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Diagnosis of Systemic AL-Type Amyloidosis Revealed by Severe Restrictive Cardiomyopathy: Case Report and Literature Review

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Abstract **Case Report**

Amyloidosis refers to a group of systemic diseases whose common feature is the extracellular accumulation of insoluble fibrillar proteins in tissues (heart, reins, digestive tract). Several types of amyloidosis have been described; the primary (AL) and the secondary (AA) forms are by far the most frequent. AL amyloidosis is rare but not exceptional disease, with a prevalence of 500new cases per year in France. It is related to be precipitation in tissues of monoclonal light chains of immunoglobulin in the form of fibrils. Its diagnosis is histological based on the biopsy analysis of an affected organ or on non-invasive biopsies (subcutaneous fat, accessory salivary glands, etc) with the detection of amorphous deposits stained by congo red with dichroism and birefringence in polarised light, which is the reference examination. But the diagnostic approach can also be done by thioflavin staining which is very sensitive but not specific for amyloidosis and always requieres a diagnostic confirmation by congo red staining. We report the case of a patient with severe restrictive cardiomyopahy and presenting a set of paraclinical arguments specific for amyloidosis whose diagnosis was made by thioflavin staining.

Keywords: AL amyloidosis, restrictive cardiopmyopathy, diagnosis.

INTRODUCTION

AL amyloidosis belongs to the group of conformational diseases. It is a rare but not exceptional disease, with an estimated prevalence of 500 new cases per year in France [1, 2]. It is related to be precipitation in tissues of monoclonal light chains of immunoglobulin in the form of fibrils. The diagnostic approach is not always easy, especially when the disease is not accessible by biopsy. Nevertheless, some specific paraclinical arguments as reported in cardiac and renal involvement can reinforce the diagnostic presumption of amyloidosis. The specific diagnosis is based on histological analysis of biopsy of an affected organ or on non-invasive biopsies by the demonstration of amorphous deposits stained by congo red with dichroism and birefringence in polarised light [3]. However, thioflavin staining is also a good alternative for the detection of amyloidosis because of its extreme sensitivity [4], especially when there are paraclinical arguments in favor of diagnosis of amyloid involvement.

CASE REPORT

We report the case of a 57-year-old farmer, without cardiovascular risk factors or comorbidities, who consulted for dyspnea classified as NYHA II evolving for one year and worsening three months before being admitted, becoming NYHA III associated with paroxysmal palpitations. The physical examination noted: hypotension (90/60 mmHg), arrhythmia, right heart failure (lower limbs edemas, jugular veins spontaneous turgidity, hepatomegaly with a smooth border and a hepatic arrow at 18 cm, hepato-jugular reflux); splenomegaly grade 3 of Hackett classification.

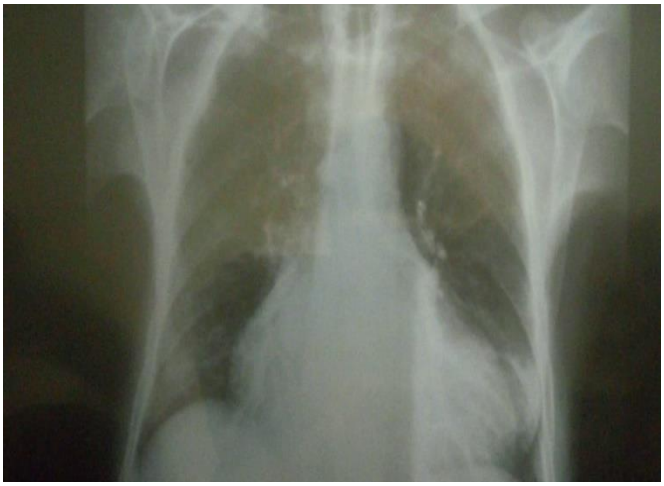

Fig 1: Frontal chest X-ray showing a 70% cardiomegaly with an important right overhang, some bilateral interstitial opacities with hilar overload

