Echocardiography as the first diagnostic clue to rapidly progressive systemic AL amyloidosis secondary to a plasma cell myeloma associated with multiple site thrombosis. A case report

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Abstract

AL-amyloidosis is a rare but complex disease, with a severe prognosis, cardiac involvement being found in half of the patients. The rapid increase of the LV wall thickness predicts an unfavorable evolution. We report the case of a 63-year-old man diagnosed with AL-amyloidosis, with cardiac involvement, secondary to a plasma cell myeloma associated with multiple site thrombosis. Specific echocardiographic methods such as tissue Doppler imaging and speckle tracking provided crucial diagnostic and prognostic information.

Keywords: cardiac amyloidosis; echocardiography; tissue Doppler imaging; speckle tracking.

Introduction

Amyloid light-chain (AL) amyloidosis is a relatively rare disease, with an estimated incidence of 9 cases/million inhabitant/year in developed countries, affecting especially patients aged over 65 years [1]. It is closely related to myeloma and affects multiple organs, an evidence of cardiac involvement being found in half of the patients. The evaluation of cardiac amyloidosis has crucial prognostic importance because the presence of heart failure in these patients reduces the average survival period in the lack of specific treatment from 24 months to under 9 months [2]. Hemostasis is frequently affected by AL-amyloidosis, which predisposes to both bleeding and thrombotic complications [3].

Although patients with amyloidosis need extensive evaluation, including cardiac magnetic resonance imaging (MRI) and histopathological examination, given the multiorgan involvement and the large number of complications that can occur, simple and widely available diagnostic tools such as ECG and echocardiography often prove to be very useful in these cases.

We report a case of AL-amyloidosis, with rapidly progressive cardiac hypertrophy and dysfunction, in which echocardiographic methods such as tissue Doppler imaging and speckle tracking had a decisive role in establishing the correct diagnosis, while other examinations considered to be more specific, such as abdominal fat tissue biopsy, were at first inconclusive.

Case report

A 63-year-old male patient presented with inspiratory dyspnea at minimum effort and massive peripheral edema which started insidiously 3 months ago, but in the last week these symptoms were accompanied by orthopnea and vertigo. He also presented an ischemic stroke in the left medium cerebral artery (confirmed by a cer-

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Fig 1. a) Tissue Doppler Imaging evaluation of the LV lateral wall showing systolic and diastolic dysfunction (reduced peak systolic (S wave) and diastolic (e' wave) velocities. E/lateral e' = 20.6); b) Speckle tracking echocardiography showing reduced peak systolic longitudinal strain of the basal segments of the LV compared to the apical segments; c) Speckle tracking echocardiography showing reduced peak systolic circular strain of the basal segments of the LV.

ebraal computed tomography (CT) scan), with complete neurological recovery one month previously and had received topical corticosteroids in the last two months for palpebral dermatitis. The first medical evaluation performed 10 weeks before admission raised the suspicion of a restrictive cardiomyopathy. At that moment, the cardiac echography revealed a mild left ventricular (LV) hypertrophy (interventricular septum = 14 mm, LV posterior wall = 13 mm), preserved ejection fraction of the LV (56%, Simpson's biplane method), but a severe diastolic dysfunction, with a restrictive profile of the mitral flow (E/A > 2). Also, the left atrium was enlarged (anteroposterior diameter = 48 mm and area = 25 mm²) and a small pericardial effusion (end-diastolic thickness = 4 mm) was detected. The cardiac MRI performed at that moment was suggestive of cardiac amyloidosis, but the abdominal fat tissue biopsy was negative. For that reason, the diagnosis of amyloidosis was excluded, and the patient received specific medical therapy for heart failure with preserved LV ejection fraction.

At admission physical examination revealed massive peripheral edema, hepatomegaly, jugular turgescence and abolished vesicular murmur at the right lung base, bilateral palpebral ecchymosis. The cardiac exam showed regular heart rhythm, 92 beats/min, third heart sound gallop and a mitral systolic murmur. The resting electrocardiography revealed sinus rhythm, microvoltage, prolonged QT interval (corrected QT = 478 ms) and negative T waves in precordial leads. The NT-proBNP levels were exceedingly increased (>30000 pg/ml).

The echocardiographic reevaluation showed a severe concentric LV hypertrophy (interventricular septum = 20.4 mm, LV posterior wall = 19.6 mm), increased myocardial echogenicity, with moderate systolic dysfunction (ejection fraction = 36%, Simpson's biplane method), and restrictive profile of the transmitral flow (E/A ratio =

2.8, E wave deceleration time = 85 ms). Tissue Doppler parameters were also suggestive for a severe diastolic dysfunction, the E/lateral e' ratio being 20.6 (fig 1a).

