Cardiac Amyloidosis Presenting as Recurrent Syncope

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Cardiac amyloidosis is an uncommon disease that is rarely diagnosed clinically. In this study, we present a case of a 63-year-old man with recurrent syncope and elevated troponin I levels. The patient’s coronary angiography showed no significant stenosis. An implantable cardioverter-defibrillator was implanted into the patient due to episodes of ventricular tachycardia. The diagnosis of cardiac amyloidosis was made by endomyocardial biopsy. The patient died of a combination of cardiogenic shock and rapid deterioration of renal function. Although cardiac amyloidosis is rarely diagnosed, it should be considered as a differential diagnosis in patients with recurrent syncope, because it is potentially treatable.

Key Words: Cardiac amyloidosis • Syncope • Troponin I • Ventricular tachycardia

INTRODUCTION

Cardiac amyloidosis is defined as the presence of amyloid deposition in the heart. Cardiac amyloidosis, together with advanced cardiac involvement can result in a significant morbidity and mortality rate among patients. Although early diagnosis is a critical step in treating cardiac amyloidosis, diagnosis is usually delayed because amyloid deposition can involve multiple systems with a wide variety of clinical appearances. In this article, we presented a case of cardiac amyloidosis with recurrent syncope complications. The discussion of the case's clinical presentations that may provide insight for early diagnosis in future patients.

CASE REPORT

A 63-year-old man with cardiovascular risk factors of hypertension, hyperlipidemia, diabetes mellitus, and obstructive sleep apnea was admitted because of recurrent syncope over the past three months. There the patient has no family history of cardiovascular or neurological diseases. Upon admission, his blood pressure, pulse rate, body temperature, and respiratory rate were 93/46 mmHg, 92 bpm, 36.3 °C, and 26 breathes/minute, respectively. Clinical examination of the patient demonstrated macroglossia, clear breathing sound, normal heart sounds without murmurs, orthostatic hypotension, and significant pitting edema and ecchymosis over both lower legs. At a inclination of 45°, the patient exhibited engorgement of the jugular vein, where the filling level of the jugular vein was 7 centimeters vertical height above the sternal angle. Laboratory studies revealed that the patient had a markedly elevated brain natriuretic peptide level of 3260 pg/mL (normal < 100 pg/mL) and a troponin I level of 0.92 ng/mL (normal < 0.5 ng/mL). The patient electrocardiogram (ECG) (Figure 1A) showed low electrocardiographic voltages. The patient was first diagnosed with hypothyroidism due to a normal adrenal function test with a low level of serum free thyroxin (0.6 ng/ml, normal 0.80-2.0 ng/ml) and an increased level of serum thyroid stimulating hormone (8.54 μU/ml, normal 0.25-4.0 μU/ml). The thyroid hormone, thyroxin, was administered per diagnosis. In echocardiography, the systolic function was normal de-
spite that the patient had a thickened left ventricle wall and a small global pericardial effusion (Figures 1B, C). Diastolic dysfunction was confirmed with Doppler mitral inflow velocity and Doppler imaging of mitral annulus, where a reversal of the E/A ratio, and a E/E’ ratio of 20.5 was observed, respectively (Figures 1D, E). Additional coronary angiography was performed on the patient due to an elevated troponin I level, however, no significant stenosis was observed. One week later the patient developed paroxysmal atrial fibrillation (PAF), junctional escape rhythm, and defibrillation terminated sustained ventricular tachycardia (VT). Electrophysiological study with entrainment revealed a re-entrant VT (Figure 2A) and confirmed sick sinus syndrome (SSS), therefore an implantable cardioverter-defibrillator was implanted accordingly. The patient also exhibited peripheral neuropathy, which was confirmed by electromyography and nerve conduction velocity studies. Furthermore, a hemorrhaging gastric ulcer was also found in the patient. The other biochemical analyses showed the following results: serum albumin level of 2.0 g/dL (normal 3.5-5.0 g/d), total cholesterol level of 334 mg/dL (normal 130-200 mg/dL), triglyceride level of 393 mg/dL (normal 35-150 mg/dL), and a spot urine protein to creatinine ratio of 10.5. The patient was diagnosed with nephrotic syndrome due to his biochemical data and general edema condition. We attempted to a renal biopsy because the patient exhibited a rapid deterioration of renal function. However, the biopsy failed as a result of patient’s intolerance. Finally, the patient was diagnosed with cardiac amyloidosis through endomyocardial biopsy, where the sample was stained with Congo red and examined under a polarized microscope (Figures 2B, C).

