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CASE REPORT

Diagnostic approach to cardiac amyloidosis: A case report☆

Andreia Fernandes[a,*], Francisca Caetano[a], Inês Almeida[a], Luís Paiva[a], Pedro Gomes[a], Paula Mota[a], Joana Trigo[a], Ana Botelho[a], Maria do Carmo Cachulo[a], Joana Alves[b], Luís Francisco[c], António Leitão Marques[a]

[a] *Serviço de Cardiologia, CHUC – Hospital Geral, Coimbra, Portugal*
[b] *Serviço de Anatomia Patológica, CHUC – Hospital Geral, Coimbra, Portugal*
[c] *Serviço de Hematologia, CHUC – Hospital Geral, Coimbra, Portugal*

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Abstract The authors present a case of systemic amyloidosis with cardiac involvement. We discuss the need for a high level of suspicion to establish a diagnosis, diagnostic techniques and treatment options. Our patient was a 78-year-old man with chronic renal disease and atrial fibrillation admitted with acute decompensated heart failure of unknown cause. The transthoracic echocardiogram revealed severely impaired left ventricular function with phenotypic overlap between hypertrophic and restrictive cardiomyopathy. After an extensive diagnostic workup, which included an abdominal fat pad biopsy, the final diagnosis was amyloidosis.

PALAVRAS-CHAVE
Amiloidose;
Miocardiopatia hipertrófica;
Miocardiopatia restritiva;
Insuficiência cardíaca

Amiloidose cardíaca – abordagem diagnóstica, a propósito de um caso clínico

Resumo Os autores apresentam um caso de amiloidose sistémica com envolvimento cardíaco e discutem a importância de um elevado índice de suspeição para o diagnóstico, os meios de diagnóstico e as opções terapêuticas à luz do conhecimento atual. Homem de 78 anos, com antecedentes de doença renal crónica e fibrilhação auricular, admitido por insuficiência cardíaca aguda de etiologia desconhecida. O ecocardiograma transtorácico mostrou ventrículo esquerdo não dilatado, com compromisso severo da função sistólica global com *overlap* fenotípico de

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* Corresponding author.
E-mail address: andreiafvf@gmail.com (A. Fernandes).

miocardiopatia hipertrófica e restritiva. Após estudo complementar alargado, o diagnóstico definitivo de amiloidose foi obtido por biópsia da gordura abdominal.

Case report

A 78-year-old man, with no cardiovascular risk factors but a history of paroxysmal atrial fibrillation and chronic renal disease (National Kidney Foundation stage IV), was admitted to the cardiac care unit for acute heart failure (HF) of unknown cause, in New York Heart Association (NYHA) class IV. He reported exertional dyspnea and worsening peripheral edema over the previous two months. He now complained of dyspnea on minimal exertion, orthopnea and paroxysmal nocturnal dyspnea, peripheral edema and increased abdominal circumference, apparently decreased urine output, and upper limb paresthesia. Physical examination showed anasarca, blood pressure 114/81 mmHg, heart rate (HR) 67 bpm and 90% oxygen saturation in room air.

Diagnostic exams revealed type 2 respiratory failure with acidosis (pH 7.24; PaO_2 58 mmHg, $PaCO_2$ 55 mmHg, HCO_3 23.6 mmol/l, and lactates 2.66 mmol/l); normocytic anemia (hemoglobin 12.1 g/dl), with no increase in inflammatory markers; NT-pro-BNP 43 300 pg/ml; hyponatremia (Na+ 132.7 mmol/l); worsening of chronic renal disease (urea 24.8 mmol/l and creatinine 207.8 μmol/l); and evidence of hepatic congestion (alkaline phosphatase 183 U/l), with increased transaminases (glutamic oxaloacetic transaminase 161 U/l and glutamic pyruvic transaminase 297 U/l). The chest X-ray showed alveolar interstitial infiltrate with a butterfly pattern. The electrocardiogram (ECG) showed sinus rhythm, HR 67 bpm, first-degree atrioventricular block, low voltage in the frontal leads and complete left bundle branch block (Figure 1).