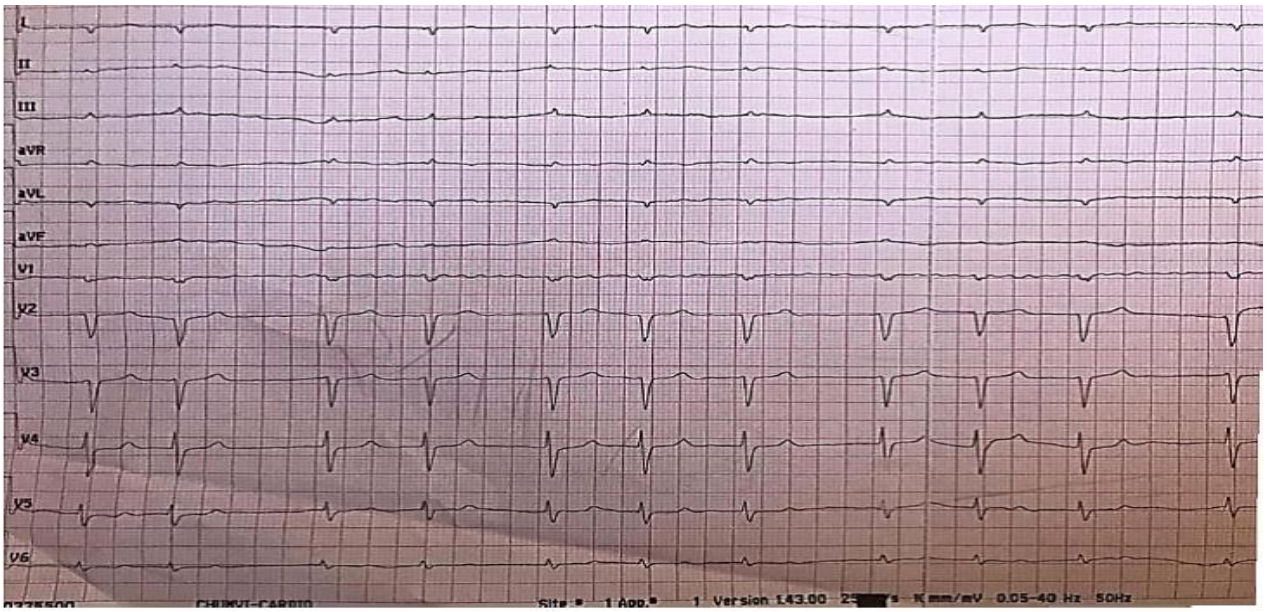

Fig 2: Electrocardiogram showing atrial fibrillation (70 cycles/min), right axis with diffuse microvoltage, anteroseptal and lateral high Q waves

