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An intriguing case of primary amyloidosis with cardiac involvement: Symptomatic and echocardiographic improvement with thalidomide treatment

Il-Young Oh, Hyung-Kwan Kim, Yong-Jin Kim, Dae-Won Sohn *, Young-Bae Park

Division of Cardiology, Department of Internal Medicine, Seoul National University College of Medicine, 28 Yongun-Dong, Chongno-Gu, Seoul 110-744, Korea

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Abstract

Patients with primary amyloidosis (AL) have poor prognosis with a median survival of one to two years. In patients with symptomatic cardiac involvement, prognosis is even worse with the reported median survival of 6 months. One patient, diagnosed as AL amyloidosis with cardiac involvement, was treated with thalidomide and showed remarkable improvement in functional capacity, cardiac function, and various laboratory parameters without any significant adverse effect and, therefore, we report the case with the review of literatures.

Keywords: Primary amyloidosis; Thalidomide; Cardiac function

1. Case report

A 52-year-old man was admitted for the frequent syncope. He complained of generalized weakness, dyspnea on exertion, and pedal edema 8 months prior to admission. He also had a 2-month-history of several episodes of syncope or pre-syncope when he either hurried upstairs or worked strenuously.

Examination revealed heart rate of 98 beats/min, blood pressure of 130/70 mmHg, and respiratory rate of 18/min. Hepatomegaly and splenomegaly were noted. Chest radiography showed enlarged cardiac size with hilar bulging. Laboratory parameters included an increase in alkaline phosphatase value (326 IU/L), hemoglobin level of 10.6 gm/dL, Bence Jones proteinuria in urine immunofixation electrophoresis (468 mg/day), monoclonal gammopathy (kappa type) in serum immunoelectrophoresis, and plasma cell dyscrasia in bone marrow examination. The electrocardiographic and echocardiographic findings are depicted in Figs. 1 and 2A, respectively. We performed endomyocardial biopsy, where a typical picture of apple-green birefringence after Congo red staining was found (Fig. 3).

On the basis of our findings, the diagnosis of primary (AL) amyloidosis with cardiac involvement was confirmed. He was started on low dose diuretics to reduce pulmonary congestion, which was discontinued due to azotemia. Thereafter, he had been treated with thalidomide (300 mg/day) and dexamethasone (only for initial 6 months). His functional capacity began to improve dramatically 3 months after treatment and further improvement was observed by a 17-month thalidomide treatment. On the latest visit to an outpatient clinic when he completed 20 months of thalidomide treatment, he was able to climb mountains and has not experienced syncope any longer. Hepatomegaly, splenomegaly, anemia and Bence Jones proteinuria completely disappeared. The alkaline phosphatase value was returned to normal range. An echocardiogram performed 17 months

* Corresponding author. Tel.: +82 2 2072 2855; fax: +82 2 764 4281.
E-mail address: dwsohn@snu.ac.kr (D.-W. Sohn).

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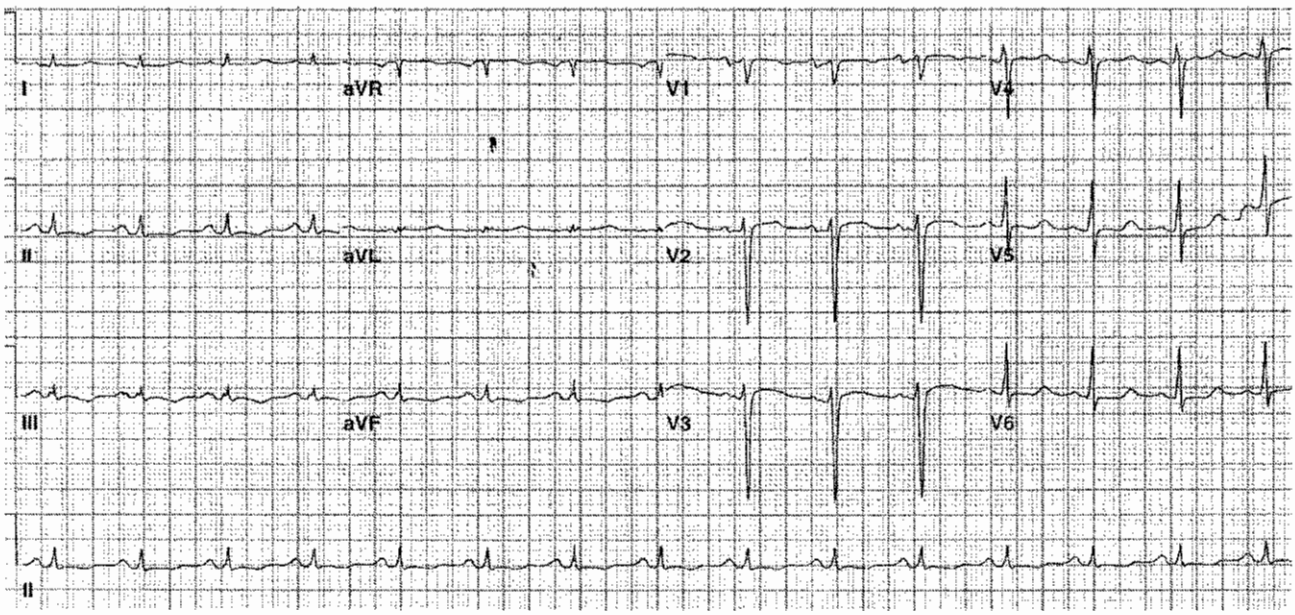

