—Report on Experiments and Clinical Cases—

Sudden Death in a Case of Cardiac Amyloidosis Immediately after Pacemaker Implantation for Complete Atrioventricular Block

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Abstract

We report a patient with cardiac involvement associated with primary amyloidosis presenting marked left ventricular (LV) wall thickening, severely decreased systolic and diastolic function, and complete atrioventricular block (CAVB), who died suddenly of cardiac arrest caused by electro-mechanical uncoupling occurring immediately after permanent pacemaker implantation. Post mortem examination showed no procedural complications such as cardiac or venous perforation. The heart was densely infiltrated with amyloid fibrils, especially in the extracellular tissues surrounding the papillary vessels.
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Key words: primary amyloidosis, pacemaker failure, electro-mechanical uncoupling

Introduction

Cardiac involvement has been known to be a critical prognostic factor in primary amyloidosis[1,2]. Extensive deposition of amyloid fibrils in the heart causes severe heart failure and fatal arrhythmia. We report a patient with cardiac amyloidosis associated with complete atrioventricular block (CAVB) who died suddenly of cardiac arrest caused by electro-mechanical uncoupling occurring immediately after permanent pacemaker implantation.

Case Report

A 65-year-old-male was admitted for treatment of congestive heart failure refractory to conventional medical treatment. Four months earlier, he had begun to experience dyspnea on exertion and progressive fatigue. After a three-month hospitalization in another hospital, he was transferred to our hospital. Upon clinical examination, blood pressure was 96/64 mmHg, and there were moderate peripheral edema and ascites. A grade 3/6 midsystolic murmur was heard best at the lower left sternal border. A slight decrease in the white blood cell count (3,400/mm^3) was noted, but other blood cell counts were normal. Also, there were no abnormalities in blood chemistry values except that for total cholesterol (112 mg/dl). M protein was discovered on serum electrophoresis. Immunoelectrophoresis of the urine proved the presence of monoclonal kappa isotype immunoglobulin. Bone marrow examination revealed

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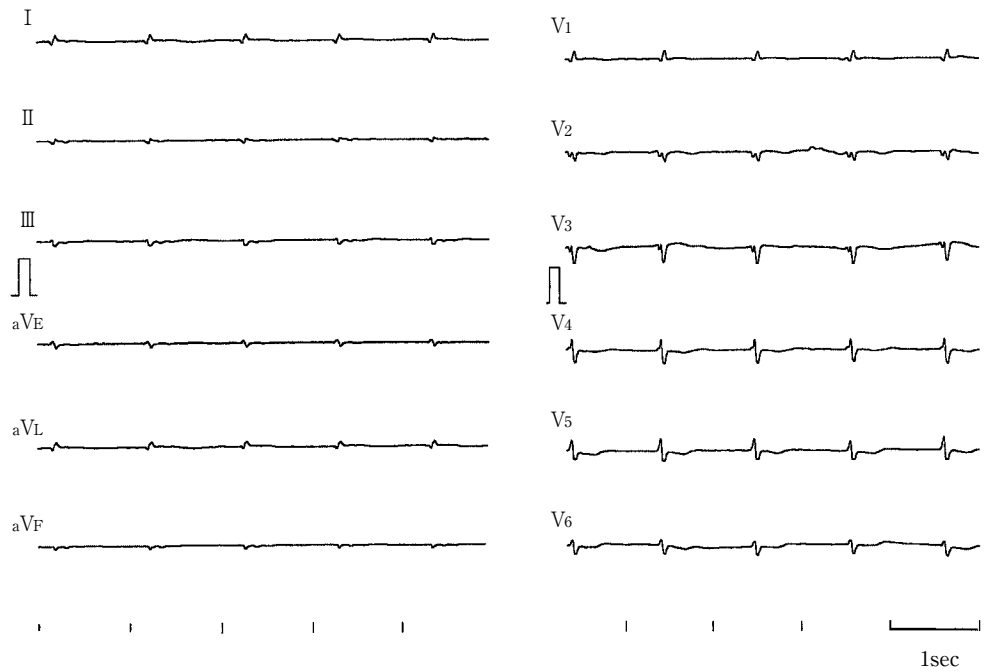

