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A Case of Cardiac Dysfunction Associated with Monoclonal Gammopathy of Undetermined Significance

The monoclonal gammopathies (MG) are monoclonal neoplasms related to each other by virtue of their development from common progenitors in the B lymphocyte lineage. Cardiac dysfunction in patients with MG is not well established. We experienced a case of cardiac dysfunction associated with MG identified by echocardiography and biopsy. Fifty nine year-old man was admitted because of dyspnea for several months. Echocardiography revealed diastolic dysfunction showing restrictive physiology with elevated left ventricular filling pressure. Bone marrow (BM) studies and immunoelectrophoresis were compatible with monoclonal gammopathy of undetermined significance. Endomyocardial, BM, and enteral biopsies for ruling out for amyloidosis (Congo-red stain) were negative. This is the case of non-amyloidotic light chain deposition cardiomyopathy.

Key Words : *Ventricular Dysfunction; Paraproteinemias; Echocardiography*

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INTRODUCTION

The monoclonal gammopathies (MG) are monoclonal neoplasms related to each other by virtue of their development from common progenitors in the B lymphocyte lineage. The clinical manifestations of MG relate to the expansion of the neoplastic cells, to the secretion of cell products, and to some extent to the host's response to the tumor (1, 2).

There have been numerous reports of multiple myeloma and related disorders with systemic amyloidosis associated with heart involvement (3-7). However, cardiac dysfunction associated with MG has scarcely been reported. We report a case of cardiac dysfunction associated with MG in which the diagnosis was made by echocardiography and biopsy.

CASE REPORT

A 59-yr-old man visited outpatient clinic for evaluation of progressive dyspnea on exertion and chest discomfort for 4 months. He had no remarkable medical and family history.

On the physical examination, his height was 170 cm, weight 77 kg, the blood pressure 104/66 mmHg, the heart rate 76/min, the respiratory rate 20/min, and the body temperature 36°C. He had clear mentality, chronic ill-looking appearance and clear sclerae. Jugular venous distension was noted, but no cervical and axial lymphadenopathy was observed. The heart sounds were regular without murmur, but presystolic gallop (S4) was checked. The breath sounds were clear without rales or wheezing. Abdominal examination revealed normal bowel sounds without any palpable mass. There was no definite pitting edema. Otherwise the physical findings were unremarkable.

The blood cell counts were as follows: the hemoglobin 13.0 gm/dL, the white blood cell count 6,700/μL, and the platelet count 198,000/μL. According to the serological biochemical assay, fasting blood sugar was 107 mg/dL, Na^+ 142 mEq/L, K^+ 4.0 mEq/L, Ca^{2+} 9.6 mg/dL, P^- 3.7 mg/dL, blood urea nitrogen 12 mg/dL, creatinine 0.9 mg/dL, total protein 7.0 g/dL, albumin 4.3 g/dL, aspartate transaminase 20 IU/L, alanine transaminase 22 IU/L, alkaline phosphatase 188 IU/L, lactate dehydrogenase 285 IU/L, and beta-2 microglobulin 1.7 mg/L (normal; 0.8-2.2). Urinalysis showed trace amount of proteinuria, and the urine Bence-Jones protein was suspected. Serum protein electrophoresis study was normal. On the immunochemistry findings, IgG was 1,052 mg/dL (normal; 700-1,600), IgA 105 mg/dL (normal; 70-400), IgM 49 mg/dL (normal; 40-230), and IgE was elevated as 385 IU/mL (normal; 10-180). In serum and urine immunoelectrophoresis study, lambda type MG was shown (Fig. 1).

The chest radiography film showed a slightly enlarged cardiac silhouette and there was no pulmonary congestion. There was no bony lesion on plain skull radiography. Electrocardiography (ECG) showed regular sinus rhythm, intermittent atri-

al premature beats, poor R wave progression, and Q wave in precordial leads (Fig. 2).

