allowing diagnosis of cardiac involvements by amyloid infiltration, enabling a targeted and qualified patient care, as early diagnosis of amyloidosis remains a challenge for clinical medicine.

Authors' contributions

Research conception and design: Lima CJM; Data acquisition: Gouveia GNM; Data analysis and interpretation: Gomes CAM; Manuscript writing: Gonçalves BKB; Critical revision of the manuscript's major intellectual content: Falcão SNRS.

Potential Conflicts of Interest

No potential conflict of interest relevant to this manuscript was reported.

Sources of Funding

This study had no external funding sources.

Academic Association

This study is not associated to graduate programs.

References

1. XavierFC. Amiloidose:revisão bibliográfica [dissertação]. Portugal: Universidade da Beira Interior; 2008.
2. Kholova I, Niessen HW. Amyloid in the cardiovascular system: a review. J Clin Pathol.2005;58(2):125-33.
3. Pellikka PA, Holmes Jr DR, Edwards WD, Nishimura RA, Tajik AJ, Kyle RA. Endomyocardial biopsy in 30 patients with primary amyloidosis and suspected cardiac involvement. Arch Intern Med. 1988;48(3):662-6.
4. Barbosa MM, Nunes MCP, Campos Filho O, Camarozano A, Rabis-choffsky A, Maciel BC, et al.; Sociedade Brasileira de Cardiologia. Diretrizes das indicações da ecocardiografia. Arq Bras Cardiol. 2009;93(6 supl 3):e265-e302.
5. Silva CES. Ecocardiografia: princípios e aplicações clínicas. Rio de Janeiro (RJ): Revinter; 007.
6. Hartmann A, Frenkel J, Hopf R ,Baum RP, Hor G, Schneider M, et al. Is technetium 99m pyrofhosphate scintigraphy valuable in the diagnosis of cardiac amyloidosis? Int J Card Imaging. 1990;5(4):227-31.
7. Selvanayagam JB, Hawkins PN, Paul B, Myerson SG, Neubauer S. Evaluation and management of the cardiac amyloidosis. J Am Coll Cardiol. 2007;50(22):2101-10.
8. Rahman JE, Helou EF, Gelzer-Bell R, Thompson RE, Kuo C, Rodriguez ER, et al.Noninvasive diagnosis of biopsy-proven cardiac amyloidosis. J Am Coll Cardiol. 2004;43(3):410–5.
9. Bhandari AK, Nanda NC. Myocardial texture characterization by two-dimensional echocardiography. Am J Cardiol. 1983;51(5):817-25.
10. Al-Zahrani GB, Bellavia D, Pellikka PA, Dispenzieri A, Hayman SR, Oh JK, et al. Doppler Myocardial imaging compared to standart two dimensional and doppler echocardiography for assessment of diastolic function in patients with systemic amyloidosis. J Am Soc Echocardiogr. 209;22(3):290-8.