Case 3/2014 - 81-Year-Old Patient Hospitalized for Decompensated Heart Failure

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JJSA is an 81-year-old male patient hospitalized for decompensated heart failure. At 71 years of age, he experienced progressive dyspnea that lasted for 1 month and an episode of palpitation that lasted for 1 day and arrived at at the emergency department. He gave history of undergoing cardioversion in the past. He was then referred to the outpatient clinic of the InCor in October 1995. He also reported that he had long-term pulmonary arterial hypertension and had undergone surgery for the removal of an intracranial hematoma in the past.

Physical examination, during the first consultation (October 30, 1995), revealed the following: heart rate of 76 beats per minute (bpm), systemic blood pressure of 120/80 mmHg, normal findings on chest auscultation. However, cardiac auscultation revealed normal heart sounds, regular rhythm, and a systolic murmur (1+/4+) in the aortic area. Abdominal examination did not reveal any abnormalities and the patient did not have pedal edema.

ECG (October 30, 1995) showed sinus rhythm with atrial extrasystoles, heart rate of 100 bpm, and signs of right atrial overload (small QRS complex in lead V_1 and normal in lead V_2) as shown in Figure 1.

Four days later, he sought emergency medical assistance because the dyspnea had worsened. Physical examination (November 3, 1995) showed the patient was in a stable condition, had tachypnea (respiratory rate of 24 breaths per minute), heart rate of 80 bpm, and systemic arterial pressure of 90/70 mmHg. Chest auscultation revealed decreased breath sounds at the base of the right lung and crepitations at the base of the left lung. Cardiac auscultation revealed a regular rhythm with the heart sounds were muffled in both systolic and diastolic phases. There were no murmurs or pericardial rub. The liver was palpated 3 cm below the right costal margin and there was swelling of the right calf. Chest X-ray revealed right atrial opacification; ECG showed no changes.

The results of the laboratory tests were as follows: hemoglobin 16.9 g/dL, hematocrit 39%, leucocytes 5,500/mm^3 (60% neutrophils, 33% lymphocytes, and 7% monocytes), platelets 244,000/mm^3, sodium 145 mEq/L, potassium 4.3 mEq/L, urea 39 mg/dL, creatinine 1.7 mg/dL, and blood glucose 97 mg/dL. Room-air pulse oximetry showed pH 7.34, pO_2 66 mmHg, pCO_2 33 mmHg, oxygen saturation 94%, bicarbonate 22 mEq/L, base excess −8 mEq/L.

Pulmonary perfusion/ventilation scintigraphy (November 3, 1995) showed hypoperfusion in the right upper lobe, anterior basal and lateral basal segments of the right lower lobe, lateral basal segment of the left lower lobe, and anterior segment of the left upper lobe. Ventilation was normal except in the base of the right lung, where it was decreased. The examination indicated a parenchymatous pathology in the base of the right lung and thromboembolism in the other pulmonary regions (Figure 2).

The patient received oxygen supplementation via nasal catheter (1 L/min), intravenous heparin (1.000 U/h), 40 mg of oral furosemide, and 37.5 mg of oral captopril daily.

On the third day of hospitalization the patient showed tachycardia, and ECG revealed atrial flutter with atrioventricular block 2:1 (Figure 3). The patient underwent cardioversion and sinus rhythm was maintained (Figure 4) with amiodarone (600 mg daily).

The dyspnea ameliorated and the patient remained hemodynamically stable. He was discharged on the seventh day of hospitalization and was prescribed warfarin (5 mg), captopril (38.5 mg), furosemide (40 mg), and digoxin (0.25 mg) daily.

Echocardiographic evaluation (June 25, 1996) revealed the following measurements: aorta 33 mm, left atrium 52 mm, right ventricle 30 mm, left ventricle (diastole/systole) 64/55 mm, and ejection fraction 36%. There was thickening of the aortic valve without stenosis, moderate tricuspid insufficiency, diffuse hypokinesis of both ventricles, and the systolic pressure of the right ventricle was estimated as 77 mmHg, with signs of pulmonary arterial hypertension (pulmonary valve corrected with absent A wave). Serological tests for Chagas disease was negative.

Echocardiographic evaluation performed later (February 10, 1999) revealed the following measurements: aorta 34 mm, left atrium 47 mm, right ventricle 33 mm, left ventricle (diastole/systole) 64/51 mm, and ejection fraction 49%. There was thickening of the aortic valve with without stenosis, moderate tricuspid insufficiency, diffuse hypokinesis of both ventricles, and the systolic pressure of the right ventricle was estimated as 79 mmHg, with signs of pulmonary arterial hypertension (pulmonary valve corrected with absent A wave).

Keywords

Amyloidosis / diagnosis; Heart Failure / complications; Multiple Myeloma; Pulmonary Embolism.