The echocardiography revealed dilated both atria, concentric left ventricular (LV) hypertrophy (end-diastolic interventricular septum thickness=13 mm and end-diastolic posterior wall thickness=13 mm, respectively). Both LV dimension and LV ejection fraction were within normal limits. On the Doppler study, ratio of early mitral inflow (E) to late filling velocity (A) (E/A) was 3.0, deceleration time was 135 msec. Tissue Doppler showed 4.03 cm/sec of early diastolic mitral annular velocity (E') with E/E' ratio of 21.6, suggesting restrictive physiology of diastolic dysfunction with elevated LV filling pressure (Fig. 3). There was scanty amount of pericardial effusion without definite evidence of constriction.

Bone marrow (BM) aspirate smears showed normocellular marrow particle, and estimated M:E ratio was 1.71:1. The granulocyte series were normal in number and showed good maturation sequences. Plasma cells were increased and counted up to 6.8% of absolute neutrophil count compatible with monoclonal gammopathy of undetermined significance (MGUS) (Fig. 4). There were no amorphous eosinophilic amyloid material in both H&E and Congo-red staining for ruling out amyloidosis for endomyocardial (Fig. 5A), BM, and enteral biopsies. However, immunostaining for lambda light chain in myocardium showed positive result (Fig. 5B).

The presentation was clinically consistent with non-amyloidotic light chain deposition cardiomyopathy (8). He was managed conservatively with low-dose vasodilators and diuretics, and his symptom mildly resolved. After 9 months follow up, he readmitted for aggravated heart failure, and died due to intractable heart failure and ventricular arrhythmia in the end.

DISCUSSION

In this case, we suspected restrictive cardiomyopathy from ECG and echocardiographic findings. Since cardiac amyloidosis should be considered in any elderly patient with restrictive cardiomyopathy of unknown cause (3, 9, 10), we took multiple site biopsies including endomyocardium and rectum, which showed no birefringence with Congo-red stain when viewed under polarized light. In a patient who presents with

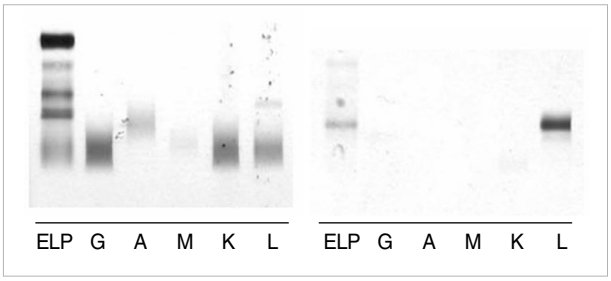

Fig. 1. In serum (left) and urine (right) immunoelectrophoresis study, lambda type monoclonal gammopathy was shown.

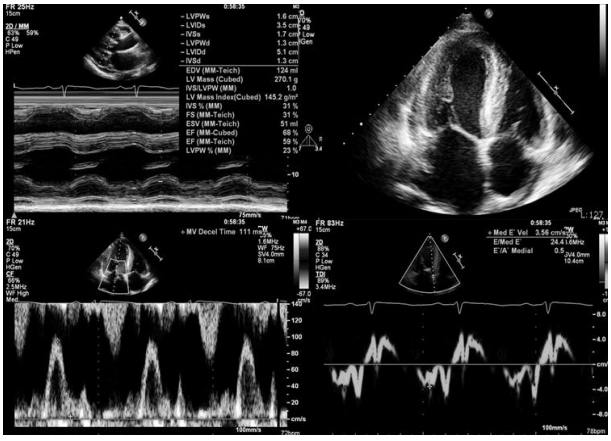

Fig. 3. Echocardiography demonstrated increased thickness of the left ventricle (LV) wall and both atrial enlargement and normal systolic function with normal wall motion. Mitral inflow and mitral anular Doppler tissue velocities showed grade 3 diastolic dysfunction and high E/E', suggesting markedly elevated LV filling pressure.