Fig. 1 Electrocardiogram recorded on the day of admission. The voltage of QRS complex was distinctively low and P wave was obscure in all leads. R-R interval was regular.

approximately 10% plasma cells. Abdominal skin and fat biopsy demonstrated the deposition of AL amyloid , indicating primary amyloidosis . Cardiomegaly and bilateral pleural effusion were noted on chest X-ray. An electrocardiogram (ECG) showed left axis deviation and low voltage QRS wave with a rate of 50 (**Fig. 1**). Transthoracic echocardiography (TTE) demonstrated left ventricular hypertrophy (intraventricular septal thickness: 16 mm, posterior wall thickness: 20 mm) and impaired diastolic and systolic left ventricular (LV) function (ejection fraction 41%) (**Photo 1**).

After admission, the patient's clinical condition had improved on intravenous administration of diuretics and dopamine. However, the P wave on the ECG became invisible and the heart rate gradually decreased to a range of 35 to 50 bpm, depending on the dose of dopamine. We thought that this degree of bradycardia was an indication for permanent pacemaker implantation.

On the day of the implantation, blood pressure was 104/68, heart rate 38 bpm, and electrolytes within normal range. Atrial and ventricular leads were inserted through the left subclavian vein under fluoroscopy. Although atrial electronic impulse was

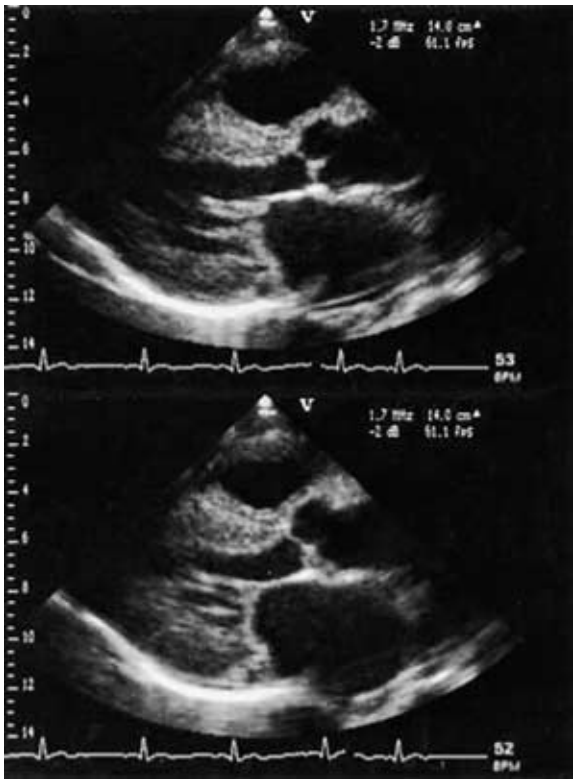

Photo 1 Long-axis images from 2-dimention parasternal view.[Upper pannel: end-diastolic image, lower pannel: end-systolic image] Remarkably thickened left ventricular wall with sparkling was recognized.