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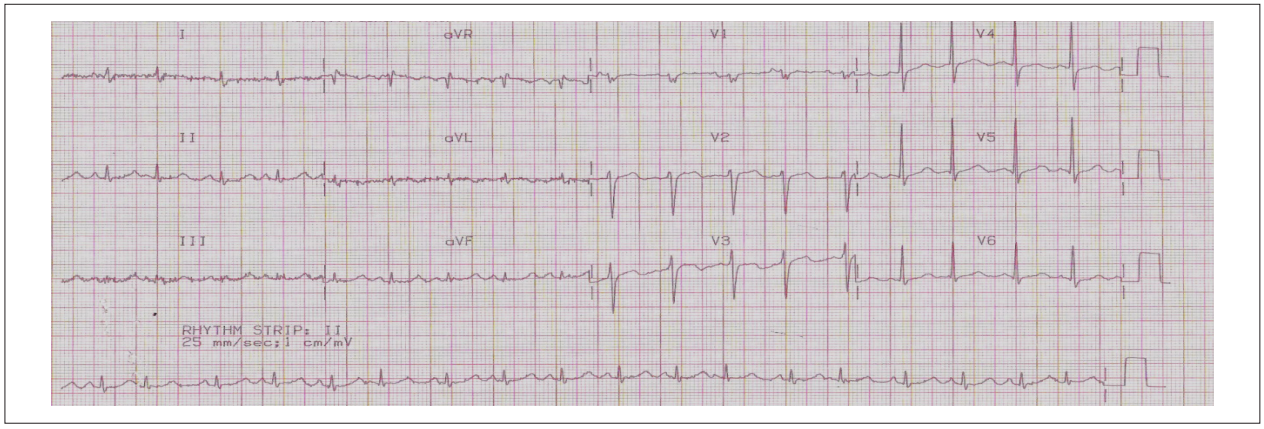

Figure 1 – *Electrocardiogram showing sinus rhythm and right atrial overload.*

The patient always experienced dyspnea on moderate exertion and there were several episodes of atrial flutter with subsequent 2:1 atrioventricular conduction, and the control of coagulation was irregular.

Laboratory tests performed in 2004 showed the following results: TSH 9.54 μU/mL, total cholesterol 112 mg/dL, HDL-C 47 mg/dL, LDL-C 53 mg/dL, triglycerides 52 mg/dL, creatinine 1.1 mg/dL, and glucose 87 mg/dL.

From 1999 onwards, the patient's daily medication consisted of spironolactone (25 mg), enalapril (40 mg), furosemide (40 mg), carvedilol (12.5 mg), digoxin (0.25 mg), and warfarin (5 mg).

An X-ray obtained on May 10, 2005, revealed right pleural thickening with opacification of the right costophrenic angle and the lower third of the right hemithorax.

A laboratory evaluation performed in January 2005 showed that creatinine had increased to 1.9 mg/dL. An analysis performed later (February 2006) showed an even higher level of 2.3 mg/dL, with urea of 66 mg/dL.

In February 2006, the laboratory tests results were as follows: total cholesterol 84 mg/dL, triglycerides 44 mg/dL, potassium 4.8 mEq/L, sodium 144 mEq/L, creatinine 2.3 mg/dL, urea 66 mg/dL, glucose 78 mg/dL, and PT-INR 1.6. The urinalysis results were as follows: density 1.01, pH 5.0, protein 0.6 g/L, free hemoglobin +++, leucocytes 56,000/mL, and erythrocytes 30,000/mL.

The patient was in a stable condition until March 3rd, 2006, when he sought medical assistance because of worsening dyspnea worsening and pedal edema (present for 10 days). He reported having stopped his medication approximately 1 month before.

Physical examination (March 3, 2006) revealed anasarca, heart rate of 80 bpm, systemic arterial pressure of 90/70 mmHg, lungs with decreased breath sounds in the base of the left lung. Cardiac auscultation showed irregular rhythm, muffled heart sounds, and a systolic murmur (++/4+) in the tricuspid area. There was abdominal swelling without tenderness, and bowel movements were present. Scrotal and pedal edema were present (++++/4+).

ECG (March 3, 2006) revealed an irregular rhythm without a visible P wave, frequent ventricular extrasystoles, low-voltage QRS complexes in the frontal plane and in V_4 to V_6 leads, and left bundle branch block (Figure 5).

The laboratory tests performed on March 3, 2006 showed the following results: erythrocytes 4.4 million/mm^3, hematocrit 43%, hemoglobin 14.4 g%, leukocytes 2,900/mm^3 (neutrophils 56%, eosinophils 2%, lymphocytes 32%, monocytes 16%), platelets 70,000/mm^3, PT-INR 1.8, magnesium, 1.9 mEq/L, calcium 4.76 mEq/L, creatinine 3.3 mg/dL, urea 124 mg/dL, potassium 4.8 mEq/L, sodium 140 mEq/L, and glucose 88 mg/dL.

The patient received 40 mg of furosemide intravenously and was prescribed 120 mg of furosemide, 37.5 mg of captopril, and 0.5 mg of digoxin daily.

The patient was diagnosed with congestive cardiac failure and malnutrition, thrombocytopenia, lymphopenia, and pneumonia. He was further prescribed 2 g of ceftriaxone as antibiotic prophylaxis.

The patient remained hypotensive and was administered intravenous dobutamine.

The laboratory test results on the second day of hospitalization (March 4, 2006) revealed the following: erythrocytes 3.7 million/mm^3, hemoglobin 12.7 g/dL, hematocrit 36%, MCV 97 μm^3, leukocytes 2,300/mm^3 (neutrophils 60%, eosinophils 2%, lymphocytes 25%, and monocytes 13%), platelets 54,000/mm^3, urea 127 mg/dL, creatinine 3.3 mg/dL, potassium 4.8 mEq/L, and sodium 145 mEq/L. In the afternoon that day, the patient suffered a cardiorespiratory arrest and died despite the attempts for cardiopulmonary resuscitation.