Transthoracic echocardiography revealed left ventricular (LV) size at the upper limit of normal (end-diastolic diameter 60 mm), with increased wall echogenicity, severe hypertrophy of the interventricular septum (20 mm) and moderate hypertrophy of the other walls (posterior wall 15 mm; LV mass index 200.1 g/m^2); severe biatrial dilatation (left atrial area 37 cm^2/m^2) (Figure 2A and B); severely impaired LV systolic function (ejection fraction 27% by Simpson's method, with global longitudinal strain of −3%); hypocontractile right ventricle (tricuspid annular plane systolic excursion 12 mm); LV filling pattern suggestive of restrictive cardiomyopathy (deceleration time 145 ms, septal E′ 3 cm/s, lateral E′ 4 cm/s, and mean E/E′ ratio 29.5); right ventricular/right atrial gradient 43 mmHg; dilated inferior vena cava (2.3 cm) without inspiratory collapse; a small circumferential pericardial effusion; and interatrial septal hypertrophy.

Cardiac magnetic resonance imaging (CMRI) was not performed since the patient had a hip prosthesis.

Anticongestive therapy and a positive inotropic agent (levosimendan) were begun, together with noninvasive ventilation, resulting in progressive clinical improvement.

Given the findings of severe LV hypertrophy and low voltage on the ECG, a diagnosis of amyloidosis was considered. Abdominal fat pad biopsy confirmed the presence of amyloid deposits, exhibiting green birefringence after staining with Congo red.

Laboratory tests showed increased beta-2 microglobulin (4.98 mg/l), erythrocyte sedimentation rate 32 mm/h, C-reactive protein 5.0 mg/dl, calcium 2.07 mmol/l, phosphorus 1.05 mmol/l, parathyroid hormone 171 pg/ml, negative tumor markers and normal autoimmune parameters. Serum protein immunofixation revealed an IgG monoclonal spike (11.8 g/dl), with no changes in urine protein immunofixation. The ratio between kappa and lambda light chains was 1.22 (7.29:5.98 g/dl). After discussion with the hematology department, myelography and bone marrow biopsy were performed, which showed no plasma cell proliferation. No mutations were identified in genes coding for transthyretin proteins.

Based on the above findings, a diagnosis of systemic amyloidosis with cardiac involvement was made. The type of fibril involved was not determined, and ^{99m}Tc-DPD scintigraphy was not performed to establish the type of amyloidosis.

The patient was readmitted four months later for decompensated HF in NYHA class IV, followed by progressive worsening of his general state, culminating in death due to pulseless electrical activity.

Discussion

Amyloidosis is a systemic disease first described by Rudolph Virchow in 1854.[1] It is caused by extracellular deposition of insoluble fibrils of low molecular weight proteins[2,3] that form beta sheets.[4] Over 30 different proteins are known to be involved in the disease,[5] of which the most common forms are light-chain amyloidosis (AL), amyloid A amyloidosis (AA) and transthyretin-related amyloidosis (ATTR).[6,7]

Despite the heterogeneity in their structure and function, these proteins are deposited in the form of amyloid in various organs, locally or systemically, and can cause multiple organ dysfunction (Table 1).

Cardiac amyloidosis is the result of amyloid deposits in the heart,[8] the most common presentation in the West being restrictive cardiomyopathy, while in around 5% of cases, it may mimic hypertrophic cardiomyopathy.[9]

Cardiac involvement is found in around 50% of patients with AL amyloidosis,[10] in isolation in 5% of these,[11] but is rare in AA amyloidosis. ATTR amyloidosis also frequently affects the heart, although the endemic mutation in Portugal is more typically associated with neurological manifestations (familial amyloid polyneuropathy). Senile