A case of dyspnea and periorbital rash

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A 75-year-old woman presented with dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, and edema. Macroglossia, generalized petechiae, raccoon eyes sign, and peripheral neuropathy were present, and an echocardiogram showed cardiac dilatation and left ventricular systolic dysfunction. Rectal biopsy and immune fixation electrophoresis confirmed the diagnosis of AL amyloidosis.

Amyloidosis is a group of diseases caused by extracellular deposition of insoluble polymeric protein fibrils in tissues and organs. Symptoms vary widely depending upon the site of amyloid deposition. Cardiac involvement may occur, with or without clinical manifestations, as a part of systemic amyloidosis or as a localized phenomenon and is associated with a poor prognosis (1). We describe a case of a 75-year-old woman with primary amyloidosis presenting as full-blown cardiac failure and classical cutaneous manifestations. The diagnosis was established by rectal biopsy and immunofixation electrophoresis.

CASE REPORT

A 75-year-old woman presented with gradually progressive breathlessness and pedal edema for 3 years with acute worsening of symptoms. There was associated orthopnea and paroxysmal nocturnal dyspnea. Edema initially started in the lower limbs and later involved the whole body and face. She had a history of easy bruisability and noticed spontaneous ecchymotic patches for a couple of years with no other significant bleeding manifestations. She also gave a history of enlargement of the tongue, which made chewing and talking difficult, and a swelling just below the jaw for 2 years. Her relatives had noticed discoloration around the eyes for 1 year. Apart from this, she had paraesthesia of extremities, which was worse in a cold climate, constipation, and urge incontinence. Her sleep was disturbed at night, and she had daytime somnolence and a history of snoring, which was suggestive of obstructive sleep apnea. She had had no significant illnesses in the past, and there was no similar illness among her family members.

On examination, the patient had significant pallor and pedal edema. Macroglossia, petechiae, and ecchymosis in the periorbital area (raccoon eyes) and the perioral region

(Figure 1) and over the trunk and extremities were present. Her pulse rate was 110 beats/minute; blood pressure, 120/90 mm Hg; and respiratory rate, 24 breaths/minute. Her jugular venous pressure was also elevated. Respiratory system auscultation revealed bilateral crepitations and rhonchi. There was cardiomegaly, with an audible S3 and pansystolic murmur. The nervous system examination showed a sensorimotor type of peripheral neuropathy.

A routine blood examination showed mild anemia with normal cell counts and a normal erythrocyte sedimentation rate. Her hemoglobin was 10 g/dL. A peripheral smear showed normocytic normochromic anemia, and a bone marrow biopsy showed mild plasmacytosis with 12% plasma cells. She had mild hyponatremia, a mild increase in activated partial thromboplastin time and prothrombin time, and a moderately raised fasting level of low-density lipoprotein; other biochemical tests were within normal limits. Urine examination showed a trace of albumin without hematuria and pyuria. Urine protein excretion was 0.981 g/day. A Bence Jones protein test and free light chain

Figure 1. Photograph of the patient, showing bilateral periorbital rash (raccoon eyes) and macroglossia.

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Figure 2. Two-dimensional echocardiography showing concentric left ventricular (LV) hypertrophy (LVH) with a granular speckling pattern. LA indicates left atrium.

assay in urine were negative. Serum electrophoresis showed no M band, but serum immunofixation electrophoresis was positive for amyloid light chain. The serum kappa was 9.3 mg/L, and lambda was elevated with 76.5 mg/L. The immunoglobulin assay showed an IgG of 75 mg/dL, IgM of 33 mg/dL, and IgA of 40 mg/dL. Serum levels of N-terminal prohormone of brain natriuretic peptide were elevated at 16,000 pg/mL.

A chest x-ray showed bilateral mild pleural effusion. Echocardiographic evaluation showed concentric left ventricular (LV) hypertrophy with a granular speckling pattern (*Figure 2*), global LV hypokinesia, moderate LV systolic dysfunction (ejection fraction 37%), restrictive LV filling, moderate pulmonary arterial hypertension, and mild pericardial effusion. The patient's rectal biopsy was positive for amyloid deposits by hematoxylin and eosin staining (*Figure 3*) and Congo red staining. The Congo red stain examined under polarized light showed apple green birefringence. Her electrocardiogram showed low voltage complexes with normal axis and rhythm.

Based on the clinical picture and the study results, a diagnosis of primary amyloidosis was made. Treatment was started for heart failure, and the patient improved with supportive measures. She was discharged, with treatment planned for amyloid, but unfortunately she died of progressive heart failure within a few weeks of the diagnosis.

Figure 3. Hematoxylin and eosin staining showing deposition of dense homogeneous eosinophilic amyloid distributed extracellularly.

DISCUSSION

In primary amyloidosis, the fibrillary protein is AL type. A few patients have some form of plasma cell dyscrasias or other form of lymphoproliferative disorders, but most do not. The disease progresses rapidly. Macroglossia is the pathognomonic feature of AL amyloidosis. Easy bruisability due to deposition of amyloid and deficiency of factor X and cutaneous ecchymoses, especially if around the eyes, may be seen. The heart and kidneys are the most commonly affected organs. Mortality is high in patients with cardiac involvement (2). Increased atrial septal wall thickening and granular speckling in the myocardium are highly specific for differentiating cardiac amyloidosis from other causes of LV hypertrophy (3). With early diagnosis, there is better response to therapy and prolonged survival (4).

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