Clinical aspects

An 81-year-old man hospitalized for worsening dyspnea. The patient reported having systemic arterial hypertension for 10 years, with a history of electrical cardioversion for the treatment of cardiac arrhythmia and having been hospitalized in the past for decompensated heart failure.

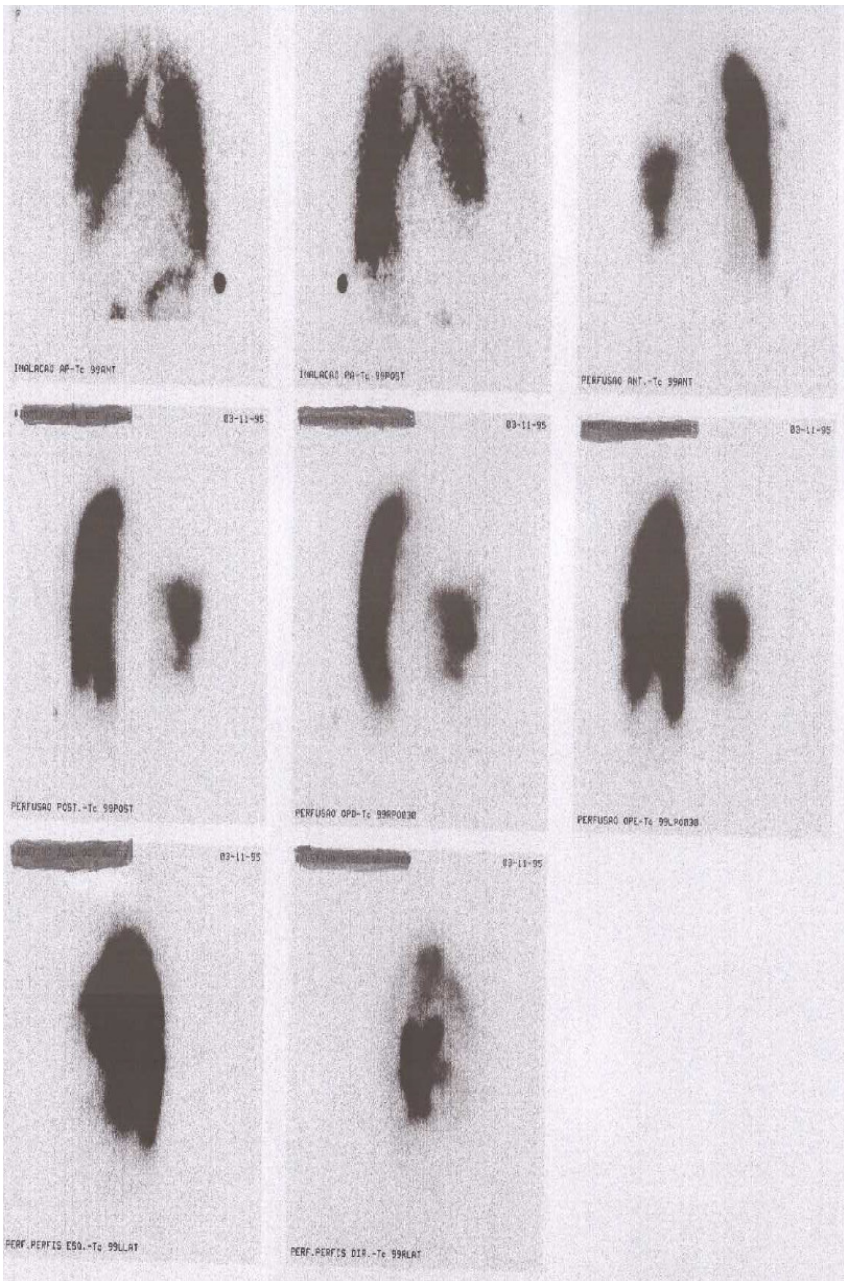

Figure 2 – *Pulmonary perfusion/ventilation scintigraphy showing hypoperfusion in the right upper lobe, anterior basal and lateral basal segments of the right lower lobe, lateral basal segment of the left lower lobe, and anterior segment of the left upper lobe, and decreased ventilation in the base of the right lung.*

During the penultimate hospitalization he had tachypnea and hypoxemia with the swelling of the right calf. Chest X-ray revealed opacification of the right lung base. On the basis of this data, the most probable diagnosis was pulmonary thromboembolism[1].

The clinical diagnosis was confirmed by perfusion/ventilation scintigraphy, which showed hypoperfusion with preserved ventilation. The complementary test most currently used is angiotomography of the pulmonary arteries, which is an alternative less invasive than the gold standard technique of pulmonary angiography. Pulmonary perfusion/ventilation scintigraphy has an important role as it diagnoses 30%–50% cases, although it may have a high rate of inconclusive results[1].

