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Case Report Open Access

Atrioventricular Conduction Disturbance Revealing Cardiac Amyloidosis in Young Adults: A Report of Two Cases

[*]Lobna Laroussi, Afef Ben Halima, Marouane Boukhris, Zied Ibn Elhadj, Hendkeskes, Sonia Marrakchi, Ikramn Kammoun, Faouzi Addad, Salem Kachboura

[*]Cardiology department, AbderrahmenMami Hospital-Ariana, Faculty of Medicine of Tunis, University Tunis El Manar, Tunisia

Abstract

Introduction

Amyloidosis is uncommon in young adults. Cardiac involvement is usually characterized by the presence of a restrictive cardiomyopathy. We report two cases of symptomatic conduction disorders, which were associated with cardiac amyloidosis in young patients.

Case reports

Case 1: A 30-year-old man consulted for loss of consciousness. Electrocardiogram showed a first-degree atrioventricular block alternating with complete atrioventricular block and sino atrial block. At echocardiography, we noted biatrial dilatation. The histopathological examination of labial biopsy was in favour of AL amyloidosis. A dual chamber pace maker was implanted. After 10 years of follow up, the patient was asymptomatic but he developed atrial fibrillation.

Case 2: A 37-year-old woman was admitted for syncope. She had no previous medical history, no family history of sudden cardiac death or syncope. There was a first degree atrioventricular block on the ECG with PR duration of 480 ms. Echocardiographic study showed an abundant circumferential pericardial effusion without signs of hemodynamic repercussion. The electrophysiological exploration was in favor of a nodal block. She was implanted by a dual chamber pacemaker. She underwent a surgical drainage of the pericardial effusion. The histological examination of the biopsy was in favor of AL amyloidosis. After a follow up of two years, the patient was asymptomatic.

Conclusion

Cardiac amyloidosis should be suspected in young patients with conduction disorders. These patients are usually brought to be implanted with a pacemaker. After the implantation, patients did not complain dizziness or loss of consciousness suggesting that their symptoms were due to conduction disorder.

Keywords

Cardiac Amyloidosis; Conduction Disorders; Atrioventricular Block

Introduction

Amyloidosis is an uncommon pathology, with an age-adjusted incidence varying from 6.1 to 10.5 per million person-years [1]. The contemporary understanding of amyloidosis points to a group of complex systemic disorders involving the extracellular deposition of insoluble fibrils composed of a variety of serum proteins (amyloid), resulting in tissue involvement. Amyloid deposition can be either localized or systemic (all organs except the brain) [2-3].

***Corresponding author:** Lobna Laroussi, Cardiology department, AbderrahmenMami Hospital-Ariana, Faculty of Medicine of Tunis, University Tunis El Manar, Tunisia. E-mail: lobna_laroussi@hotmail.com

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Cardiac amyloidosis can be isolated to the heart, but it is often associated with other organs involvement [3, 4]. Cardiac involvement may either be clinically patent or only detected on routine investigation in patients with non-cardiac symptoms [4]. The presence and the severity of cardiac involvement depend on the amyloidosis type and the importance of amyloid deposition [4]. This cardiac involvement may occur in the three main types of amyloidosis: acquired monoclonal light-chain, transthyretin-related hereditary amyloidosis (ATTR) and senile amyloidosis.

Electrocardiography and transthoracic echocardiography represent important diagnostic and prognostic tools in patients affected by cardiac amyloidosis. Cardiac involvement is usually characterized by the presence of an infiltrative/restrictive cardiomyopathy with classical echocardiographical findings, which have been already well described [5, 6]. Major electrocardiographic conduction disturbances might also be frequently associated.

We report two cases of symptomatic conduction disorders revealing cardiac amyloidosis in young patients.

Case reports

Case 1

A 30-year-old man with history of deep vein thrombosis and positive anti-cardiolipin antibodies was referred to our department for several episodes of loss of consciousness over the previous 3 years leading to several traumas. No prodromes were reported.

