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Primary Cardiac Amyloidosis Mimicking Interstitial Lung Disease and Bleeding Diathesis: A Case Report

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ABSTRACT

Primary amyloidosis is a rare systemic disease due to various organ involvements that can lead to atypical clinical findings. In this article, we discuss a case of primary cardiac amyloidosis in a patient presenting with bleeding eyelids and interstitial lung disease.

INTRODUCTION

Amyloidosis is a multisystemic disease characterized by amyloid fibril deposits in the extracellular compartments of various organs [Dubrey 1995]. Primary systemic amyloidosis, which is a subtype, is a rare disease characterized by deposition of immunoglobulin light chain. Cardiac involvement may be seen in up to 50% of primary amyloidosis cases [Cueto-Garcia 1985]. In this article, we discuss a patient with primary amyloidosis who presented with bleeding diathesis and interstitial lung disease findings.

CASE REPORT

A 39-year-old man presented with exertional dyspnea, fatigue, subconjunctival bleeding in both eyes following vomiting, and straining and petechial bleeding on the face and eyelids. He was hospitalized with the pre-diagnoses of collagenosis and vasculitis in the Department of Chest Disease. Cardiomegaly was detected on chest x-ray, and he was consulted by a cardiologist. On physical examination, blood pressure was 140/80 mmHg, pulse rate was 100 beats/min, and a grade 2/6 systolic murmur on the apical region was heard. His electrocardiography revealed low voltage on limb leads and QS waves on V1-4 leads. There were no pathological findings on the laboratory examinations, and specific coagulation assays were within normal limits. Transthoracic echocardiography was performed because of the cardiomegaly detected on chest x-ray and the ischemic cardiomyopathy and pericardial effusion pre-diagnoses. Mild pericardial effusion, diffuse myocardial hypertrophy, diffuse granular increase on the whole myocardial echogenicity, thickening of the mitral and aortic valves and the interatrial septum, patent foramen ovale (0.3 cm in size), and biatrial dilatation were detected on transthoracic echocardiography (Figure 1). In addition, there was moderate mitral regurgitation and a restrictive left ventricular filling pattern (E/A ratio >2; deceleration time = 120 ms). On tissue Doppler, peak lateral mitral annulus Em wave velocity and Sm wave velocity were measured as 4.4 cm/s and 6.8 cm/s, respectively. Left ventricular ejection fraction was 50%. Upon these echocardiographic findings, cardiac magnetic resonance imaging was performed because of the infiltrative cardiomyopathy pre-diagnosis that revealed a diffuse increase of left and right ventricular wall thickness, thickening of the interatrial septum, and pericardial effusion (Figure 2A). Diffuse hyperenhancement was observed on the delayed contrast-enhanced magnetic resonance images following gadolinium injection (Figure 2B). On the right-left heart catheterization, systemic pulmonary artery pressure and the difference of left and right ventricular end-diastolic pressure were calculated as 50 mmHg and 7 mmHg, respectively. Square root sign and deep x and y decline were seen on the ventricular diastolic pressure tracing and on the right atrium pressure tracing, respectively. Coronary angiography results were normal. Endomyocardial biopsy was performed from the right ventricle. Dense amyloid deposition was seen with Congo red staining of the biopsy specimen, and diagnosis of amyloidosis was confirmed with apple-green birefringence under polarized light (Figure 3). Immunohistochemical staining revealed light-chain (AL) amyloidosis. The results of protein electrophoresis, blood and urine immune fixation tests, and bone x-rays performed for the exclusion of multiple myeloma were normal. Normocellular bone marrow and dense amyloid infiltration were present on the bone marrow biopsy. Plasmocyte rate was <5%. Interstitial thickening was present on high-resolution computed tomography, and mucosal hyperemia and congestion were seen on bronchoscopy. Bronchoscopic biopsy confirmed amyloid deposition. There were no other abnormal findings in the tests

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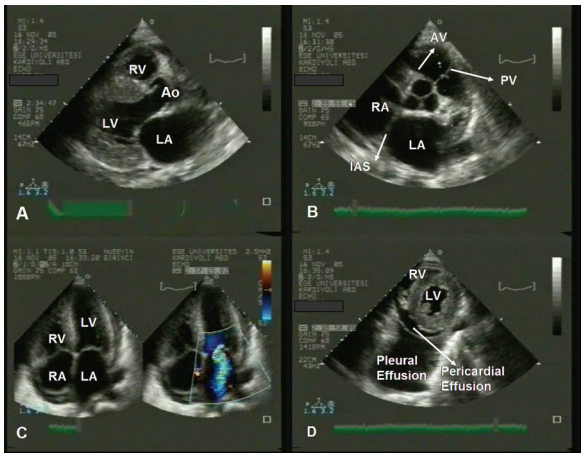

Figure 1. Parasternal long- and short-axis views (A, B, D) and apical 4-chamber (C) view show concentric left ventricular hypertrophy, thickening of the interatrial septum, myocardial granular sparkling texture, patent foramen ovale, mitral regurgitation, and pleural and pericardial effusion. RV indicates right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium; Ao, aorta; IAS, interatrial septum; AV, aortic valve; PV, pulmonary valve.

performed for other organ involvements. The patient was discharged after hematology consultation to be evaluated for chemotherapy and/or autologous peripheral blood stem cell transplantation.