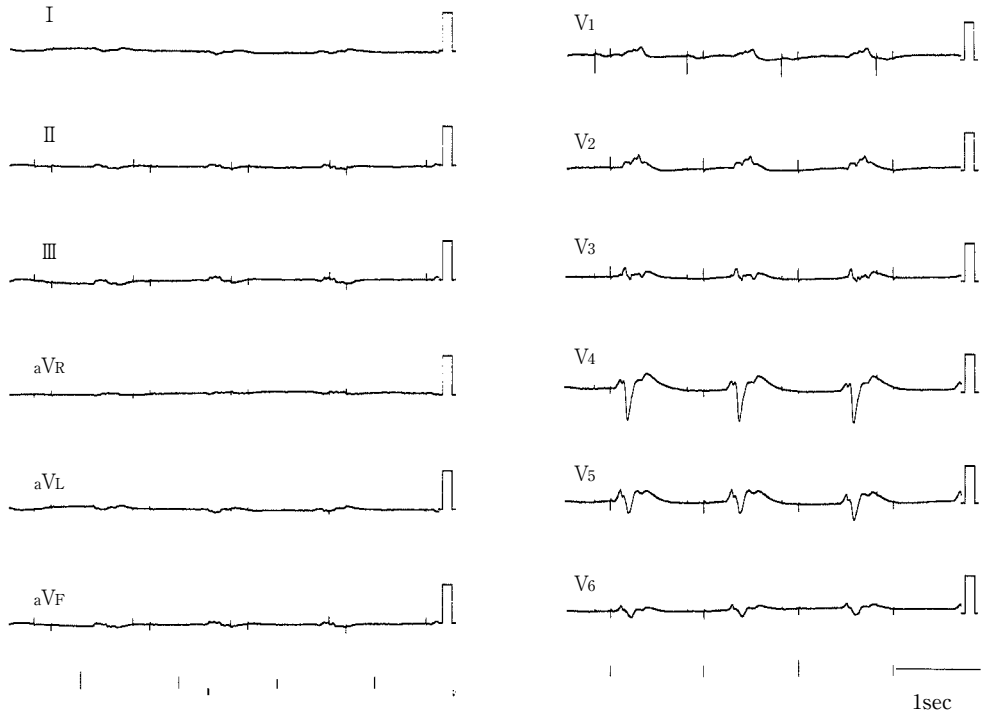

Fig. 2 Electrocardiogram recorded immediately after unstable hemodynamics in the operating room. QRS complex was independent of pacing spike indicating pacing failure and atrioventricular junctional rhythm.

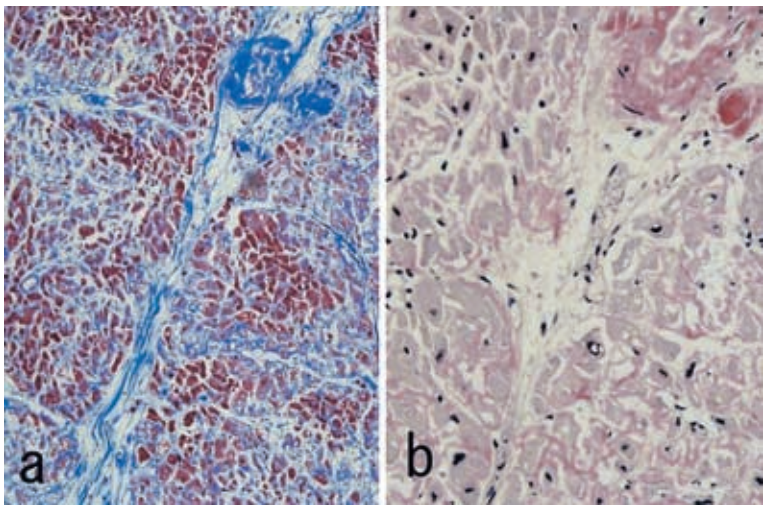

Photo 2 **a)** Extensive deposition of amyloid fibrils in the left ventricular myocardium in a the histological section with Masson Stain (×40). **b)** Deposition of amyloid fibrils especially in interstitial tissue surrounding capillaries as demonstrated by the pink reticular pattern of the Cong-Red Stain (×100).

barely detected by intracardiac ECG, its pacing and sensing thresholds were significantly impaired. The pacing threshold of the right atrium (RA) was higher than 10 V and the sensing threshold was 0.3 mV. The pacing threshold of the right ventricle (RV) was 0.6 V and its sensing threshold was 13.5 mV. Ventricular rhythm was completely independent of the atrial impulse, which indicated CAVB. Since we obtained the highest atrial sensing threshold at the free wall, the pacing lead was placed in the right

atrial free wall instead of the right appendage. Another lead was placed in the right ventriclular endocarium and the pacemaker started working with fixed A-V sequential pacing mode. Approximately 5 minutes after the procedure of pacemaker implantation was completed, the patient suddenly began convulsing and his level of consciousness fell. Arterial pulse was not palpable and the ECG showed pacing failure with atrioventricular junctional escaped rhythm (**Fig. 2**). We immediately transferred him to the intensive care unit and performed TTE. No pericardial or pleural effusion was observed but contraction of the LV disappeared. Despite intensive treatment with cardiac massage and intravenous infusion of beta adrenergic receptor agonists to resuscitate this patient, he finally died due to cardiac arrest 4 hours after the onset of electromechanical uncoupling.