On admission, blood pressure was 120/70 mmHg without orthostatic hypotension, and heart rate was regular (50 bpm). Rest electrocardiogram (ECG) showed a first degree atrioventricular block (PR=400 ms) alternating with complete atrioventricular block and sino atrial block.

Chest x-ray found a cardiothoracic ratio of 0, 58. At echocardiography, the left ventricle was not dilated (diastolic diameter= 55 mm and systolic diameter=39 mm) with no thickened left ventricle wall (inter ventricular septum=11mm). The systolic and diastolic functions were normal [Figure 1]. Both right and left were dilated: 43 cm^2 and 33cm^2, respectively.

Holter-ECG monitoring showed an average frequency of 52 bpm. Along the 24 hours, there was an alternating junctional rhythm with atrioventricular and sino atrial block. In addition, we found 40 pauses; the longest one was 2615 ms [Figure 2].

Figure 1: Transmitral Doppler showing a normal diastolic function

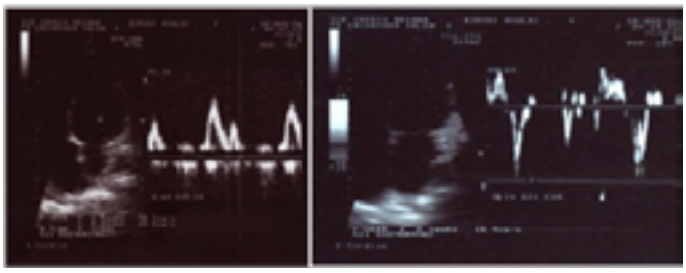
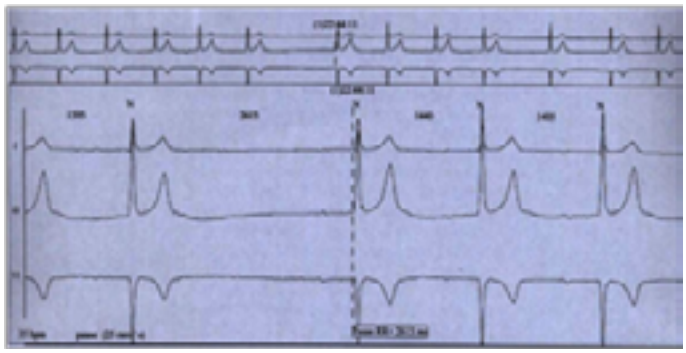


Figure 2: Holter monitoring showing a long pause of 2615 ms.



Serum electrophoresis was normal (no increase in gamma globulin). There was no Bence-Jones protein. The labial biopsy was performed. The histopathological examination showed interstitial deposits of extracellular homogeneous eosinophilic material with affinity for Congo red stain and typical apple-green birefringence under polarized light, characteristic of amyloid substance. Immuno-histochemical stains were positive for AL (primary) amyloidosis expressing the lambda light chain.

The diagnosis of cardiac amyloidosis was then confirmed. Since the patient was very symptomatic with frequent syncope leading to several trauma, we decided to implant a dual chamber pacemaker.

After 10 years of follow up, the patient is asymptomatic with no more syncope but he developed atrial fibrillation with increase in right and left atrial volumes. Oral anticoagulation was indicated despite CHADS Vasc score of 0

Case 2

A 37-year-old woman was admitted for lipothymia with previous episodes of syncope. She had no previous medical history; no family history of cardiovascular disease, sudden cardiac death or syncope was reported.

On physical examination, blood pressure was 100/60 mmHg without orthostatic hypotension and heart rate was 60 bpm. ECG revealed a first degree

atrioventricular block (PR duration of 480 ms).

The Holter ECG recording showed the presence of sinus bradycardia with a mean heart rate of 53bpm with an alternation between episodes of Luciani Wenckebach, 2/1 atrio ventricular block and sino-atrial block

Echocardiography found an abundant circumferential pericardial effusion without hemodynamic signs of tamponade. Left ventricle was not dilated (diastolic and systolic diameters: 43mm and 22mm, respectively). The systolic function was normal with no thickened left ventricle wall (inter ventricular septum=10mm). No atrial dilatation was observed, and diastolic function was normal.

