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# Severe heart faillure of amylootic etiology

## *Insuficiência cardíaca grave de etiologia amiloidótica*

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**ABSTRACT:** Amyloidosis is a systemic disease caused by the extracellular deposition of insoluble fibrils of low molecular weight proteins in various tissues. It can be classified in the following forms: primary, secondary, hereditary, and senile systemic. We report the case of a 75-year-old male patient who was admitted due to a cardiologic emergency with progressive edema in the lower limbs, which started four months prior. Thirty days before admission he presented dyspnea from medium to small effort, evolving at rest, and in decubitus (cardiac failure - functional class IV). Upon physical examination, he presented as conscious, tachypneic, afebrile, hydrated, hypochromic (1+/4+), jaundiced (2+/4+), and acyanotic, with jugular stasis at 45°. The cardiac rhythm was regular with normal heart sounds. A systolic murmur was noted in the mitral focus (2+/6+), with fixed unfolding of the second sound, blood pressure of 80/40 mmHg, and heart rate of 84 bpm. The admission electrocardiogram showed regular sinus rhythm, 1st degree atrioventricular block, low voltage in the frontal plane leads, electrically inactive zone in the anteroseptal region, and left bundle branch conduction disorder. Chest X-ray revealed increased cardiac area, a pattern of pulmonary congestion, and bilateral pleural effusion, which was more pronounced on the left. A transthoracic echocardiogram was performed, showing enlarged right cardiac chambers, mildly depressed right ventricular systolic function, moderate to severe tricuspid insufficiency, moderate pulmonary hypertension, left ventricular hypertrophy, left ventricular dysfunction, and bright granular echogenicity. Ultrasonography of the abdomen showed heterogeneous texture of the liver and spleen, suggestive of granulomatous disease. Subsequently, hepatic biopsy was performed, supporting the hypothesis of infiltrative disease caused by cardiovascular amyloidosis. The patient evolved with a lowered level of consciousness and acute renal failure, undergoing hemodialysis and transfer to the Coronary Unit, where he suffered fatal cardiorespiratory arrest.

**Keywords:** Heart failure/etiology; Amyloidosis/etiology; Aged.

**RESUMO:** A amiloidose é uma doença sistêmica causada pela deposição extracelular de fibrilas insolúveis de proteínas de baixo peso molecular em diversos tecidos. Pode ser classificada nas formas: primária, secundária, hereditária e sistêmica senil. Relatamos o caso de um paciente masculino, 75 anos, que deu entrada em emergência cardiológica com quadro progressivo de edema em membros inferiores iniciado há quatro meses. Trinta dias antes do internamento passou a apresentar dispneia de médios para pequenos esforços, evoluindo para dispneia ao repouso e em decúbito (insuficiência cardíaca – classe funcional IV). Ao exame físico apresentou-se em estado geral regular, consciente, taquidispneico, afebril, hidratado, hipocorado (1+/4+), ictérico (2+/4+), acianótico e presença de estase jugular a 45°. O ritmo

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cardíaco era regular em dois tempos e bulhas, normofonéticas, com sopro sistólico em foco mitral (2+/6+) desdobramento fixo da segunda bulha; pressão arterial de 80x40 mmHg e frequência cardíaca de 84 bpm. O eletrocardiograma de admissão mostrou ritmo sinusal regular, bloqueio atrioventricular de 1º grau, baixa voltagem em derivações de plano frontal, zona eletricamente inativa em região ântero-septal e distúrbio de condução pelo ramo esquerdo do feixe de His. Radiografia de tórax com área cardíaca aumentada, padrão de congestão pulmonar e derrame pleural bilateral, mais acentuado à esquerda. Também foi realizado ecocardiograma transtorácico que evidenciou câmaras cardíacas aumentadas à direita, função sistólica de ventrículo direito levemente deprimida, insuficiência tricúspide moderada a importante, hipertensão pulmonar moderada, hipertrofia de ventrículo esquerdo, disfunção de ventrículo esquerdo e achado de ecogenicidade granular brilhante. Ultrassonografia de abdome mostrou fígado e baço com textura heterogênea, sugestivo de doença granulomatosa. Posteriormente foi realizada biópsia hepática que confirmou a hipótese de doença infiltrativa determinada pela amiloidose cardiovascular. Paciente evoluiu com rebaixamento de nível de consciência e insuficiência renal aguda, sendo realizada hemodiálise e transferência para Unidade Coronariana, onde apresentou parada cardiorrespiratória e evolução para óbito.