DISCUSSION

Amyloidosis is a rare systemic disease leading to organ and tissue dysfunction due to extracellular protein deposition. It is classified according to the type of deposited protein. It is referred to as primary amyloidosis if there is immunoglobulin light-chain deposit (AL), as in our case. Primary amyloidosis may be seen also in multiple myeloma and Waldenström macroglobulinemia. However, these 2 diseases were excluded in our case.

Amyloid deposits may be seen in the heart, kidney, liver, and other organs in primary amyloidosis [Dubrey 1998]. Cardiac involvement has been detected in up to 50% of primary amyloidosis cases [Cueto-Garcia 1985]. However, clinically relevant cardiac findings were present only in one third of these patients. Restrictive cardiomyopathy, bradyarrhythmias, tachyarrhythmias, ischemic heart disease, valvular heart disease, and constrictive pericarditis may develop. The most frequent cardiac manifestation is restrictive cardiomyopathy [Cueto-Garcia 1985], as in our case. Restrictive cardiomyopathy was confirmed by echocardiography and catheterization in our case. Cardiac amyloidosis usually presents with symptoms of right ventricular failure. However, there was no right ventricular failure in our case. One of the most important characteristics of cardiac amyloidosis is the presence of low voltage on electrocardiography despite left ventricular hypertrophy on echocardiography. Also, pseudoinfarction pattern and bradyarrhythmias and tachyarrhythmias may be seen on

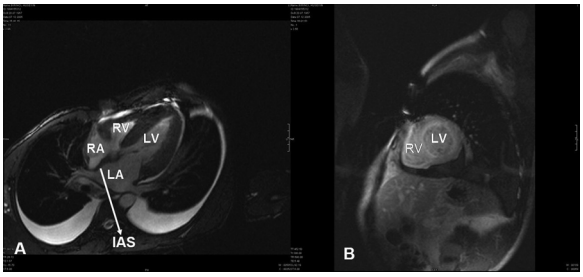

Figure 2. Precontrast cardiac magnetic resonance image shows increased left ventricular, right ventricular, and interatrial septal thickening (A). Short-axis delayed contrast-enhanced magnetic resonance image shows left and right ventricular diffuse enhancement (B). RV indicates right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium; IAS, interatrial septum.

electrocardiography [Dubrey 1998]. The most characteristic finding on echocardiography is the increased myocardial echogenicity referred to as granular sparkling [Falk 1987]. Furthermore, echocardiography reveals left and right ventricular wall and interatrial septal thickening, atrial dilatation, valvular thickening, and Doppler findings consistent with restrictive cardiomyopathy. Cardiac magnetic resonance imaging is also helpful for diagnosis. On cardiac magnetic resonance imaging, postcontrast delayed hyperenhancement in the myocardium is seen in addition to ventricular wall and interatrial septal thickening [Sueyoshi 2006]. In our case, echocardiographic data were confirmed by cardiac magnetic resonance imaging findings. The definitive diagnosis of cardiac amyloidosis is made by demonstrating amyloid infiltration with Congo red stain on an endomyocardial biopsy [Gertz 1999]. In addition to this, amyloidosis subtype should be determined by immunohistochemical staining. High-dose chemotherapy and autologous peripheral blood stem cell trans-

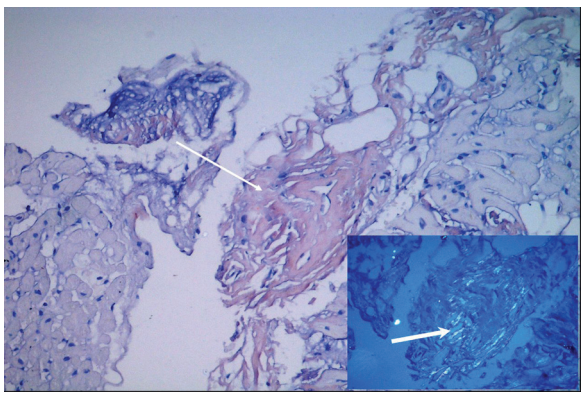

Figure 3. Extracellular amyloid deposition with Congo red staining (thin arrow) and amyloid deposits that have apple-green birefringence under polarized light (bold arrow) are seen on the endomyocardial biopsy specimen of the right ventricle.

plantation are the current treatment for primary amyloidosis [Skinner 2004]. If cardiac involvement is present, a poor prognosis is reported for primary amyloidosis [Gertz 1999]. The median survival is 6 months after the onset of heart failure [Grogan 2000]. Our case was diagnosed relatively early because of the cardiac findings and will be evaluated for chemotherapy and/or bone marrow transplantation without losing time. Amyloidosis may also present with subcutaneous bleeding of the eyelids [Landa 2004]. These ocular findings are an important sign in the context of AL amyloidosis, as in our case. Our case is the first one in the literature diagnosed as primary systemic amyloidosis with cardiac amyloidosis and presenting with interstitial pulmonary disease and ocular findings.

In conclusion, primary amyloidosis may manifest with many atypical clinical findings. Cardiac involvement with typical findings may be detected as a result of detailed examination and primary amyloidosis may be diagnosed in these patients. Cardiac amyloidosis should be considered in patients with low voltage and a pseudoinfarction pattern on electrocardiography in addition to left ventricular hypertrophy on echocardiography, and the diagnosis should be clarified by further investigations. Thus, a chance of early treatment may be obtained in primary amyloidosis, which has a poor prognosis.

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