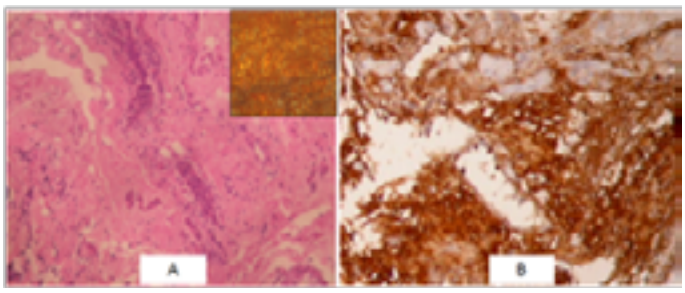
Blood count and biology tests were normal. Antinuclear antibodies and rheumatoid factor were negative, and thyroid function was normal. Lyme serology was negative and no Koch bacillus was found in the sputum.

The electrophysiological exploration was in favor of a nodal block: (AH=253 ms, HV=54 ms, Wenckebach point = 60 beats / min; refractory period of the atrio-ventricular node=1000ms). Atropine administration did not change the heart rate beating and the conduction parameters.

Hence, the patient was implanted by a dual chamber pace maker. She also underwent a surgical drainage of the pericardial effusion and a biopsy was performed. The histological examination showed a thickened pericardial tissue remodeled by large deposits of amorphous eosinophilic substance with affinity for Congo red stain and showed apple-green fluorescence under a polarizing microscope. In immunohistochemistry, amyloid deposits are AL type expressing the lambda light chain [Figure 3].

Figure 3: a : Pericardial tissue remodeled by large amyloid deposits with a yellow-green birefringence under polarized light

b: Immunohistochemistry: amyloid deposits by anti-lambda antibodies confirming that it is an AL amyloidosis



The diagnosis of cardiac amyloidosis was then confirmed. After 2 years of uneventful follow, the patient is asymptomatic.

Discussion

The heart can be involved in all types of systemic amyloidosis, particularly in systemic senile amyloidosis (SSA) and some forms of transthyretin-related hereditary amyloidosis (ATTR). Cardiac involvement in light chain (LC) amyloidosis (AL) is the most frequent, expressing the lambda isotype in 70% of cases. Whereeas in secondary amyloidosis, cardiac involvement is rare and clinically non-significant [4].

In our two observations, cardiac involvement was associated with LC amyloidosis (AL) expressing the lambda isotype.

Cardiac manifestations are mainly due to diastolic dysfunction, also known as heart failure with preserved ejection fraction (30- 50% of cases) [4, 7, 8]. Restrictive cardiomyopathy could be observed in 30% of cases; while, valvular insufficiency and stenosis due to endocardial involvement are rarer [8, 9, and 10]. In our two patients, there was neither systolic nor diastolic dysfunction.

Patients may also complain typical angina secondary to coronary flow abnormalities and microvascular involvement [12].

Disturbances of conduction and arrhythmia are common manifestations of cardiac amyloidosis [14, 15]. Several types of arrhythmia have been reported; the most common is atrial fibrillation [10, 11]. In our two patients conduction disorders revealed the disease.

There are few studies of long term electrocardiographic monitoring in patients affected with amyloidosis. The incidence of serious arrhythmias and disturbances of conduction have been underestimated. Symptoms such as dizziness and syncope have probably been erroneously ascribed to orthostatic hypotension which is a common feature of all types of systemic amyloidosis [16]. Sudden death, occurring in 15% of cases of cardiac amyloidosis, may also be a manifestation of arrhythmias or conduction disturbances [15].