**Descritores**:Insuficiência cardíaca/etiologia; Amiloidose/etiologia; Idoso.

## INTRODUCTION

Amyloidosis is a systemic disease caused by the extracellular deposition, in the amyloid form, of insoluble fibrils of low molecular weight proteins in many tissues. It can be classified in the following forms: primary, secondary, hereditary, and senile systemic. Age above 50 years, being male, having a history of chronic infections or inflammatory diseases, and a family history of amyloidosis are the main predisposing factors for this condition[1,2].

The primary form is the most common systemic amyloidosis, with a mean age of diagnosis at 60 years, and male predominance of 2:1. Cardiac involvement is present in approximately 50% of patients, with worsening of symptoms and poor prognosis. Once the diagnosis is made, the median survival is six months[3].

## CASE REPORT

A 75-year-old male patient was admitted due to a cardiologic emergency with progressive edema in the lower limbs, which started four months prior, and progression from dyspnea to orthopnea in the last thirty days (cardiac failure - functional class IV). The patient presented with positive epidemiology for Chagas Disease and Schistosomiasis, and had been taking a regular dose of hydrochlorothiazide (25 mg/day) for the past two years to treat his systemic arterial hypertension. On the physical examination he presented as conscious, tachypneic, afebrile, hydrated, hypochromic (1+/4+), jaundiced (2+/4+), and acyanotic, with jugular stasis at 45°. Vesicular murmurs were present in both hemithoraces, but decreased in bases and with fine crepitus until the middle third on the right. The patient had a respiratory rate of 24 ipm and arterial oxygen saturation of 92%. In the cardiovascular evaluation, visible and palpable ictus cordis was observed in the 5th left intercostal space, occupying a digital pulp, but without mesocardial impulse. The cardiac rhythm was regular with normal heart sounds. A systolic murmur was noted in the mitral focus (2+/6+), with fixed unfolding of the second sound, blood pressure of 80/40 mmHg, and heart rate of 84 bpm. The abdomen was globose, flaccid, and painful below the right costal border and xiphoid appendix. The liver was palpable at 5 cm below the right costal border, and presence of abdominal wall edema with signs suggestive of ascitic fluid were noted. Upon examination of the extremities, both the upper and lower limbs exhibited symmetrical pulses. Lower limb edema (LLE) (2+/4+) without calf padding was also present. For further evaluation, laboratory tests (Table 1), electrocardiogram (ECG) (Figure 1) (regular sinus rhythm, 1st degree atrioventricular block, low voltage in frontal plane shunts, electrically inactive zone in the anteroseptal region, and left bundle branch conduction disorder), chest X-ray (Figure 2) (increased cardiac area, a pattern of pulmonary congestion, and bilateral pleural effusion, more pronounced on the left). Transthoracic echocardiography (TTE) showed increased right heart chamber size, mildly depressed right ventricular (RV) systolic function, significant tricuspid regurgitation, moderate pulmonary hypertension, LV dysfunction (ejection fraction 44%), bi-atrial dilatation, and bright, granular echogenicity. Abdominal ultrasonography was performed, showing heterogeneous texture of the liver and spleen, an aspect suggestive of granulomatous disease, as well as pleural effusion on the left, and mild ascites. Chest tomography demonstrated normal heart size and preservation of vascular structures, consolidation components and atelectasis in the lower lobe of the left lung, focus with frosted glass attenuation in the inferior lingular segment, with an inflammatory-infectious pattern and moderate, bilateral pleural effusion. Abdominal radiography revealed distension of the intestinal loops and absence of gas in the rectal ampulla. Due to suspected depositive disease, a liver biopsy was required, which confirmed the diagnosis of amyloidosis. Diuretic therapy with spironolactone was started, but two days later the patient progressed with a serum potassium level of 5.58 mEq/L, and spironolactone was replaced with furosemide EV to decrease edema of LLE, in addition to starting simethicone and antiemetics. The patient evolved with difficulty for clinical compensation in the ward. Even with diuretic substitution, he presented acute renal failure, requiring hemodialysis. The patient progressed with a lowered level of consciousness, and was transferred to the Coronary Unit, where he suffered a bronchospasm and fatal cardiorespiratory arrest.

