Conduction system in cardiac amyloidosis: two cases succumbed to cardiac arrest

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Key words:
Amyloidosis;
Conduction system.

The present article reports the histological study of the conduction system in 2 cases of cardiac amyloidosis. The discrepant anatomical and clinical evidence yet confirmed the need for accurate ECG controls in all cases. Indeed, while in the first case evident lesions of the conduction system were revealed by surface ECGs, the second case did not exhibit significant ECG abnormalities but the right atrium and the His bundle showed slight fibro-amyloid involvement, as potential forerunners of high-risk arrhythmias.

(Ital Heart J 2001; 2 (12): 932-934)

Received September 14, 2001; revision received October 3, 2001; accepted October 4, 2001.

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The clinical and pathological aspects of cardiac amyloidosis have long been studied[1-4], but research in the last decade has focused special attention on the biochemical classification[5-7] of the amyloid substance and on its deposition in different parts of the organ, in particular the right atrium and on the inherent arrhythmic manifestations[8-10]. However, little attention has been paid to the involvement of the conduction system[11,12], notwithstanding the awareness that right atrial amyloidosis has been seen to encompass and/or affect the sinoatrial node region and the pacemaker itself thus resulting in impaired atrial impulse formation and conduction. Senile amyloidosis[13], often involving the heart, seems to present with the same typical predilection for the conduction system. It is characterized by amyloid deposits around the nutritional artery and in the specialized myocardium. Interstitial fibrosis may also be present. These alterations underlie the abnormalities in the arousal of rhythm and/or its transmission to the ordinary myocardium. This awareness can perhaps be useful for the clinical differential diagnosis with diabetic cardiopathy, the histological diagnosis of which (i.e. on bioptic specimens) can be doubtful whenever the paraprotein interstitial deposits and/or an associated amyloidosis concur in elderly patients. Indeed the involvement of the conduction system with inherent block does not seem to characterize diabetic cardiopathy.

For the foregoing reasons, the authors thought it worthwhile to present 2 cases of cardiac (senile?) amyloidosis. A complete histological analysis of the alterations in the conduction system which probably underlie the related ECG abnormalities is presented.

In the second case, despite some involvement of the sinoatrial node and of its atrial approaches, there is no ECG evidence of anomalous impulse formation and intra-atrial conduction.

Description of cases

Case 1. B.A., a 57-year-old woman. Ten days prior to admission in the emergency ward, the patient developed symmetric and non-obstructive hypertrophic cardiomyopathy-related congestive heart failure and anasarca. Echocardiographic evaluation revealed a marked biventricular wall thickness with only a virtual evidence of the cavity in systole, biatrial dilation and pleuropericardial effusion. At the time of admission the patient was in shock and her systolic blood pressure was 70 mmHg. She lost consciousness and succumbed to asystole and respiratory arrest (autopsy no. 24/97).

Only the data inherent to the heart will be reported: volume and weight increased (540 g); diffuse, marked wall thickening; in the posteroseptal wall a small, pale, soft area was detected.

Histologically, diffuse amyloid deposits may be seen (Fig. 1), particularly in the right atrium. The deposits were occasionally surrounded by multinucleated giant cells. The sinoatrial node, its connections with the atrial myocardium, the His

bundle (Fig. 2) and both bundle branches were all involved. The histological picture was consistent with the ECG features (Fig. 3).

Case 2. L.R., a 45-year-old woman. From childhood the patient complained of muscular and arthritic-like pains. She had never been treated. These myoarthritic symptoms became more severe during the first pregnancy and the diagnosis of sickle cell anemia was established. The patient's two sisters presented with a similar clinical picture. Later on she was splenectomized and symptoms improved (only a few sporadic painful attacks persisted). At the time of hospital admission, after 3 months of dyspneic, painful thoracic crises, besides confirmation of sickle cell anemia, renal amyloidosis was also diagnosed at biopsy; the ECG (Fig. 4) did not exhibit any significant anomalies. Echo-Doppler revealed tricuspid insufficiency with slight pulmonary hypertension which was in contrast with the marked systemic hypertension. Later on, during the last week before demise, the edema worsened and tachycardia as well as thoracic pain and dyspnea persisted until death (autopsy no. 5/98).

Only the autoptic data of the heart will be recorded: weight 340 g with normal diameters and wall thickness. Histologically, amyloid periarteriolar deposits were seen in the right atrium. Mild His bundle fibrosis (Fig. 5) was also present. These histological anomalies were not related to any significant changes in the surface ECGs.