The patient’s progressively severe hypotension and deterioration of renal function resulted in oliguria, pulmonary edema, and metabolic acidosis within two weeks after the endomyocardial biopsy. Furthermore, the patient’s cardiac rhythm became completely pacemaker-dependent. The invasive hemodynamic monitoring revealed that the patient was in cardiogenic shock, which had led to multiorgan failures. Despite of inter-
ventions such as inotropes, continuous veno-venous hemofiltration, and ventilator support, the patient’s condition continue to deteriorate. Finally, the patient died of cardiac arrest with no response to pacemaker pacing.

DISCUSSION

Amyloidosis is a disease resulted from the deposition of misfolded precursor protein. The types of amyloidosis are classified on the basis of the amyloidogenic protein such as light chains, transthyretin, and serum amyloid. The protein can occur in multiple organs and can cause a variety of clinical manifestations. Cardiac amyloidosis constantly occurs with significant dysfunction in combination with other major organs. Cardiac amyloidosis is a leading cause of early death because the disease can result in congestive heart failure and arrhythmias. The incidence of amyloidosis is unclear due to the greatly underdiagnosed light chain (AL) amyloidosis at predominantly affects the heart. The incidence of AL cardiac amyloidosis has an estimated annual incidence rate of 6 to 10 cases per million population in western countries. In contrast, the prevalence of cardiac amyloidosis in Taiwan is uncertain, and lacked public health survey. Our case demonstrated several important clinical features of cardiac amyloidosis such as syncope, nephrotic syndrome, soft-tissue infiltrations (such as macroglossia and obstructive sleep apnea), vascular infiltrations (such as myocardial ischemia, gastrointestinal bleeding and ecchymosis), and autonomic neuropathy. Syncope commonly occurs in cardiac amyloidosis patients and is a sign of poor prognosis. Syncope can be caused by ventricular arrhythmia, restrictive cardiomyopathy combined with autonomic neuropathy, or the involvement of conduction system.

The most common electrocardiographic findings of cardiac AL amyloidosis are low QRS voltages (46%) and pseudo-infarct patterns (47%). Arterial fibrillation (AF) and atrial flutter are the most common type of arrhythmias (20%). High-degree atrioventricular AV block (3%) or VT (1%) is rarely found. In our presented case, both tachyarrhythmia (PAF and VT) and bradycardia (SSS and junctional escape rhythm) were present. Even though the various problems of the conduction system may reflect the severity of myocardial infiltration, the correlation between pathophysiology of re-entrant VT and cardiac amyloidosis remained unclear.

Typical appearance of cardiac amyloidosis in echocardiography includes concentric ventricular thickening with right ventricular involvement, and poor biventricular long-axis function with normal or nearnormal ejection fraction. Other imaging findings may include a speckled or granular myocardial appearance, biventricular dilatation, and valvular and intratral septal thickening. Therefore, low QRS voltages on the ECG and increased mass on echocardiography in the absence of hypertension in our patient are highly suggestive of infiltrative cardiomyopathy.

In the presented case, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and high-sensitivity troponin had proven to be clinically sensitive and useful markers for cardiac amyloidosis. Increased troponin concentrations can reflect the poor prognosis of the patient. The concentration of NT-proBNP can also be used to predict the response of therapy. Currently, the gold standard for demonstrating amyloidosis deposition is a tissue biopsy such as endomyocardial, rectal...
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submucosal, abdominal fat, and kidney and bone marrow biopsy. The presence of amyloid deposition should be confirmed by Congo red staining. Endomyocardial biopsy has a great sensitivity (almost 100%) in determining diffused cardiac involvement, and when performed by experts, it is a relatively safe procedure. In addition, endomyocardial biopsy can differentiate cardiac amyloidosis from the other type of infiltrative myocardial conditions. The treatment goal can be classified into two aims: treatment for heart failure, and therapy to prevent further amyloid deposition. In our case, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and beta-blockade were halted due to severe patient postural hypotension. Otherwise, the patient did not receive further chemotherapy to reduce amyloid production due to poor patient performance status.

In conclusion, early diagnosis of cardiac amyloidosis is crucial because patients with advanced cardiac involvement are ordinarily too ill for chemotherapy. Although cardiac amyloidosis is uncommon, our presented case demonstrated several important clinical features such as heart failure, recurrent syncope, and typical echocardiographic and electrocardiographic results (except for VT). Cardiac biomarkers such as high-sensitivity troponin, and NT-proBNP are sensitive markers in determining cardiac involvement and prognosis. Early diagnoses of amyloid deposits are critical in improving the outcomes of this uncommon, yet now potentially treatable disease.

REFERENCES