CASE REPORT

Multiple Myeloma a Rare Cause of Heart Failure with Reduced Ejection Fraction

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ABSTRACT

Multiple myeloma (MM) is one of the plasma cell disorder. It is a malignant condition of plasma cell derived from single clone. The incidence of myeloma increases with age. The mean age of diagnosis is 69 years. MM is more common in males than females. The incidence of MM is lowest in people from developing countries including Asia. Although MM may have cardiac manifestations but heart failure with reduced ejection fraction (HFrEF) or dilated cardiomyopathy is unusual presentation. We report a case of multiple myeloma that rarely presented as dilated cardiomyopathy.

Key words: Multiple myeloma, plasma cell disorder, single clone, dilated cardiomyopathy, heart failure with reduced ejection fraction.

INTRODUCTION

Multiple myeloma is a malignancy arising from the plasma cell. MM accounts for ~ 10% of all haematological cancers[1,2]. Most of the patients are elderly and mean age at presentation is 69 years[3]. Many of these patients have cardiovascular risk factors or comorbidities at diagnosis[4]. MM itself directly and indirectly affects cardiac function.

In multiple myeloma cardiac involvement has been associated with severe prolonged disease because of its complication[5]. Amyloid deposition in myocardium has been one of the cause of dilated or restrictive cardiomyopathy and heart failure[6,7]. In all amyloid light-chain (AL) cases cardiac involvement is estimated in up to 50% cases[8,9]. The hyperviscosity syndrome has been associated with congestive heart failure[10]. In addition, ischemic heart disease may occur as a result of one or more of these mechanisms associated with other risk factors like age, marked anemia or underlying coronary artery disease. We describe one case with well defined multiple myeloma presenting as heart failure with reduced ejection fraction (HFrEF).

CASE REPORT

A 61-year-old female have progressive dyspnea on exertion since 2 months. She also had both lower limb swelling since 15 days. Along with these she had orthopnea, pedal edema with rapid deterioration requiring admission. She was known case of hypothyroidism, and hypertension for which she was on regular treatment with thyroxin 50 mcg and telmisartan 40 mg and hydrochlorothiazide 12.5 mg daily.

Her blood pressure was 140/90 mm Hg, pulse rate 98 per minute; respiratory rate 26 per minute, and temperature 98.8°F. A physical examination revealed basal crackles in lungs, pedal edema and raised jugular venous pressure.

Laboratory tests revealed hemoglobin 8.1 gm/dl (N: 12.0- 15.0), total leukocyte count 5100/ Cumm (*N*: 4000- 10000), platelet count 1.20 lac/Cumm (N: 1.50- 4.50), serum creatinine level at 1.5 mg/dl (*N*: 0.5-1.4), bood urea 44.3mg/dl (N:15- 45), the sedimentation rate was 50 mm at the first hour, and lactate dehydrogenase (LDH) was normal at 200 U/L (*N*: 105- 248). serum uric acid 6.8 mg/dl (*N*: 2.5- 7.5), SGPT 111.8 U/L (*N*: 10- 40) Serum alkaline phosphatase 204.8 U/L (*N*: 110- 310), serum protein 10.9 g/dl (*N*: 6.4- 8.5), serum albumin 2.8 g/dl (*N*: 3.2- 5.5)

The bone marrow examination revealed occasional megakaryocytes and myeloid erythroid ratio 5.5:1. 36% plasma cells present. Differential distribution of cells of myeloid series are within normal limits. Findings suggestive of multiple myeloma.

Serum protein electrophoresis shows total protein 11.6 (*N*: 6.4- 8.2), albumin 2.82 (*N*: 3.30 -5.70), beta-2 globulin 4.71 (*N*: 0.10- 0.50), gamma globulin 2.69 (*N*: 0.50- 1.60). Myeloma band detected. (**Figure: A**).

Serum immunoglobulin parameter (Method: immunenelphelometry), total IgA 71.900 g/L (*N*: 0.52-4.68), total IgG 1.95 g/L (*N*: 6.5- 16.4), total IgM < 0.17 g/L (*N*: 0.39- 3.38).