**Table 1 -** Laboratory tests

| Variable | Found Value | Reference Value |
|---|---|---|
| Hematocrit | 27% | 36 – 50% |
| Hemoglobin (g/ dL) | 9.9 | 12 - 17 |
| White blood cells (nº/ $mm^3$) | 11.3 x $10^3$ | 5 – 11 x$10^3$ |
| Platelets (nº/ $mm^3$) | 148 x $10^3$ | 150 – 400 x $10^3$ |
| INR | 1.32 | ≤ 1.0 |
| Urea (mg/ dL) | 93 | 15 - 45 |
| Creatinine (mg/ dL) | 3.21 | 0.5 – 1.3 |
| Sodium (mEq/ L) | 128 | 135 - 145 |
| Potassium (mEq/ L) | 4.48 | 3.5 – 5.5 |
| Chloride (mEq/ L) | 95.2 | 95 - 105 |
| PCR (mg/ dL) | 142 | < 0,5 |
| Calcium (mg/ dL) | 9.25 | 8.5 – 10.5 |
| Albumin (g/ dL) | 2.65 | 3.5 – 5.0 |
| Urine Analysis | Absence of Nitrite | Absence of Nitrite |
| Proteinuria | 3+/ 4 | Absence |
| Hemoglobinuria | 4+/ 4 | Absence |

INR: International Normalized Ratio; PCR: C-reactive protein

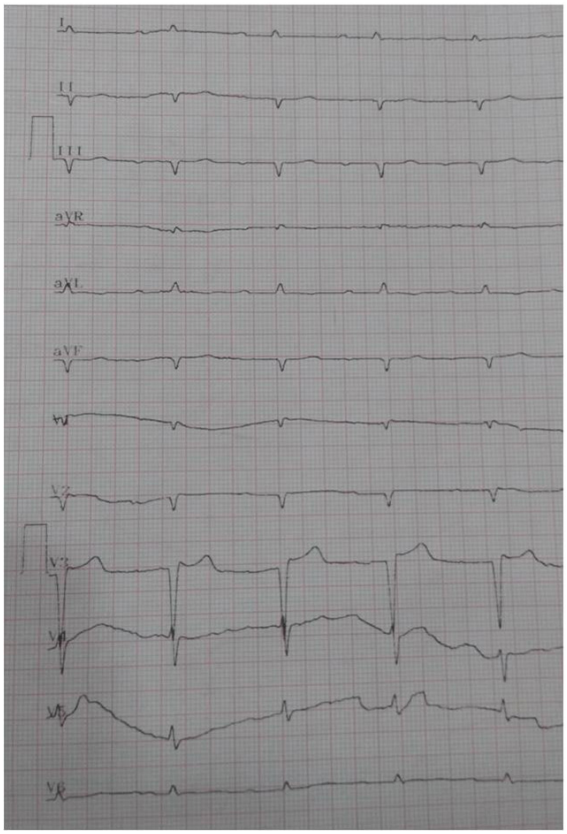

**Figure 1 -** Electrocardiogram showing regular sinus rhythm, 1st degree atrioventricular block, low voltage in frontal plane leads, electrically inactive zone in the anteroseptal region, and left bundle branch conduction disorder

