

Cardiac Amyloidosis: A Case Report of Seven Patients

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Abstract

Introduction: Cardiac amyloidosis is a rare and under-diagnosed disease. The objective of this study was to collect cases of cardiac amyloidosis in patients hospitalized in the cardiology department of the Centre Hospitalier Intercommunal Alençon-Mamers (CHICAM). Patients and Methods: This was a retrospective descriptive study of the records of patients diagnosed with cardiac amyloidosis. The study took place in the cardiology department of the CHICAM over 12 months (from January 1, 2020 to December 31, 2020). We included the files of patients in whom the diagnosis of cardiac amyloidosis was confirmed on the basis of clinical, echocardiographic, biological, scintigraphic and cardiac MRI evidence. Results: Seven patients were included. The mean age was 86.71 years. Six men for one woman. Most of the patients were in heart failure. There was one case of periorbital ecchymosis. Troponinemia was increased in three patients, NTproBNP was always high with a mean of 1000 ng/L. Cardiac echography showed a hyperbright septum in four cases, concentric hypertrophy of the left ventricle with a mean interventricular septum in diastole of 13.85 mm. Six cases were senile transthyretin amyloidosis (TTR), one case was mutated transthyretin amyloidosis (TTRm). Two cases of death were noted. Conclusion: Cardiac amyloidosis has a poor prognosis due to delayed diagnosis.

Keywords

Cardiac Amyloidosis, Echocardiography, Heart Failure, Myocardial Scintigraphy

1. Introduction

Cardiac amyloidosis is a rare disease that belongs to the infiltrative cardiomyopathies and corresponds to deposits of substances in the myocardial tissue resulting in structural abnormality and/or impairment of cardiac function [1] [2]. There are between 1000 and 5000 new cases per year in the United States [3] [4]. Classically, there are two types of infiltration: extracellular infiltration represented by pathologies such as cardiac amyloidosis or cardiac sarcoidosis; and intracellular infiltration represented by Fabry disease or iron overload [2]. The clinical manifestations result from the location and type of these amyloid deposits, as well as from the toxicity of certain soluble precursors (for example immunoglobulins) [5]. Two precursors are responsible for the three types of cardiac amyloidosis: light chains (LC) of immunoglobulin, involved in AL amyloidosis; mutated transthyretin (TTR), involved in hereditary amyloidosis (ATTR-h); and wild-type TTR involved in senile amyloidosis (ATTR-wt) [5]. This pathology, long considered rare, is very underestimated and diagnosed too late [6]. Echocardiography and magnetic resonance imaging (MRI) are complementary in the diagnostic approach, but these two examinations do not allow to distinguish the different forms of amyloidosis (AA, AL, mutated TTR). Scintigraphy may point to the transthyretin forms [7]. The prognosis of this condition is poor because of the delay in diagnosis. The aim of this study was to collect cases of cardiac amyloidosis in patients hospitalized in the cardiology department of the Centre Hospitalier Intercommunal Alençon-Mamers.

2. Patients and Methods

This is a retrospective descriptive study of the records of patients diagnosed with cardiac amyloidosis. The study took place in the cardiology department of the CHICAM over 12 months (from January 1, 2020 to December 31, 2020).

- 1) Selection criteria
- 2) Inclusion criteria

We included the files of patients in whom the diagnosis of cardiac amyloidosis was confirmed on the basis of clinical, echocardiographic, biological, scintigraphic and cardiac MRI arguments.

3) Criteria for non-inclusion

Patients with suspected but unconfirmed amyloidosis were not included. We studied:

*Sociodemographic variables (age, sex);

*Clinical (right or left heart failure, chest pain, syncope, orthostatic hypotension) or extracardiac (including digestive, neurological, skin or kidney);

- *Paraclinical:
- electrocardiographic data;
- Biological data (NTproBNP, troponinemia, inflammatory assessment, liver assessment);
- serum protein electrophoresis; search for serum free light chains; urinary

protein electrophoresis;

- radiological (search for cardiomegaly with a cardiothoracic ratio greater than 0.5 and signs of overload);
- echocardiography with first of all an interventricular septal thickness superior to 12 mm in the absence of arterial hypertension or other cause of left ventricular hypertrophy;
- MRI for morphological abnormalities;

MRI for morphological abnormalities; -diphsophonate scintigraphy for cardiac amyloid deposits.

*Therapeutic variables: we analyzed the symptomatic treatment, particularly that of heart failure, but also the specific treatment.

- The average time between the onset of symptoms and the diagnosis

- The evolution in 12 months of the included patients.

We expressed the qualitative variables in percentage and the quantitative ones in average.

3. Results

A total of seven (07) patients were collected during this period. The average age of our patients was 86.71 years. We noted six (06) men for one woman.

The average delay between the diagnosis and the first symptoms was 16 months. The main cardiac manifestations were: heart failure (6/7), chest pain (2/7). An extracardiac localization (periorbital ecchymosis) was present in one patient (Table 1).

The ECG abnormalities found were atrial fibrillation (5/7) (**Figure 1**), atrial flutter (1/7), sinus dysfunction (2/7).

In five cases, the chest X-ray showed cardiomegaly.

Cardiac echocardiography showed a hyperbright septum in four cases, concentric left ventricular hypertrophy (Figure 2) with a mean interventricular septum in diastole (IVSd) of 13.85 mm, mean left ventricular election fraction (LVEF) at diagnosis was 51%, two cases of moderately tight calcified aortic stenosis (CAS), global strain was altered in two patients (Figure 3).

Cardiac MRI was abnormal in six of seven cases. Salivary gland biopsy was

Characteristics	N = 07
Male gender	06
Average age	86.71 years
Cardiac manifestations	
Heart failure	06
Chest pain	02
Extracardiac manifestations	
Periorbital ecchymosis	01

Table 1. Characteristics of the study population.