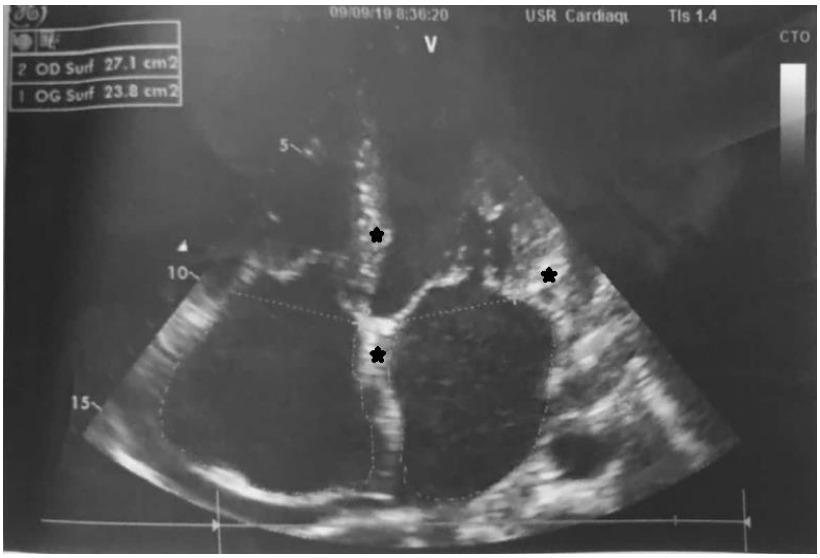

Fig 3: Transthoracic echocardiography showing a non- dilated and, hypertrophied left ventricle of 12mm with preserved systolic function, a dilated, hypertrophied right ventricle with preserved systolic function, pulmonary hypertension and dilated inferior vena cava

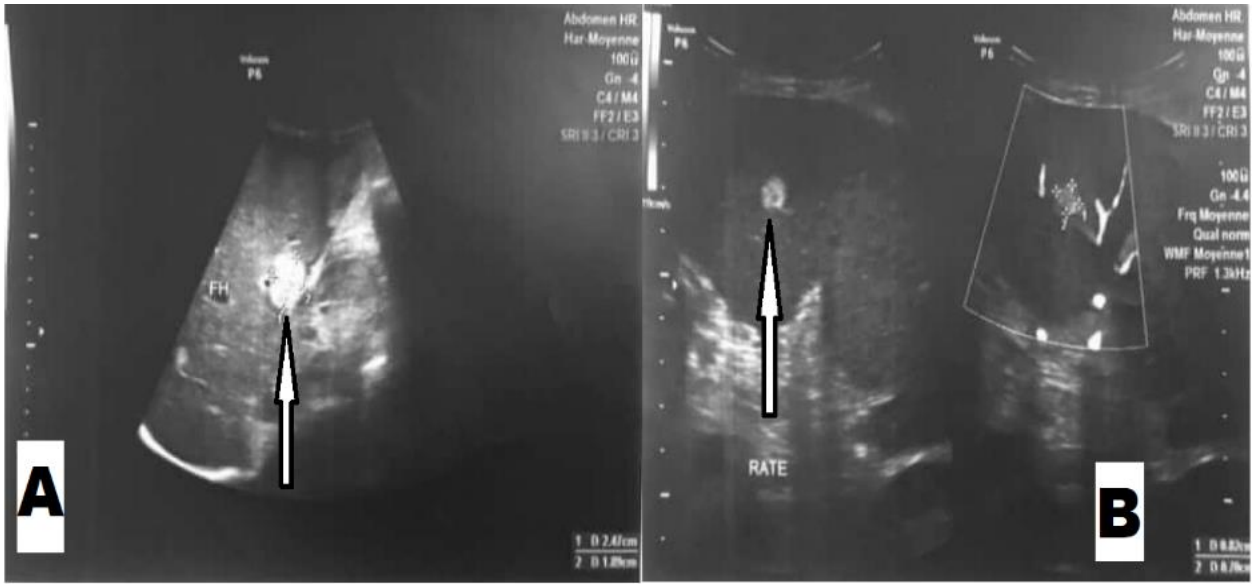

Fig 4: Abdominal ultrasound showing cardiac liver with signs of portal hypertension,two nodules in hepatic segments IV and VI measuring 8 and 29 mm respectively(A), a medio-splenic nodule measuring 8×7mm(B)

The blood count showed a regenerative anemia (8g/dl), the direct coombs test was negative, the sedimentation rate was accelerated (115mm) and serum ferritin was high (1514ng/ml), but serum iron, transferrin and transferrin saturation coefficient were normal making the possibility of hemochromatosis unlikely. To assess the severity of restrictive cardiomyopathy we used the Mayo Clinic score which was score III with troponins 240ng/L (N≤ 13) and NT-ProBNP 23000pg/ml(N≤125). Pathological examination after salivary gland biopsy showed focal, perivascular amyloid deposits on thioflavin staining. In the search for systemic involvement, particulary renal, the 24-hour proteinuria was positive (380g/L) with presence of light chain proteins of lambda type in urine(Bence-Jones proteins).