Fig. 1. Electrocardiography showed low voltages in the limb leads in contrast to the increased left ventricular wall thickness in echocardiogram.

after thalidomide treatment showed improved systolic function with the wall motion of left ventricle normalized (Fig. 2B).

2. Discussion

AL amyloidosis, a plasma cell dyscrasia related to multiple myeloma, is characterized by an autonomous proliferation of plasma cells with an overproduction of monoclonal immunoglobulins [1]. It carries a worse prognosis with a median survival of one to two years, which falls to only 6 months with symptomatic heart involvement [2]. In general, patients who have AL amyloidosis present with more than one of the following seven syndromes [3]: (1) cardiomyopathy with or without congestive heart failure, (2) nephrotic-range proteinuria with or without renal insufficiency, (3) hepatomegaly with dramatic increase in alkaline phophatase value, (4) axonal peripheral neuropathy, (5) autonomic neuropathy manifested by orthostatic hypotension, and bladder and/or bowel dysfunction, (7) soft tissue involvement leading to arthropathy and enlargement of the tongue and submandibular glands, frequently with jaw and limb claudication.

To date, melphalan, corticosteroid, and colchicine have been the most widely used drugs to treat AL amyloidosis with limited success [4]. Recently, 4′-iodo-4′-deoxydoxorubicin, which has an affinity for amyloid fibrils, and stem cell

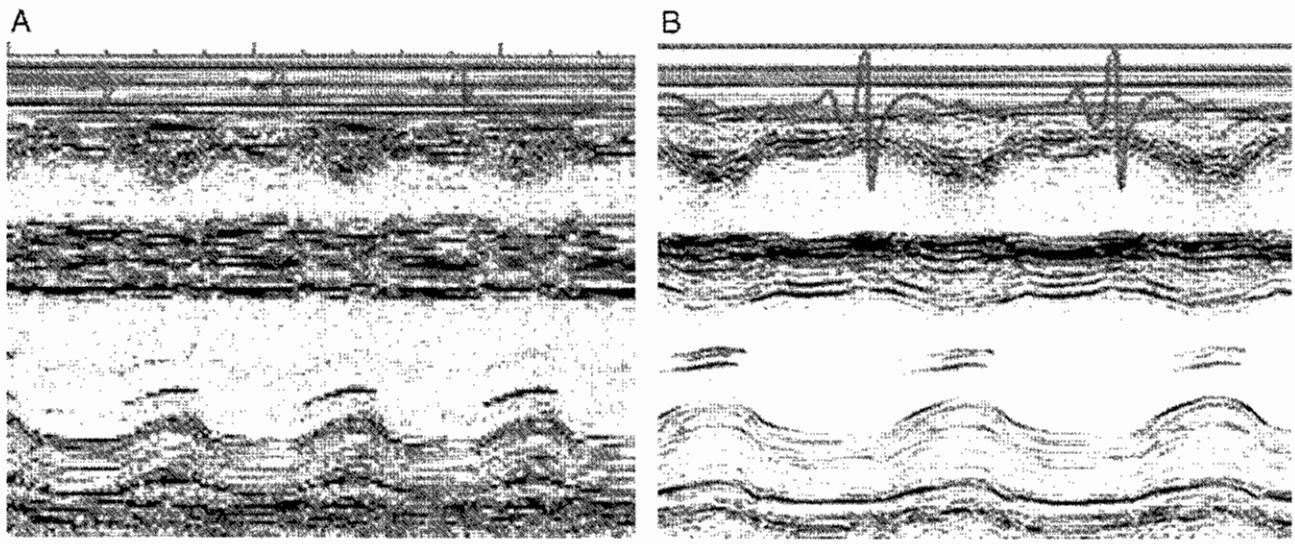

Fig. 2. The systolic function of the left ventricle, calculated by ejection fraction, improved from 35% at the diagnosis (Left panel) to 57% 17 months after treatment with thalidomide (Right panel).