Both left and right atria were enlarged (LA area = 35 mm² and RA area = 33 mm²). Speckle tracking echocardiography noticed reduced strain in the basal segments of the LV, with normal kinetics in the apical segments (fig 1b,c).

The longitudinal systolic function of the right ventricle was also impaired, with a tricuspid annular plane systolic excursion (TAPSE) of 13 mm and a moderate degree of arterial pulmonary hypertension was present (pulmonary artery systolic pressure (PAPs) = 60 mmHg, inferior cava vein = 27 mm, with 20% inspiratory collapse). The pericardial effusion was larger compared to the previous examination (18 mm at the LV posterior wall and 15 mm anterior to the right ventricle) and a right pleural effusion was also observed.

Because the echocardiography was highly suggestive for cardiac amyloidosis, the abdominal fat tissue biopsy was repeated using another puncture site, this time confirming the AL type amyloidosis with Lambda chains. Bence Jones proteinuria test was positive (kappa chains = 374 mg/L and lambda chains = 314 mg/L). The bone marrow biopsy from the iliac crest established the diagnosis of plasma cell myeloma.

Due to the sudden worsening of the patient's symptoms with elevated D-dimer plasmatic values, a pulmonary embolism was suspected. The thoracoabdominal CT scan detected a thrombus in a segmentary branch of the left pulmonary artery and a splenic infarction of 25 mm. The Doppler ultrasound of the lower limbs identified a bilateral deep vein thrombosis (left popliteal and internal saphenous veins, right infrapopliteal veins) as a probable source for the emboli.

The evolution of the congestive syndrome was slightly favorable under specific heart failure treatment. Anti-

coagulants were also administered. He was transferred to the Hematology Department for initiation of the specific therapy, but one week later developed a cardiac arrest that did not respond to resuscitation.

Discussions

Although abdominal fat tissue biopsy is considered to be an accurate diagnostic method in systemic amyloidosis, the cardiac echocardiography was the examination that guided the medical approach. The rapidly progressive cardiac hypertrophy and depreciation of both left and right ventricular function, with wall motion abnormalities highly suggestive for cardiac amyloidosis, detected by speckle tracking imaging, enforced the anatomopathological reevaluation of the patient and emphasized the correct diagnosis.

Speckle tracking cardiac ultrasound is able to differentiate between primary or secondary LV hypertrophy and storage diseases and to detect intrinsic myocardial dysfunction before the depreciation of the LV ejection fraction. While patients with hypertrophic cardiomyopathy have reduced strain in the interventricular septum, in patients with cardiac amyloidosis reduced strain in basal segments of the LV with apical sparing can be observed [4]. That same aspect was found in our patient.

The clinical exam and paraclinical tests can be misleading in the early stages of amyloidosis, resulting in an incorrect diagnosis. What was at first diagnosed as a palpebral dermatitis proved to be actually periorbital purpura, a pathognomonic sign of AL amyloidosis [5].

It is also noticeable the abrupt worsening of the heart failure caused by cardiac amyloidosis, with increase of the LV wall hypertrophy by 45% and depreciation of the ejection fraction from 56% to 36% during 10 weeks. Other cases of fast worsening cardiac amyloidosis have been reported in literature presenting with refractory heart failure [6] or even with cardiogenic shock [7].

The rapid increase of the LV wall thickness is an important mortality predictor in patients with cardiac amyloidosis, a study published by Kristen et al showing that the deceased patients had a progression of approximately 2 mm/month and the survivors 0.2 mm/month during a 3 year follow up period [8]. In our case, the progression was 2.74 mm/month and was associated with a fatal evolution.

Hemostasis disorders are difficult to manage in patients with AL-amyloidosis secondary to plasma cell myeloma. As in many other cancer types, patients with myeloma are at high risk for thrombosis and thromboembolic events, the most frequently involved factors be-

ing immobility, malignant cells, central venous catheters, inflammation-induced prothrombotic states and chemotherapy effects [9].

Cases of bi-atrial appendage thrombosis in cardiac amyloidosis patients in sinus rhythm have been reported [10], a clinical hypothesis that could explain the ischemic stroke and the spleen infarction found in our patient.

Echocardiographic follow-up of patients with cardiac amyloidosis using new ultrasonographic techniques, such as speckle tracking, can prove very useful in the early stages of the disease, when more specific examinations, such as cardiac MRI or histopathological examination, occasionally return inconclusive results.

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