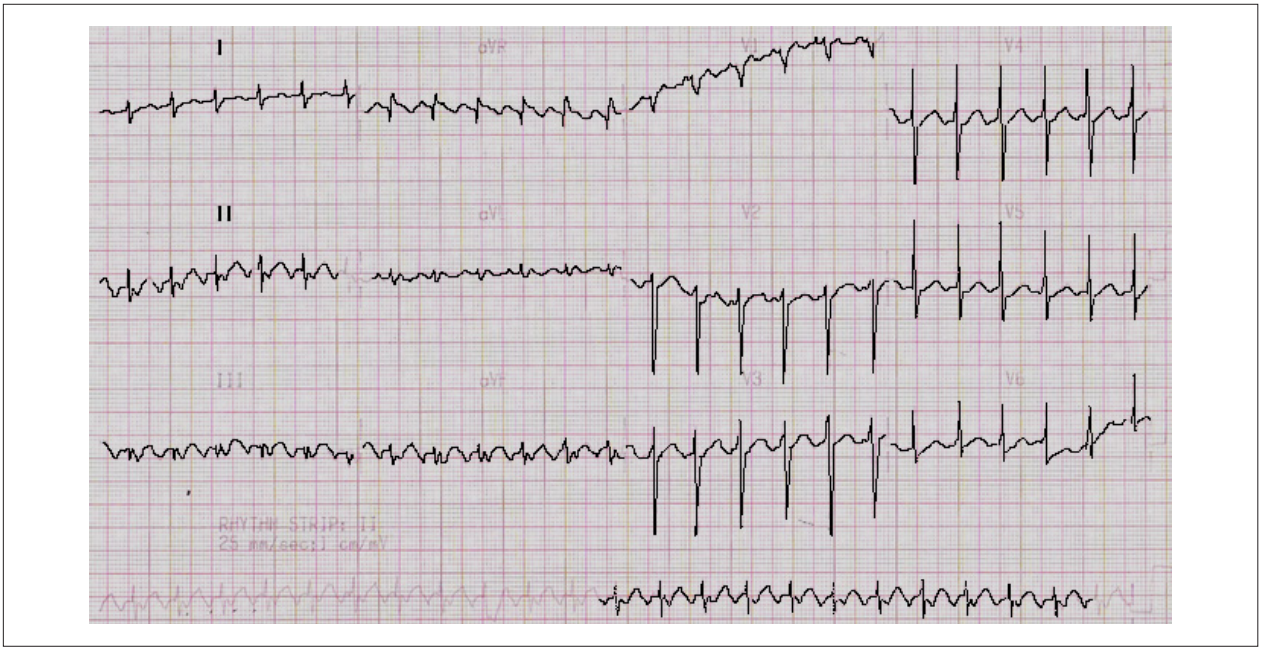

Figure 3 – *Electrocardiogram showing atrial flutter with a 2:1 atrioventricular block.*

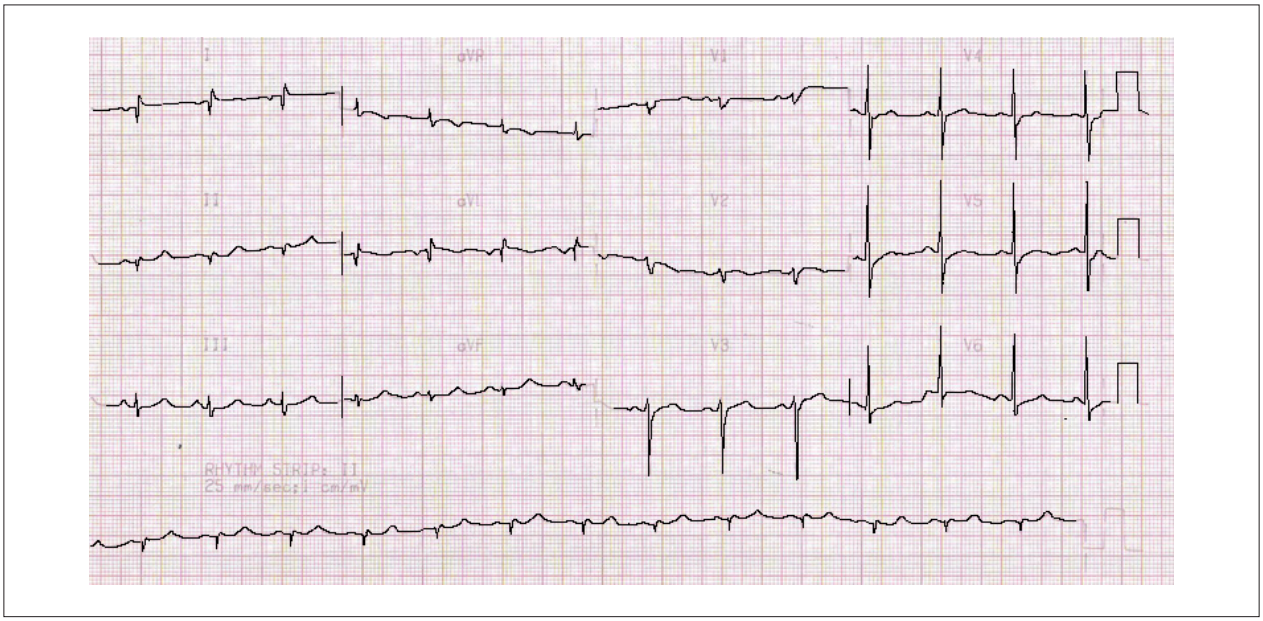

Figure 4 – *Electrocardiogram showing sinus rhythm and lateral inactive area.*

Ecocardiography revealed systolic dysfunction (left ventricular ejection fraction of 36%), enlarged left atrium (47 mm), and increased pulmonary artery pressure, a complication of pulmonary thromboembolism that is observed in up to 26% of cases[1].