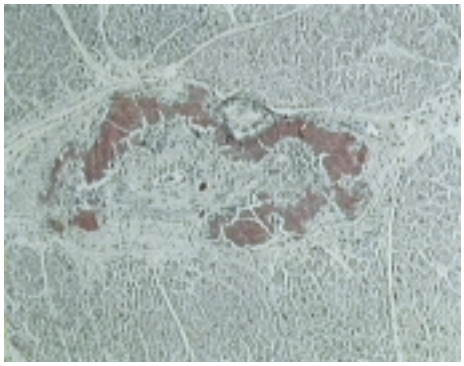

Figure 1. *Case 1. Amyloid deposits in the left ventricular wall (Congo red 100×).*

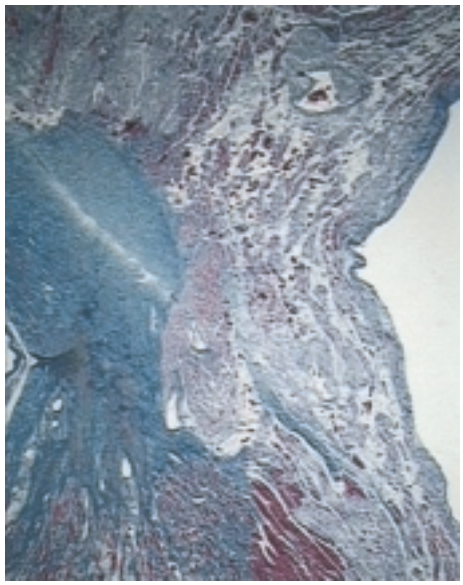

Figure 2. *Case 1. Upper His bundle showing slight patchy fibrosis (Azan Mallory 25×).*

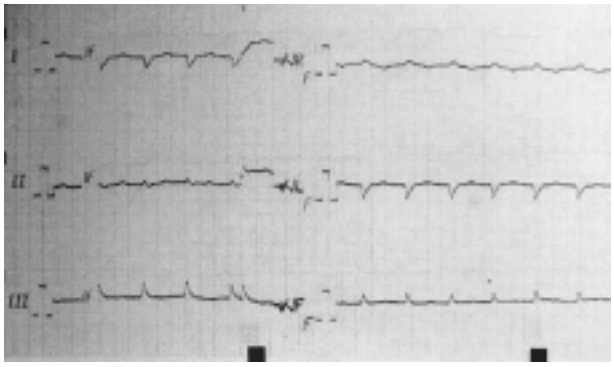

Figure 3. *Case 1.* On the upper left: *the ECG shows accelerated junctional rhythm replacing the normal sinus rhythm. This arrhythmia is due to amyloid deposits in the sinoatrial node.*