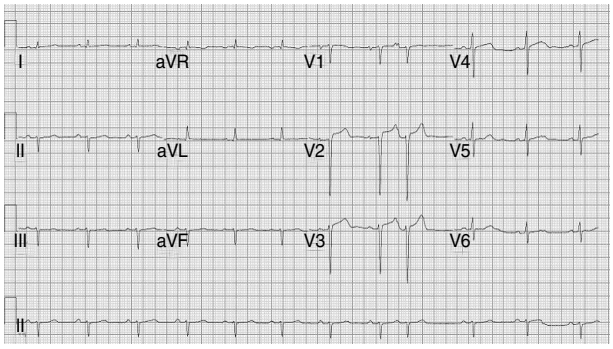

Fig. 2. Electrocardiogram demonstrated regular sinus rhythm with premature atrial beat, left axis deviation, and poor R progression on precordial leads.

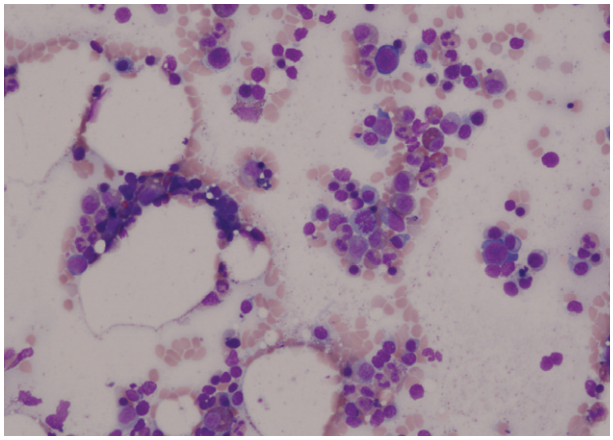

Fig. 4. In bone marrow biopsy, plasma cells were increased and counted up to 6.8% of absolute neutrophil count. (H&E stain, ×200).

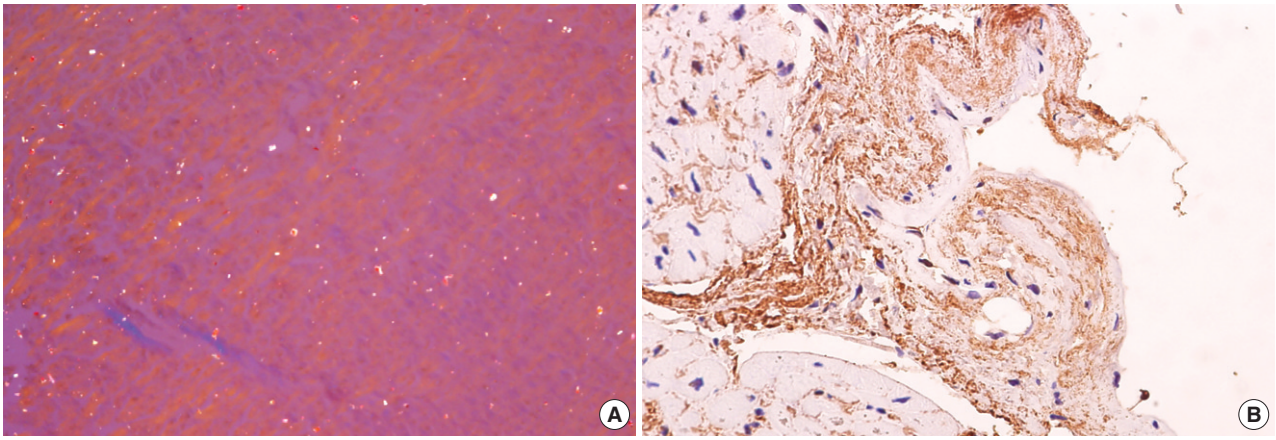

Fig. 5. (A) Right ventricular endomyocardial biopsy with Congo-red stain did not show apple-green birefringence in polarized light (×200). (B) Same specimen of immunostaining for lambda light chain showed positive for perivascular deposition of immunoglobulins (brown color, ×400).