Support therapy and anticoagulation treatment were initiated and maintained after hospital discharge.

With time, the patient improved but remained oligosymptomatic and showed progressive renal failure. He showed new cardiac decompensation after having interrupted the use of medications and was hospitalized for treatment. On admission, leukopenia, lymphopenia, and thrombocytopenia were observed. On admission, the chest X-ray showed pleural effusion and a pulmonary consolidation.

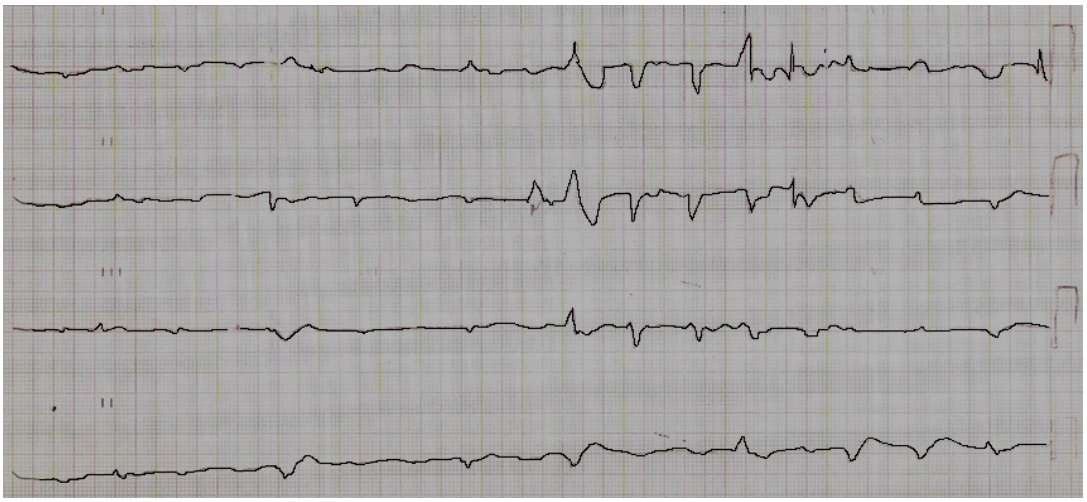

Figure 5 – *Electrocardiogram: ventricular extrasystoles, atrial fibrillation, left bundle branch block.*

The most probable diagnosis for this elderly patient, who had acute cardiac decompensation, was hypotensive, and whose chest X-ray showed consolidation, would be pneumonia and antibiotic therapy should be initiated. However, a diagnosis of myeloproliferative disorder should be considered because the patient had leukopenia, lymphopenia, and thrombocytopenia. The pulmonary thromboembolism, due to tumor embolism, may present itself as a consolidation in the chest X-ray[1].

Therefore, multiple myeloma is a possible diagnosis, because plasmocyte mutations are unique, with neoplastic proliferation of plasmocytes and production of monoclonal immunoglobulin that results in several alterations, such as cytopenia and renal failure.

Renal failure occurs in 20% patients with multiple myeloma. Renal damage is caused by the immunoglobulin light chains produced by the neoplasm. The early mortality rate is 30% among patients with myeloma who progress with renal failure and is mainly associated with sepsis[2].

Circulating immunoglobulins in multiple myeloma increase serum viscosity and allow the formation of thrombi and the occurrence of embolism. Therefore, it is reasonable to think that the patient may have had deep vein thrombosis followed by pulmonary thromboembolism, which can be an early manifestation of multiple myeloma[3].

Cardiac involvement can also occur, usually resulting in recurrent high-output decompensated cardiac failure[4]. Decompensated heart failure, in patients with multiple myeloma, can be divided into 2 subgroups: low-output failure, which is more common, and high-output failure[5].

High-output decompensated cardiac failure usually occurs in patients with with preserved left ventricular contractility or underlying structural heart disease, which leads to contractile impairment because of structural deterioration[5].

The cause of the high-output failure in multiple myeloma remains only partially understood and has been associated with several factors. These include increased splenic inflow in patients who have splenomegaly with a splenic inflow increase of 55% (in these cases, the spleen functions almost like a arteriovenous fistula), anemia, osteoclastic lesions caused by the disease, which produce substances that lead to high-heart output state[6].

Amyloidosis should be considered as a differential diagnosis or associated with multiple myeloma, because it can coexist in 10% cases[7]. Most frequently, multiple myeloma occurs first and amyloidosis develops later. Some authors have reported cases in which amyloidosis was diagnosed first; however, these cases tend to be more serious and have lower survival of approximately 1-2 years[7].

Amyloidosis is an uncommon disease and is therefore often not taken into consideration during diagnosis. It usually presents as restrictive cardiomyopathy, with systolic function preserved until its last stage. Biatrial dilation is also present, which leads to an increase in the incidence of thromboembolic events[8,9].