A post-mortem examination confirmed that the pacemaker leads were firmly mounted and that there was no cardiac or major vessel rupture. The heart weighed 550 g and the myocardium was white, thick and firm. Microscopic examination revealed amyloid fibrils densely deposited in the myocardium, including coronary arteries and veins, connective tissue, valves and conduction systems (**Photo 2a**). The infiltration was especially significant in the interstitial tissue surrounding the capillary vessels (**Photo 2b**). Amyloid fibrils were also observed in almost every systemic organ, although the infiltration was less significant than in the heart.

Discussion

Primary amyloidosis causes failure of multiple organs by deposition of amyloid fibrils consisting of the NH2-terminal amino acid residues of the variable portions of a monoclonal κ or λ light chain[2]. Among those disorders associated with primary amyloidosis, cardiac involvement is the most undesirable because of the desperately poor prognosis. The median survival of patients with AL amyloidosis presenting with heart failure is 4 to 10 months[1,3] and death is mainly attributed to congestive heart failure and cardiac arrhythmia[4,5]. No definitive treatment of primary amyloidosis with cardiac involvement has been established, although several attempts have been made[1,3]. Chemotherapy with melfalan and predonisolone has been reported to be effective for improving survival by inhibiting synthesis and deposition of amyloid fibrils[6]. Conventional medical therapy for heart failure should also be given with the caution of hypotension and cardiac arrhythmia if clinical symptoms are apparent. A permanent pacemaker is commonly used for bradycardiac arrhythmia, but no beneficial effect in reducing the risk of sudden death has been identified[1,4].

The diagnosis of cardiac amyloidosis was assigned to this patient on the basis of typical ECG and TTE findings (low voltage QRS wave and remarkable thickened left ventricular wall with sparkling) and histopathological evidence of AL amyloid in abdominal fat and skin. While receiving medical treatment for heart failure, the patient underwent permanent pacemaker implantation for gradually worsening bradycardia. We also scheduled chemotherapy with an alkylating agent to begin after pacemaker implantation. However, the patient died suddenly manifesting electro-mechanical uncoupling immediately after the implantation, which was without procedural complication.

Although several factors were speculated to be responsible for this event, no conclusive explanation can be given. Blood pressure had fallen gradually and coronary circulation might have decreased after ventricular pacing had started. The efficacy of cardiac performance with the electrical pacing from distal RV is usually attenuated because it often causes LV-RV asynchrony, especially in the heart infiltrated with amyloid fibrils[7]. The cardiac contraction, reduced by right ventricular pacing and asynchronized wall motion, could have been insufficient to maintain stable hemodynamics. As another explanation, the minimal necrosis of the surface of the endocardium caused by right ventricle electronic stimulations, which does not usually affect a normal heart, might have altered the threshold in this amyloid heart and caused pacing failure. It might also be possible that the heart was on the verge of arrest on that day and the event occurred independently of the pacemaker implantation. The

post mortem analysis revealed a dense deposition of amyloid fibrils in the whole heart including both the myocardium and conduction system, and the myocardium was found to be completely stiff and barely bendable. Amyloid fibrils had invaded the surrounding capillaries in the myocardium in particular, suggesting disturbance of the microvascular circulation and impaired coronary flow reserve. In this circumstance, myocardial ischemia could easily have been induced by a reduction of the coronary circulation without obstruction of the epicardial coronary flow[8]. This could be one possible etiology of the instability of hemodynamics during the event after pacemaker implantation.

Zenhausern et al have reported a similar case with cardiac amyloidosis who developed sudden death in hospital after infusion of dimethyl sulfoxide-cryopreserved hematopoietic stem cells showing electromechanical dissociation[9]. Although the autopsy failed to reveal the reason for the event, the heart was shown to be extensively invaded by amyloid fibrils, which is similar to the findings in our patient.

Conclusion

A patient with cardiac amyloidosis died suddenly immediately after pacemaker implantation. Considering that patients with amyloidosis have a high risk of fatal arrhythmia and that permanent pacemakers sometimes fail to work properly in the advanced stage of cardiac amyloidosis, it should always be borne in mind that such patients are continuously threatened by unexpected death even in hospital.

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