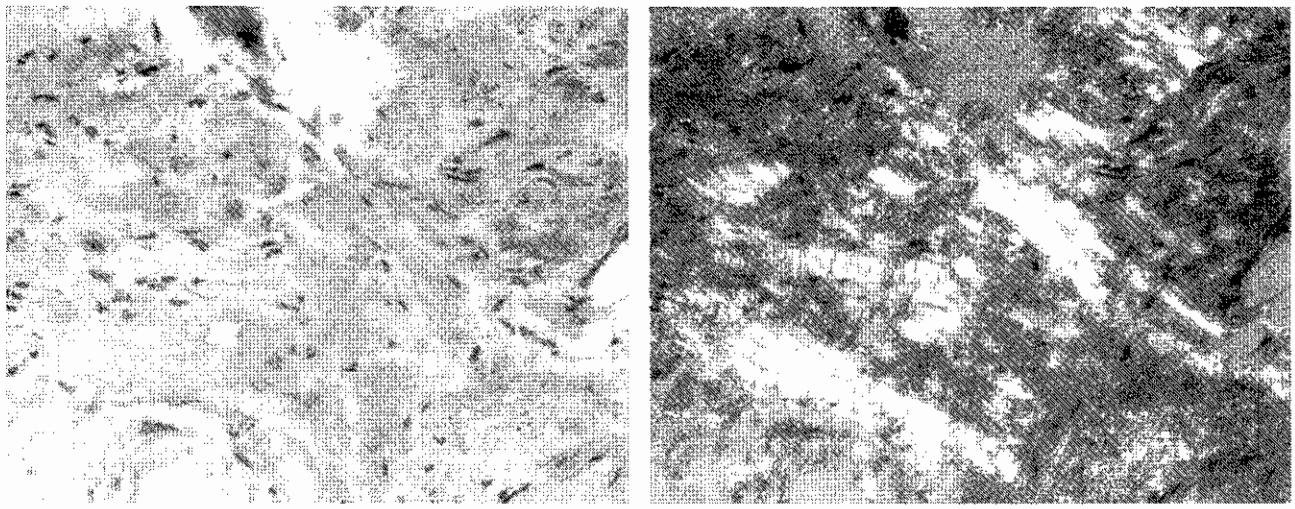

Fig. 3. Myocardial degeneration and atrophy (Left panel, × 100) and typical apple-green birefringence after Congo red stain under polarizing microscopic examination (Right panel, × 100).

transplantation, were introduced for alternative treatment option for AL amyloidosis [5,6]. Nevertheless, survival benefits from the drugs described earlier have been disappointing.

Since interest in thalidomide resurfaced in 1965 after incidental discovery of its masked effects on erythema nodosum leprosum [7], it has stood in the spotlight of various clinical fields, especially in the management of various cancers including multiple myeloma. In the early 20th century, it was used for treatment of AL amyloidosis [8,9].

In this case, thalidomide was initially chosen due to increased serum creatinine level and decreased cardiac function, in which circumstances it is difficult to prescribe melphalan or colchicine. In spite of the possibilities that thalidomide could be used for treatment of AL amyloidosis being previously suggested [8,9], there has been no definite report, to our knowledge, depicting the beneficial effects of thalidomide on cardiac functional recovery. This case is interesting in the fact that the patient had a near-complete recovery in both cardiac function and many laboratory parameters with thalidomide treatment. Although we cannot definitely conclude that AL amyloidosis has been cured in this male patient because endomyocardial biopsy was not done after treatment, the objective evidences of echocardiographic and laboratory findings suggest that thalidomide will become a promising solution to manage the patients with AL amyloidosis, to whom the treatment with melphalan or colchicine is difficult to perform. Clinical trials will be warranted to elucidate the subgroup of patients with AL amyloidosis in whom thalidomide is effective.

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