Therefore, secondary causes should be investigated in elderly patients with dilated cardiomyopathy, progressive worsening of renal function, and thromboembolic phenomena. Clinical changes primarily treated as conditions separate from the underlying disease may have a common origin of monoclonal gammopathy, which may present as amyloidosis and multiple myeloma. **(Dra. Bruna Affonso Madaloso)**

Diagnostic hypotheses: pulmonary thromboembolism, cardiac failure attributed to cardiac amyloidosis, multiple myeloma. **(Dra. Bruna Affonso Madaloso)**

Autopsy

At autopsy, the heart was heavy and enlarged; however, the chambers appeared normal. Microscopic examination showed that the primary disease was amyloidosis. This condition affected the myocardium (Figure 6) and the pericardium (Figure 7). In particular, obstructions were observed in the vascular tree of both coronary arteries, leading to the formation of areas of myocardial fibrosis. In addition, obstructions of the vessels supplying the pulmonary artery, and the aorta (vessels of the *vasa vasorum*) and of renal vessels were noted.

To investigate amyloidosis, we performed immunohistochemical analysis of immunoglobulin light chains. Kappa light-chain staining was negative and lambda light-chain staining was positive (Figure 8), indicating that the patient probably had multiple myeloma. Supporting this was the fact that he had pancytopenia and systemic signs compatible with neoplasia. In the bone marrow sample obtained at autopsy (rib, Figure 9), there was no plasmacytic proliferation or amyloid deposition; however, we cannot completely rule out the possibility that the disease was present in other locations.

The patient was hypertensive and had benign nephrosclerosis and myocardiocyte hypertrophy. In addition, he had chronic obstructive pulmonary disease. As a consequence, the patient had cardiac failure. Secondarily, he had thrombosis in the right atrium. Thus, pulmonary thromboembolism was the causative factor of death (Figure 10). **(Dr. Paulo Sampaio Gutierrez)**

Primary diagnosis: cardiovascular amyloidosis (AL type) (deposition of lambda light chain).

Secondary diagnosis: systemic arterial hypertension.

Causa mortis: pulmonary thromboembolism. **(Dr. Paulo Sampaio Gutierrez)**

Comment

The course of progression of cardiac failure suggests that the primary reason may not be amyloidosis. Possibly, the initial oligosymptomatic phase was caused by systemic arterial hypertension with hypertensive myocardiopathy. Amyloidosis had a major role in the worsening of the patient's condition and in the final outcome. Amyloid deposition was very significant in vessel walls.

In most cases, cardiovascular amyloidosis is usually diagnosed at autopsy[10]. A few years ago, we reported that <50% cases were diagnosed before patients die[11]. In particular, cardiac failure occurred in elderly patients and in patients with other diseases, as was the case with the present patient[11]. Other difficulties include the absence of low-voltage QRS complexes and the existence of systolic dysfunction. Hence, amyloidosis is suspected in cases of unusual clinical and physiopathological patterns, which normally involve younger patients; however, it occurs mostly in elderly patients who have comorbid conditions.

More than 20 proteins with anomalous conformation are known to form amyloid deposits. In the heart, the most common proteins are transthyretin (especially in senile cardiovascular amyloidosis) and light-chain amyloidosis (AL amyloidosis)[12]. AL amyloidosis appears to be more frequent; however, the number of cases of senile cardiovascular amyloidosis is increasing as a result of the aging of the population[13]. The prognosis of AL amyloidosis is worse than that of senile cardiovascular amyloidosis[14]. In the present case, lambda light-chain staining showed that the disease was AL amyloidosis, despite the patient's advanced age.

Gammopathies leading to AL amyloidosis and multiple myeloma are plasmocyte dyscrasias, but the relationship between these conditions is not direct. Only 10%-15% patients with myeloma exhibit amyloid deposition. The reverse, i.e., the number of patients with amyloidosis who present

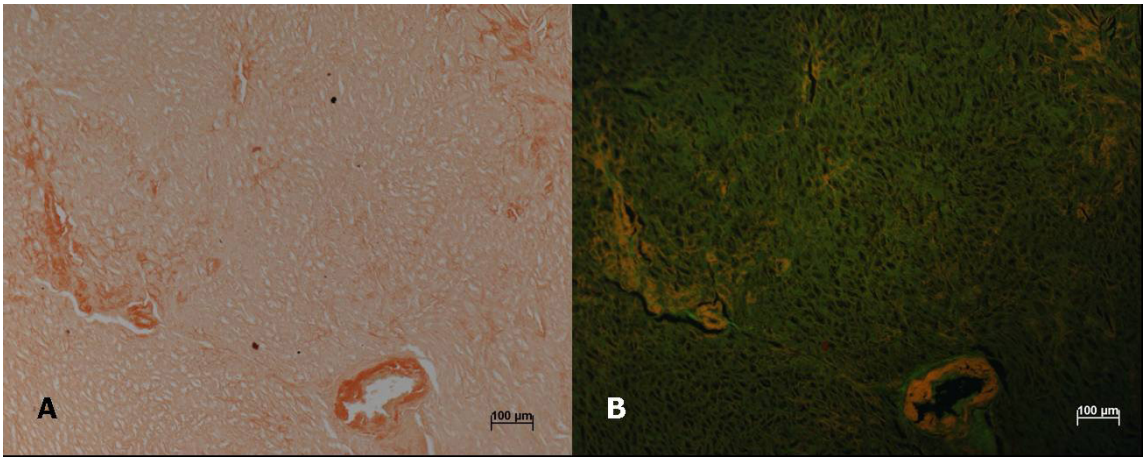

Figure 6 – *(A) Histological section of the myocardium stained with Congo red, showing amyloid deposits in small vessels and the interstitium. (B) Same area observed under fluorescence microscopy where the amyloid deposition is shown. Objective magnification: 10×.*