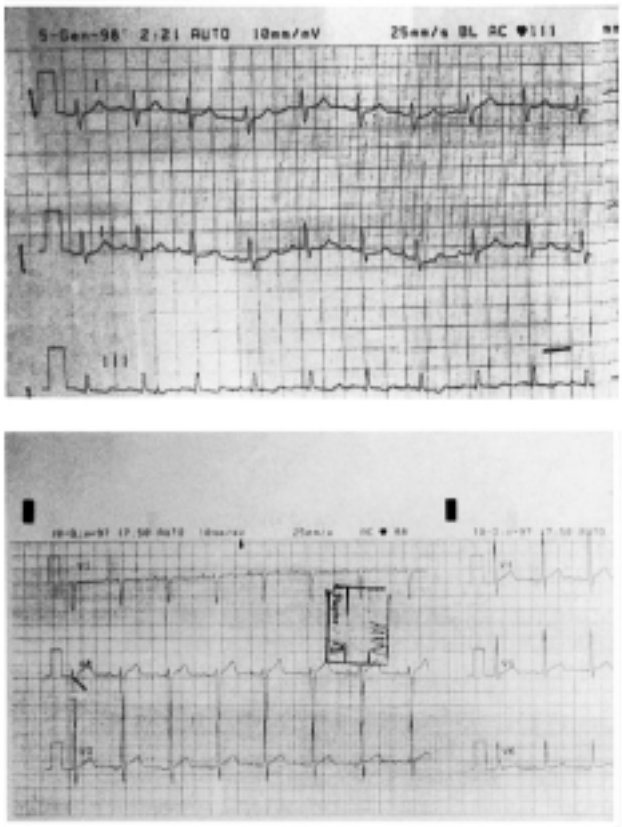

Figure 4. *Case 2. Normal ECG.*

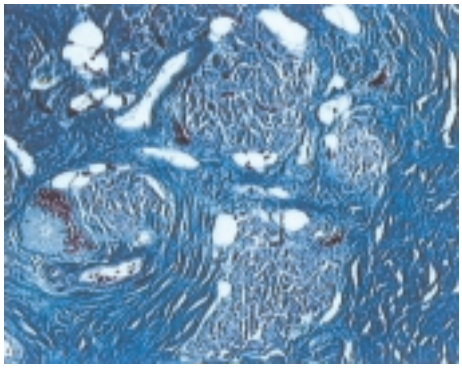

Figure 5. *Case 2. His bundle showing initial fibrosis (Azan Mallory 100×).*

Discussion

In both the studied cases, the particular vulnerability of the right atrium to amyloid deposition within the pacemaker and atrioventricular conduction pathways was confirmed. On the other hand, the arrhythmic manifestations were significantly different. As a matter of fact, in case 1 these amyloid lesions had manifested with inherent abnormalities at routine ECG, while in case 2 the conduction system abnormalities were electrocardiographically "silent". Such a wide clinical variability would not surprise an expert of the anatomical and clinical characteristics of the conduction system itself, but it does cast some doubts upon the usual diagnostic criteria for right atrial involvement in amyloidosis. The demonstrated absence of any significant impairment in impulse arousal and atrio-intraventricular conduction does not seem to suffice to clinically rule out the existence of amyloidosis of the specialized myocardium with right atrial damage; such lesions can be present even in the absence of any specific clinical symptoms and they are potentially dangerous whenever they manifest more or less suddenly. For this reason, now documented histologically, all patients with amyloidosis should be submitted to accurate clinical and instrumental evaluation. The involvement of the pacemaker and conduction system, which would not necessarily show up at routine surface ECG, may be revealed. Such a diagnosis, whenever made, might be of value in the prevention of potentially high-risk manifestations.

The above illustrated discrepancy between the clinical and pathological pictures can be even more useful when extrapolated to the clinical management of amyloidosis.

References

1. Bisceglia M, Grossi GB, Panniello G, Bertani T, Cenacchi G, Pasquinelli G. Le amiloidosi. Inquadramento clinico-patologico. Parte 1: la nosografia. Pathologica 1997; 89: 329-45.
2. Gertz MA, Kyle RA, Edwards WD. Recognition of congestive heart failure due to senile cardiac amyloidosis. Biomed Pharmacother 1989; 43: 101-6.
3. Johansson B, Westermark P. Senile systemic amyloidosis: a clinico-pathological study of twelve patients with massive amyloid infiltration. Int J Cardiol 1991; 32: 83-92.
4. Lie JT, Hammond PI. Pathology of the senescent heart: anatomic observations on 237 autopsy studies of patients 90 to 105 years old. Mayo Clin Proc 1988; 63: 552-64.
5. Jacobson DR, McFarlin DE, Kane I, Buxbaum JN. Transthyretin Pro55, a variant associated with early-onset, aggressive, diffuse amyloidosis with cardiac and neurologic involvement. Hum Genet 1992; 89: 353-6.
6. Johansson B, Wernstedt C, Westermark P. Atrial natriuretic peptide deposited as atrial amyloid fibrils. Biochem Biophys Res Commun 1987; 148: 1087-92.
7. Kisilevsky R. Proteoglycans, glycosaminoglycans, amyloid-enhancing factor, and amyloid deposition. J Intern Med 1992; 232: 515-6.
8. Dubrey S, Pollak A, Skinner M, Falk RH. Atrial thrombi occurring during sinus rhythm in cardiac amyloidosis: evidence for atrial electromechanical dissociation. Br Heart J 1995; 74: 541-4.
9. Olson LJ, Gertz MA, Edwards WD, et al. Senile cardiac amyloidosis with myocardial dysfunction. Diagnosis by endomyocardial biopsy and immunohistochemistry. N Engl J Med 1987; 317: 738-42.
10. Plehn JF, Southworth J, Cornwell JG. Brief report: Atrial systolic failure in primary amyloidosis. N Engl J Med 1992; 327: 1570-3.
11. Raineri P, Rossi L. Confronto fra ECG ed alterazioni istopatologiche in sette casi con lesioni del sistema miocardico specifico. Minerva Cardiologica 1965; 13: 1-35.
12. Stefani M, Angiero F. Histopathology of lethal conduction system involvement in a case of cardiac amyloidosis. In: Proceedings XXII International Congress of the International Academy of Pathology. Nice, 1998: 160.
13. Kyle RA, Spittell PC, Gertz MA, et al. The premortem recognition of systemic senile amyloidosis with cardiac involvement. Am J Med 1996; 101: 395-400.