Amyloid Heart: Heart Failure with Preserved Ejection Fraction – A Rare Cause of a Common Illness

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The importance of heart failure with preserved ejection fraction is gaining increasing recognition since it is responsible for half the cases of heart failure. Valvular and pericardial heart diseases, as well as right heart failure and diastolic dysfunction, are etiologies of this entity. Diastolic heart failure is more common in the elderly, in women, and in patients with hypertension. Hypertrophic cardiomyopathy, coronary heart disease, diabetes mellitus, hypertension, restrictive cardiomyopathy and infiltrative cardiomyopathies can all cause diastolic heart failure [1].

Amyloidosis can affect the heart in 50% of patients with systemic amyloidosis. Clinical manifestations include heart failure, syncope, angina, pericardial disease, involvement of the conduction system, and thromboembolism. Since the extent of cardiac involvement is a major prognostic factor in these patients, efforts should be made to reach the diagnosis as early as possible [2].

PATIENT DESCRIPTION

PATIENT 1

A 64 year old woman was admitted to our department after several months of malaise. Her clinical history included poliomyelitis in her childhood resulting in right leg weakness, back surgery at the age of 12 for spina bifida and occasional urinary incontinence with recurrent urinary tract infections since the surgery, multinodular goiter, and monoclonal gammopathy of undetermined significance for 20 years.

On arrival the patient reported weakness and twitching of her legs, loss of appetite and nausea with weight loss of 4 kg over a period of 1 month, dysphagia for fluids and solids, reflux, cough and hoarseness. A thorough ambulatory investigation revealed anemia with hemoglobin 10 g/dl (11.7–15.7 g/dl) and erythrocyte sedimentation rate 84. Thyroid ultrasound demonstrated a multinodular goiter; chest X-ray and abdominal ultrasound were normal. Electrophoresis of her urine showed 2.8 g of immunoglobulin G lambda protein, which correlated well with previous and recurrent studies over the last 20 years since MGUS was first described. On admission the patient showed no sign of distress, and apart from hypoesthesia and weakness of her legs (that were attributed to the polio) her physical examination was normal. Laboratory test revealed creatinine 0.71 mg/dl (0.5–0.9 mg/dl), albumin 30 mg/dl (34–48 mg/dl), protein 80 mg/dl (64–83 mg/dl). Electrolytes and liver function tests were normal. Electrocardiography revealed small complexes. Echocardiography demonstrated left ventricular hypertrophy with diastolic dysfunction. Soon after admission the patient underwent a fat-pad biopsy that was negative for amyloid by Congo-red stain; gastroscopy was scheduled for 2 weeks.

On her second admission, gastroscopy revealed erosive gastritis and duodenitis, and gastric biopsies were also sent for amyloid. Bone marrow biopsy was performed. During this admission she developed leg edema and was discharged although the biopsy results were pending. The gastric biopsy revealed abundant amyloid type AL, and the bone marrow biopsy showed monoclonal plasma cells lambda type with up to 60% cellularity. Blood vessels stained positive for Congo-red. The patient received fluids with allopurinol and started on a regimen of bortezomib, dexamethasone and cyclophosphamide. Dyspnea developed, peripheral leg edema worsened, and chest X-ray was consistent with pulmonary congestion and bilateral pleural effusions. The patient developed atrial fibrillation that was restored to sinus rhythm with amiodarone. She was transferred to the intermediate care chest unit with a diagnosis of amyloid heart. After stabilization she was referred to a tertiary hospital for completion of therapy where she is currently being treated.

MGUS = monoclonal gammopathy of undetermined significance

PATIENT 2

A 75 year old woman was admitted to our department with dyspnea, cough, bilateral leg edema and abdominal distension. The patient had been hospitalized repeatedly in the preceding months due to dyspnea that was attributed to heart failure exacerbations, and each time diuretics were administered but with no improvement. She suffered from hypertension, diabetes mellitus, dyslipidemia, morbid obesity, and diastolic heart failure. Her regular medications included acetylsalicylic acid, furosemide, statins, repaglinide, losartan, and inhalations of ipratropium. Prior to her first admission she underwent cardiac scintigraphy that revealed no ischemia, and chest computed tomography that demonstrated mild pericardial effusion, bilateral

moderate pleural effusion, signs of pulmonary hypertension and a small left lower lobe consolidation. Echocardiography showed left ventricular hypertrophy with mild left atrial enlargement. On admission the patient was tachycardic, tachypneic and dyspneic, and had rales on auscultation, with prolonged expiratory phase and wheezes and severe bilateral leg edema. Blood tests were consistent with creatinine levels of 2.7 mg/dl (0.5–0.9), protein 57 mg/dl (64–83), albumin mg/dl 27 (34–48), and hemoglobin 9.6 g/dl (11.7–15.7). ECG showed sinus tachycardia with no ST changes and inverted T wave in V6.

Chest X-ray revealed pulmonary congestion with bilateral pleural effusion. We found 3.9 g of protein in a 24 hour urine collection. Echocardiography showed diastolic dysfunction with left ventricular hypertrophy and a restrictive pattern. The patient was treated with diuretics and her kidney function deteriorated. She was then transferred to the intensive care cardiac unit and underwent right-sided heart catheterization with a finding of high pulmonary capillary wedge pressure. She became dialysis dependent.

Serum protein electrophoresis showed monoclonality of lambda chains. A fat-pad biopsy was positive for amyloidosis. The patient developed line sepsis and deep vein thrombosis of her right leg followed by heparin-induced thrombocytopenia. Her leg became necrotic and an above-knee amputation was performed. She was then admitted to the intensive care unit but died several days later due to septic shock.

COMMENT

We describe two women with amyloid heart presenting with heart failure and preserved ejection fraction, who differ by presentation and outcome. The 64 year old patient developed rapidly progressive heart failure and atrial fibrillation during treatment with steroids, fluids and bortezomib for systemic AL amyloidosis. The other patient, 75 years old, was hospitalized recurrently because of symptomatic heart failure unresponsive to therapy. This patient was diagnosed too late in the grim pathway of this disease.

AL amyloidosis is the most common and severe among the increasing number of amyloidosis subtypes. It often targets the heart, with an estimated survival of a few weeks after the onset of overt heart failure. Early diagnosis is of the utmost importance to improve survival. Since cardiac involvement determines both survival and treatment tolerability, risk stratification is based on troponin and N-terminal pro-brain natriuretic peptide levels [3]. Bortezomib combinations are the mainstay of therapy with reports of long-term survival, although studies are still lacking. Intermediate risk patients can either undergo autologous stem cell transplantation or combination chemotherapy. High risk patients with markedly elevated levels of NT-Pro-BNP are extremely sensitive to treatment toxicity. Since early diagnosis is of great importance, it is possible that changing the monitoring approach to MGUS will hasten diagnosis and improve survival [4].

Heart failure is a leading cause of morbidity and mortality among hospitalized patients and diastolic heart failure comprises half of those cases. Cardiac amyloidosis should be considered in adults with unexplained heart failure, left ventricular hypertrophy and low voltage on electrocardiography [2].

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NT-Pro-BNP = N-terminal pro-brain natriuretic peptide