a monoclonal gammopathy, additional testing is warranted, including examination of aspirated BM and a skeletal survey, to rule out multiple myeloma and to confirm the diagnosis of MGUS (2). So, we performed BM biopsy and confirmed MGUS, and concluded this case as a non-amyloidotic light chain deposition cardiomyopathy (8, 11) with restrictive physiology of diastolic dysfunction associated with MGUS. Light chain deposition disease, which was first reported by Randall et al. (12), is a systemic disorder characterized by the deposition of monoclonal immunoglobulin light chains in various organs. The main cardiac manifestation is congestive heart failure as a form of restrictive cardiomyopathy (13, 14). However, in rare cases, paraproteinemia can deposite as a non-fibrillary infiltrate that does not show typical amyoloidosis but resembles its clinical features as in our patient. And non-amyloidotic light chain deposition cardiomyopathy should be considered and endomyocardial biopsy may be needed for the differential diagnosis of restrictive cardiomyopathy (8, 9).

In conclusion, here we present a case showing cardiac dysfunction associated with MGUS in which the diagnosis was made by echocardiography and biopsy. We should consider cardiac involvement associated with systemic infiltrative disease, especially MG, in the differential diagnosis for patients with cardiac dysfunction of unknown cause.

REFERENCES

1. International Myeloma Working Group. *Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. Br J Haematol 2003; 121: 749-57.*
2. Blade J. *Clinical practice. Monoclonal gammopathy of undetermined significance. N Engl J Med 2006; 355: 2765-70.*
3. Shah KB, Inoue Y, Mehra MR. *Amyloidosis and the heart: a comprehensive review. Arch Intern Med 2006; 166: 1805-13.*
4. Nicolosi GL, Pavan D, Lestuzzi C, Burelli C, Zardo F, Zanuttini D. *Prospective identification of patients with amyloid heart disease by two-dimensional echocardiography. Circulation 1984; 70: 432-7.*
5. Hongo M, Ikeda S. *Echocardiographic assessment of the evolution of amyloid heart disease: a study with familial amyloid polyneuropathy. Circulation 1986; 73: 249-56.*
6. Falk RH. *Diagnosis and management of the cardiac amyloidoses. Circulation 2005; 112: 2047-60.*
7. Oh IY, Kim HK, Kim YJ, Sohn DW, Park YB. *An intriguing case of primary amyloidosis with cardiac involvement: symptomatic and echocardiographic improvement with thalidomide treatment. Int J Cardiol 2006; 113: 141-3.*
8. Buxbaum JN, Genega EM, Lazowski P, Kumar A, Tunick PA, Kronzon I, Gallo GR. *Infiltrative nonamyloidotic monoclonal immunoglobulin light chain cardiomyopathy: an underappreciated manifestation of plasma cell dyscrasias. Cardiology 2000; 93: 220-8.*
9. Kushwaha SS, Fallon JT, Fuster V. *Restrictive cardiomyopathy. N Engl J Med 1997; 336: 267-76.*
10. Kristen AV, Dengler TJ, Katus HA. *Suspected cardiac amyloidosis: endomyocardial biopsy remains the diagnostic gold-standard. Am J Hematol 2007; 82: 328.*
11. Toor AA, Ramdane BA, Joseph J, Thomas M, O'Hara C, Barlogie B, Walker P, Joseph L. *Cardiac nonamyloidotic immunoglobulin deposition disease. Mod Pathol 2006; 19: 233-7.*
12. Randall RE, Williamson WC Jr, Mullinax F, Tung MY, Still WJ. *Manifestations of systemic light chain deposition. Am J Med 1976; 60: 293-9.*
13. Nakamura M, Satoh M, Kowada S, Satoh H, Tashiro A, Sato F, Masuda T, Hiramori K. *Reversible restrictive cardiomyopathy due to light-chain deposition disease. Mayo Clin Proc 2002; 77: 193-6.*
14. Jego P, Paillard F, Ramee MP, Grosbois B. *Congestive heart failure: revealing light chain deposition disease. Eur J Intern Med 2000; 11: 101-3.*