Anatomopathological Session

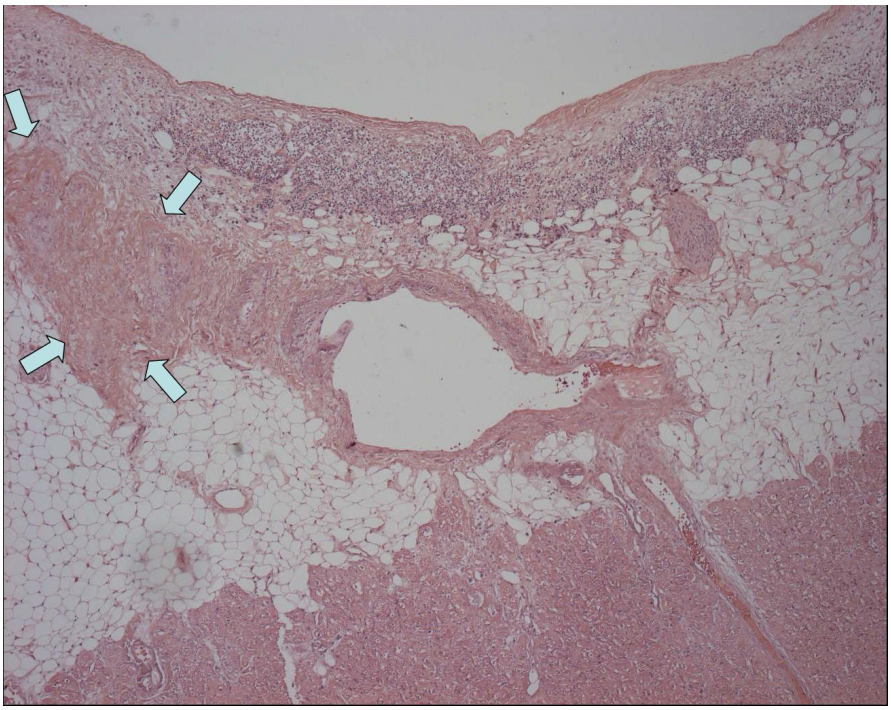

Figure 7 – *Histological section of the epicardium showing amyloid deposit indicated by arrows. Hematoxylin and eosin staining. Objective magnification: 40×.*

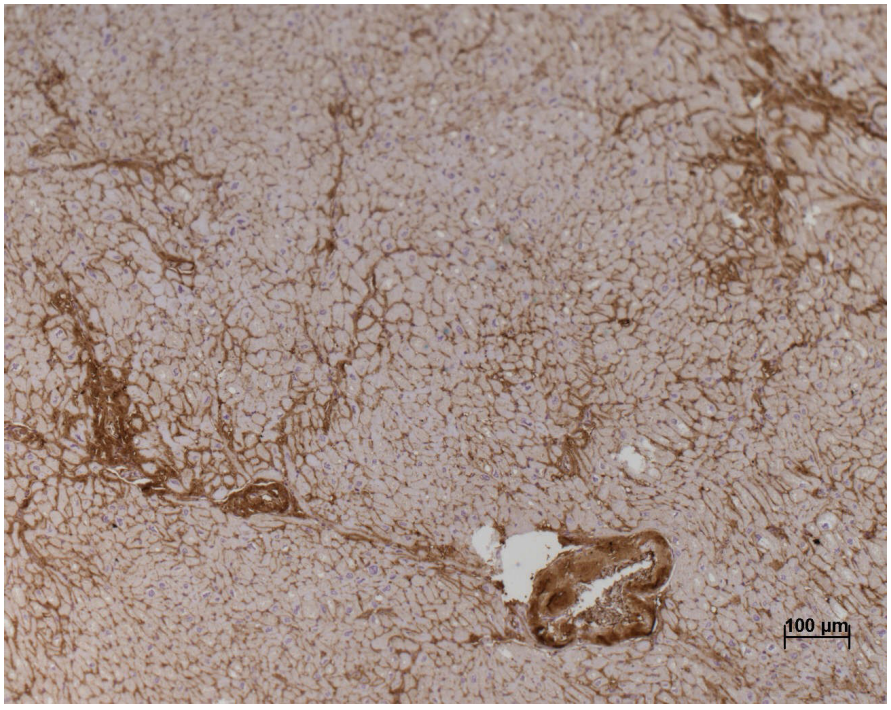

Figure 8 – *Histological section adjacent to that of Figure 6, with immunoperoxidase labeling for lambda light chain, showing positivity in the same areas of the amyloid deposition. Objective magnification: 10×.*