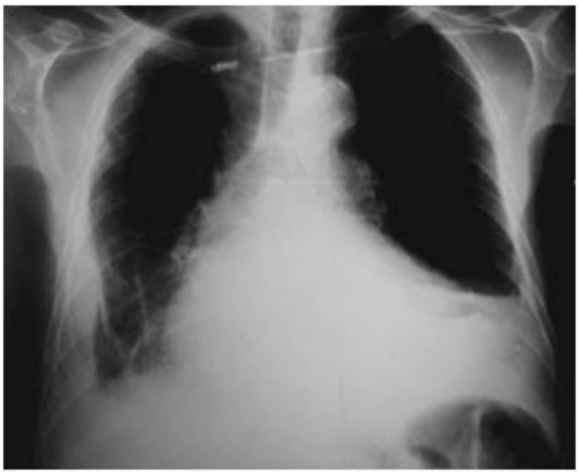

**Figure 2 -** Chest radiograph showing increased cardiac area, a pattern of pulmonary congestion, and bilateral pleural effusion, more evident on the left

## DISCUSSION

First described by Rudolph Virchow in 1954[1], amyloidosis is caused by the extracellular deposition of insoluble fibrils of low density proteins and is classified as systemic when these proteins are deposited in multiple organs. Localized amyloidosis occurs when deposition is restricted to a single organ. Another form of classification divides amyloidosis into: 1) primary (which may occur in isolation), 2) secondary (the deposit occurs as a

complication of infections or chronic inflammation). Thus, cardiac amyloidosis arises from the deposition of amyloid protein in cardiac tissue, with restrictive cardiomyopathy being the most common presentation[2].

Clinical manifestations depend on the affected organs, although nonspecific symptoms such as fatigue and/or anorexia may occur. Systemic amyloidosis usually presents with proteinuria as a first sign, due to renal involvement. Organs such as the liver, kidneys and heart may be enlarged in both primary and secondary amyloidosis[2].

It is not possible to establish a clinical presentation pattern of cardiovascular amyloidosis, and the disease should be suspected when uncontrollable chronic heart failure develops in patients older than 50 years, especially if it is associated with signs of restrictive cardiomyopathy, such as conduction disorders, low blood pressure, and atrial instability. In addition, compromise of other organs should be investigated because localized amyloidosis occurs in only 4% of the cases[3]. The clinical findings of ascending and progressive edema associated with hepatomegaly, as in the present case, suggest predominantly right heart involvement, highlighting the diagnosis of cardiopathy with diastolic restriction[4].

The gold standard for the diagnosis of cardiac amyloidosis is endomyocardial biopsy. Although associated with a low risk of complications (less than 1%), cardiac perforation with tamponade, significant vascular complication, emergency cardiac surgery, and death may occur. Therefore, in clinical practice, endomyocardial biopsy is rarely used[3]. Rahman et al.[5] compared the diagnostic efficacy of ECG and echocardiogram in conjunction with endomyocardial biopsy in patients with cardiac amyloidosis, noting that biopsy presents better diagnostic results.

Despite these results, the ECG is important to establish the diagnosis of amyloidosis. The most common finding from an ECG is low voltage in the frontal plane and low voltage of the QRS complex in limb leads[6], in addition to conduction disturbances[7], as observed in the present case. Another frequent observation is the pseudo-infarction pattern. Less frequently, paroxysmal or persistent atrial fibrillation and electrically inactive areas may occur[7].

Another important diagnostic method is echocardiography, which may show an increase in the thickness of the right and/or left ventricular walls. The visualization of increased wall thickness of the left ventricle along with the low voltage electrocardiographic pattern presents high specificity for cardiac amyloidosis. Even in asymptomatic patients, echocardiography is sensitive in detecting cardiac involvement in amyloidosis[8]. Although infrequent, finding bright, granular echogenicity also shows high specificity[9], as occurred in the present case.

Cardiac magnetic resonance imaging is also considered a good diagnostic method because it can identify myocardial and atrial septal thickening, signs of diastolic dysfunction, and a subendocardial late enhancement pattern in the LV[3]. In the case reported, the MRI was requested, but the patient died before the test.

Treatment of heart failure is primarily done by administration of diuretics. Cardiac glycosides usually do not benefit the patient's clinical condition, as in the majority of cases of amyloidosis, because diastolic dysfunction predominates. Calcium channel blockers, angiotensin converting enzyme inhibitors, and beta-blockers often induce hypotension, limiting their use in these patients. Regarding the surgical approach (cardiac transplantation) for the treatment of amyloidosis, there is no consensus in the literature and it is not indicated in advanced cases or in cases of systemic amyloidosis[10].

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