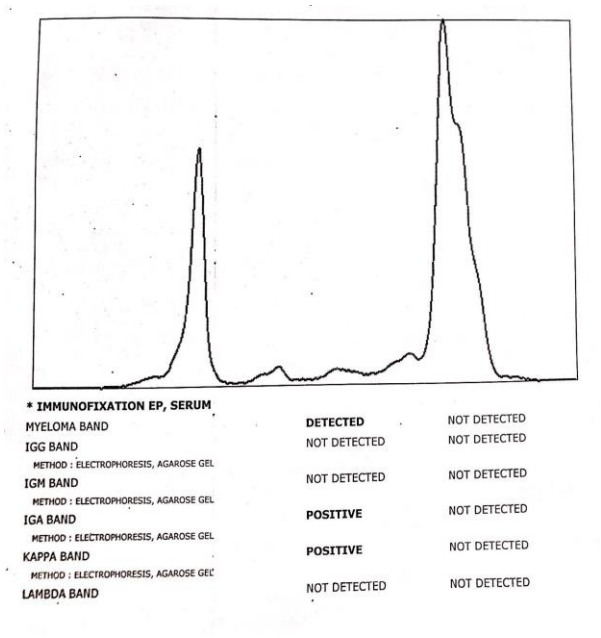

Figure A: Serum protein electrophoresis showing myeloma bands

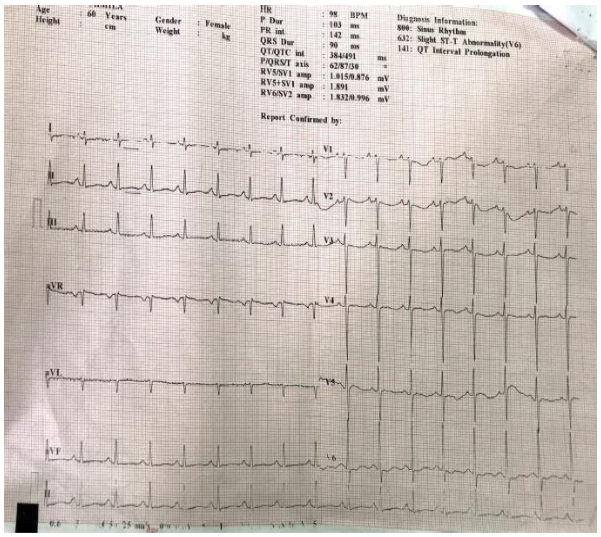

Figure B: Electrocardiogram shows sinus tachycardia, left atrial overload and slight ST-T changes in leads V5-V6.

Serum light chains level, kappa free light chain 61.70 mg/L (*N*: 3.30- 19.40), *lamda* free light chain < 5.47 mg/L (*N*: 5.71- 26.30). Serum B2-microglobulin level was 9580 ng/mL (*N*: 609.0- 2366.0).

Electrocardiogram revealed sinus tachycardia, left atrial overload and slight ST-T abnormality in V5,V6 leads. (**Figure: B**)

Doppler echocardiography showed the dilated cardiomyopathy with severe left ventricle systolic dysfunction, LVEF ~24 %, Grade I diastolic dysfunction, mild mitral regurgitation, mild tricuspid regurgitation and mild aortic regurgitation. (**Figure: C**)