In familial amyloidosis, a high prevalence of conduction disturbances has been shown, and the need for permanent pacing due to high degree AV block was relatively frequent [17, 18]. Olofsson et al. [17] demonstrated that atrioventricular and/or intraventricular conduction disturbances were found in 48 out of 71 patients (67%) with familial amyloidosis and polyneuropathy. In addition, the prevalence of conduction disturbances increased with the duration of the disease [17].

The cause of the electrocardiographic abnormalities in amyloidosis is a matter of controversy despite attempts of clinicopathological correlation. Detailed correlative studies of the involvement of cardiac conduction system in amyloidosis are few and have produced conflicting results. Some authors favour the hypothesis that infiltration of the conducting system by amyloid deposits is the main reason for the disturbances of conduction [19]. In familial amyloidosis with polyneuropathy, amyloid infiltration of the sinus node and atrioventricular conduction system is now well documented, and this seems to account for the majority of the electrophysiological disturbances of these regions [21, 22].The distribution and extent of heart infiltration by amyloid are not, however, uniform. On the other hand, other authors have concluded that direct infiltration by amyloid is of lesser importance [14]. Autonomous neuropathy due to amyloid may also contribute to the electrophysiological disturbances. In fact, in familial amyloidosis with polyneuropathy, amyloid has also been found in subepicardial neural tissue [21].

Drugs affecting impulse formation and conduction (for example: digitalis, antiarrhythmic agents, and also carbamazepine) may aggravate the dysfunction of an already compromised conduction system in amyloidosis. Therefore, they should be avoided if possible. Sensitivity to digitalis in cardiac amyloidosis has been proposed [15, 23] and binding of digoxin by amyloid fibrils was suggested to be one possible mechanism of conduction disturbance [23].

Reisinger et al. [24] sought to determine the spectrum of electrophysiologic abnormalities found in patients with cardiac involvement due to AL amyloidosis. The sinus function and the atrioventricular node was preserved in most patients, but the infra-His conduction times (HV) were usually abnormal. The mean HV interval was 79 ±18 ms (range 50 to 110), and 23 patients (92%) had an abnormally prolonged interval (>55 ms). Marked HV prolongation (>80 ms) occurred in 12 patients, 6 of whom had an interval >100 ms.

The authors also concluded that AV node conduction was borderline or within normal limits, whereas disturbances in the His-Purkinje system were common [24]. Marked prolongation of the HV interval was often seen, even in the presence of a narrow QRS complex. Moreover, a significant association between HV interval prolongation and the occurrence of sudden death was found. The finding of HV prolongation in the majority of these patients, even when the QRS complex was relatively narrow, implies that the distal conduction system is extensively infiltrated.

In non amyloid heart disease, it is postulated that the coexistence of HV prolongation and bundle branch block reflects a non homogeneous involvement of the bundle branches by the underlying pathologic process [26, 27]. In cardiac amyloidosis, the rare occurrence of complete bundle branch may be explained by the widespread, generalized and homogenous involvement of both bundle branches leading to an equivalent conduction delay in both bundle branches and would result in a narrow QRS complex but a prolonged HV interval.

Prolongation of the HV interval was common even in patients with AL amyloidosis without a history of syncope or presyncope. But caution should be applied in interpreting this finding in a patient with AL amyloidosis with syncope. Indeed, in Reisinger et al series [24], two patients died suddenly despite appropriately functioning permanent pacemakers inserted because of syncope and HV prolongation. Earlier studies of patients with prolonged HV intervals and bifascicular block [30, 31] found a markedly prolonged HV interval to be predictive of sudden death. However, the cause of sudden death, when documented, was more often due to ventricular tachyarrhythmias than to complete AV block [32, 33].

In our observations, only the second patient has an electrophysiologic exploration before the implantation of the pacemaker; the HV interval was normal but a nodal block was detected.

Conclusion

Cardiac amyloidosis should be suspected in young patients with conduction disorders. These patients are usually brought to be implanted with a pacemaker. After the implantation, they didn’t complain dizziness or loss of consciousness suggesting that their symptoms were due to conduction disorder.

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