DISCUSSION

AL amyloidosis is a serious disease affecting slightly more men than women. The average age at diagnosis in some series is estimated at 65 years but it can also affect young adults with about 10% of patients diagnosed before the age of 50 [3]. Amyloidosis can be localized or systemic; the organs most frequently affected by AL amyloidosis are the heart (50%), kidneys (50%), liver and gastrointestinal tract (25%), peripheral nerves (20%); other localizations, notably splenic with sometimes functional hypo-splenism have been described [3, 5]. Diagnosis is made by Congo red staining of a tissue biopsy sample, which shows a pathognomonic apple green dichroism under polarized light [6]. On the other hand, thioflavine staining is very sensitive to amyloid fibrils but less specific than Congo red staining. Therefore, it is recommended to confirm the results obtained with thioflavine by electron microscopy or by the Congo red [4]. However, in the case of a group of clinical and paraclinical arguments, this confirmation can be dispensed with. Indeed, amyloid heart disease, recognizable by its scintillating appearance on echocardiography, is a major prognostic factor. Approximately 60% of patients have cardiac involvement at the time of diagnosis, half of whom are symptomatic. The deposits thicken the myocardial walls, leading to a restrictive cardiomyopathy responsible for progressively increasing asthenia and dyspnea [7]. The Infiltration of the bundle of conduction can lead to conduction abnormalities, atrial and ventricular rhythm disorders. The diagnosis is sometimes difficult and often delayed. Clinical signs are not very specific: asthenia, dyspnea and edema of the lower limbs. The electrocardiographic signs are characteristic: microvoltage (QRS< 0.5 cm) in peripheral leads and pseudo-necrosis Q waves in precordial leads. The cardiac prognostic score (Mayo score) based on NT-proBNP and troponin measurement remains the most widely used in routine practice and in clinical trials [1, 3]. The Median survival for stages I, II, and III were 26.4, 10.5, and 3.5 months, respectively [3, 8]. In our case, the severe cardiac involvement was associated with a hepatosplenic involvement with splenic sequestration responsible for the profound anemia, which corroborates the literature data, which report several involvements at the time of diagnosis of AL amyloidosis [3]. The Hepatic impairment manifested by hepatomegaly associated with an isolated elevation of alkaline phosphatases without hepatocellular insufficiency is detected at diagnosis in 30% of patients. Fibroscan can help in the diagnosis [9]. The Splenic involvement is apparent when the deposits are massive, by signs of hyposplenism, with Howell-Joly bodies on the blood smear and hyperplaquettosis sometimes revealing the diagnosis. On the hematological plan, an increased bleeding problem is often observed. This is due to the coagulation factor deficiency (especially factor X which is bound by amyloid), hyperfibrinolysis and platelet dysfunction [1, 2]. Although AL amyloidosis remains an often

incurable disease, much progress has been made in recent years with the development and validation of criteria for organ damage, prognostic staging, and response to treatment (hematological and clinical). The treatment goal is to reduce the monoclonal protein responsible for the deposits to a minimum through chemotherapy drugs that are effective on the clone that synthesizes the amyloidogenic protein.

CONCLUSION

AL amyloidosis is a pathology that can be presented in an extremely diverse way and the cardiac involvement determines the prognosis of the disease. The specific diagnosis is based on Congo red staining of a tissue biopsy sample, but other less specific but very sensitive stains such as thioflavin staining support the diagnosis, especially in the presence of other criteria such as: a flickering appearance of the myocardium on echocardiography, peripheral microvoltage on ECG, Bense-Jones proteinuria on immunofixation.

Informed consents of the patient: Oral informed consent has been obtained from the patient.

Conflicts of Interest: The authors declare no conflicts of interest.

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