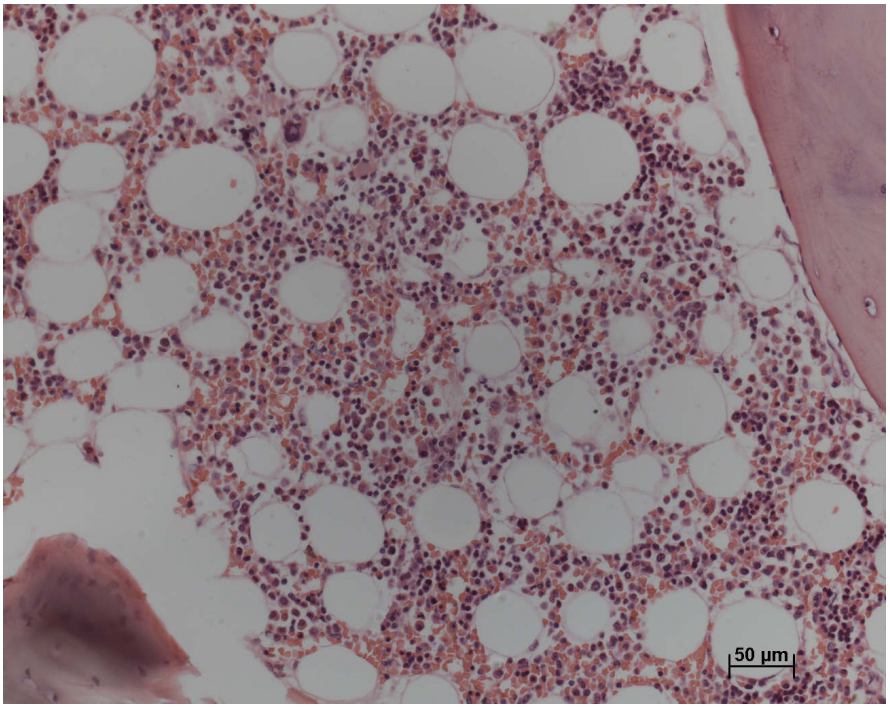

Figure 9 – *Histological section of the bone marrow showing absence of plasmacytic proliferation. Hematoxilin and eosin staining; objective magnification: 20×.*

myeloma, has been less analyzed. A study conducted with 46 patients with amyloidosis in several organs (83% with cardiac involvement) showed that 57% of them met the criteria for myeloma[15]. In the case of our patient, because amyloidosis was not clinically suspected, tests for multiple myeloma were not conducted. The bone marrow sample analyzed during autopsy did not exhibit plasmocyte proliferation; however, we cannot completely rule out the possibility that the disease was present in other locations.

Although amyloid deposition in the pericardium has been described[16], it is uncommon.

Pulmonary thromboembolism is the most frequent cause of death without diagnosis. In a survey conducted in our hospital[17], it accounted for 34% of the cases in which there were discrepancies between diagnoses and the autopsy findings.

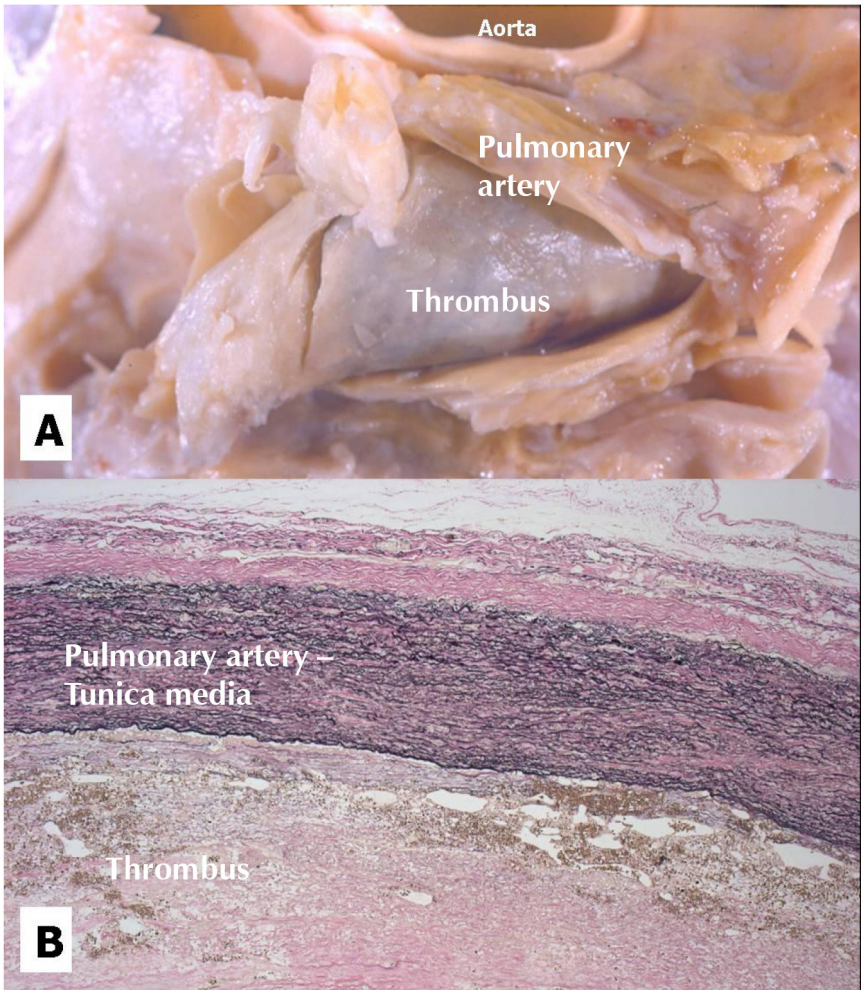

Figure 10 – *Thromboembolism of the central pulmonary artery: gross examination (A) and microscopy (B). Hematoxylin and eosin staining. Objective magnification: 5×.*

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