Figure 1. Atrial fibrillation with mean ventricular rate at 93 beats/min, anteroseptal R-wave planing, diffuse micro voltage.



Figure 2. Two-dimensional cross-sectional echocardiographic image of the four chambers showing biauricular dilatation, hypertrophy of the myocardial walls with a hyperbrilliant septum, infiltration of the mitral valves, pericardial detachment in the right retroatrial area.

performed in two patients. Troponinemia was increased in three patients, NTproBNP was always elevated with a mean of 1000 ng/L.

Six (06) cases were senile transthyretin amyloidosis (TTR), one case of mutated transthyretin amyloidosis (TTRm) for which genetic testing is in progress. The diagnosis of amyloidosis was made on the basis of the combination of the

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Figure 3. Global longitudinal strain (GLS) altered to -9% and a longitudinal strain in 4 cavities to -8.4%.

clinical picture, the appearance suggestive of cardiac amyloidosis on echocardiography or cardiac MRI and the demonstration of amyloid deposits on scintigraphy. Four (04) patients received the specific treatment of amyloidosis based on Tafamadis associated with the symptomatic treatment of the insufficiency. One patient had refused to take the specific treatment. Two patients had a pacemaker.

The evolution at 12 months was good with a clear improvement of the symptoms.

However, we noted two deaths before the beginning of the specific treatment.

4. Discussion

This study is the very first series in our department. However, the size of our sample, and the absence of salivary gland biopsy in all our patients constitute our main limitations. The presence of myocardial transthyretin deposits was initially described from autopsy series [8] [9] [10] [11]. In these series, 11% to 25% of deceased patients had transthyretin amyloid fibril deposits in the atria or ventricles. As described in the literature, transthyretin cardiac amyloidosis occurs at an advanced age beyond 70 years [6] with a male predominance, which is the case in our series with a mean age of 86.71 years. It is also important to know that most hereditary transthyretin cardiac amyloidosis becomes symptomatic after 55 years of age. This late age of onset would probably explain the underdiagnosis of this condition. Because of the aspecific clinic, the delay between the first symptom and the diagnosis is long, Isabel C et al. [12], reported in their series an average delay of 14 months. This result is comparable in our study where we found an average delay of 16 months between the symptomatology and the diagnosis. The clinical picture was dominated by heart failure followed by chest pain in two patients. We noted one case of periorbital ecchymosis. Several studies agree that the clinical symptomatology is aspecific, and the cardiac involvement is dominated by signs of heart failure [5] [6] [7] [12]. It should be noted that in some cases, the disease will be revealed by syncope secondary to conduction disorder or cardiac rhythm disorders including atrial fibrillation or atrial flutter [12].

Its electrical abnormalities were also found in our series. From a diagnostic point of view, echocardiography is the most classical examination proposed for the diagnosis of amyloid cardiomyopathy. In addition to the classical parameters allowing the diagnosis of the amyloid character of the cardiopathy (hyperbrilliant aspect of the cardiac parenchyma, thickening of the interventricular septum, thickening of the right ventricular wall, reduction of the left ventricular chamber), new parameters have been measured such as the longitudinal strain allowing the evaluation of the deformability of the heart (1). This examination was abnormal in all our patients. It also allowed us to find a calcified aortic narrowing which is often associated with cardiac amyloidosis. LVEF was preserved in the majority of cases, which is common in cardiac amyloidosis where LVEF remains preserved or minimally impaired until late in the disease, although systolic function assessed by tissue Doppler or strain analysis is rapidly impaired, with abnormalities predominating in the basal segments of the left ventricle (apical sparing) [13]. Other examinations are useful for the diagnosis, in particular cardiac MRI and bone scintigraphy. Cardiac MRI provides both a reliable diagnostic approach and prognostic information. Cardiac biomarkers (tropinine and natriuretic peptides) were elevated in our series. Elevation of these cardiac markers is very common in cardiac amyloidosis. It reflects the elevation of intramyocardial pressures and the suffering of cardiomyocytes secondary to interstitial amyloid infiltration that isolates cardiac cells from vessels. Therapeutically, all our patients benefited from conventional symptomatic treatment of heart failure associated with specific treatment with Tafamadis in four patients. Two patients refused this treatment. Although frequently prescribed in heart failure, diuretics should be used with caution in amyloidosis. Indeed, one of the consequences of the decrease in myocardial compliance is a decrease in ventricular end-diastolic volumes. The reduction in preload by diuretics may therefore worsen the reduction in systolic ejection volume, further deteriorating the hemodynamics of these patients and leading to symptomatic hypotension. For the same reason, the use of antihypertensive drugs, such as ACE inhibitors and angiotension 2 receptor blockers (ARBs), is often risky and poorly tolerated and should be avoided. Finally, the negative chronotropic effect of beta-blockers, sought in other causes of heart failure to prolong the diastolic filling phase, may deprive patients of an adaptive tachycardia that is then the only compensatory mechanism for reduced systolic ejection volume, and are therefore to be avoided. It should be noted that many patients with ATTR-wt amyloidosis already have these molecules in their usual treatment when amyloidosis is diagnosed [5]. The prognosis of this condition is poor, probably because of the delay in diagnosis; in our series we recorded two deaths. The median survival after a first episode of heart failure is less than four years [14].

5. Conclusion

Senile amyloid heart disease is an infiltrative heart disease with an underestimated frequency due to delayed diagnosis. Emphasis should be placed on the search for this condition in the presence of suggestive echocardiographic signs. However, calcified aortic stenosis in elderly subjects should be considered. The prognosis remains poor despite the advances in diagnosis and treatment in recent years.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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