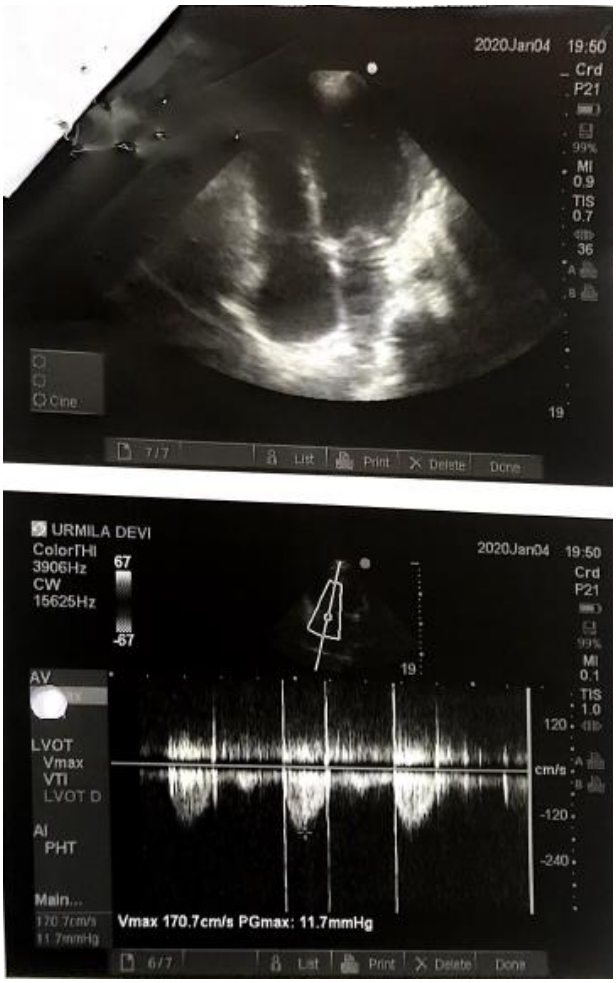

Figure C: Doppler echocardiography showed dilated left ventricle, dilated right ventricle and right atria with mild mitral regurgitation.

DISCUSSION

This 61-year-old female patient, on arrival at the hospital emergency room, with an evocative symptoms of acute decompensated heart failure; apart from the renal insufficiency and moderate anemia found during the intake assessment in the cardiology department. There was no clinical or biological symptoms of myeloma could be evoked, but the biochemical and hematological assessments at the arrival were little contributory factors.

In multiple myeloma patient's anemia is the most common hematological abnormality and commonly associated with heart failure[11]. There are specific set of clinical manifestation occur in multiple myeloma patients like hypercalcemia, renal dysfunction, anemia and bone lesion[12]. Hypercalcemia can leads to development of arrhythmias[13], renal dysfunction has been shown to increase the risk of cardiovascular disease by two to four times[14]. Anemia can also causes high-output heart failure, cardiomyopathy and arrhythmias.[15,16] Several studies showed that anemia independently increases the risk of cardiovascular morbidity and mortality particularly in old age[17].

In multiple myeloma anemia is present in up to two-third of patients and causes are multifactorial: plasma cell infiltration, decreased erythropoietin secretion due to renal dysfunction, cytokine-induced suppression of erythropoiesis, myeloablative chemotherapy and amyloidosis etc.[18].

In our case report the medullary insufficiency linked to the infiltration of the bone marrow by malignant plasma cells causes anemia, along with superadded mild renal dysfunction and heart failure.

The serum electrophoresis is one of the important test in old anemic patients that have hypergammaglobulinemia along with renal dysfunction. It can contribute to the etiologic diagnosis by screening for monoclonal gammopathies like multiple myeloma, or to explore possible other associated inflammatory conditions. The results of the assessment in this patient led us to suggest the resumption of laboratory tests for diagnostic and etiological purposes. Serum protein electrophoresis demonstrated positive myeloma band (IgA band and kappa band). Furthermore, immunonephelometry showed elevated total IgA level and elevated kappa free light chain. Beta-2 microglobulin level was also significantly high in our patient.

The bone marrow examination is the decisive test of multiple myeloma, and it helps to identify the abnormal plasma cell infiltration both quantitatively and qualitatively. The clonal bone marrow plasma cell is one of the diagnostic criteria of MM. Indeed, the diagnostic criteria was proposed in 2014 by the International Myeloma Working Group (IMWG), thus making it possible to distinguish MM, indolent MM, and monoclonal gammopathies of undetermined significance (MGUS)[19].

It is not surprising that many of the multiple myeloma patients have existing cardiovascular abnormalities. MM is primarily a disease of the elderly with high burden of cardiovascular diseases particularly manifestated in this age group.[3] Many studies demonstrated that prevalence of cardiovascular disease (including hypertension, coronary heart disease, heart failure, and stroke) was estimated to be ~40% in patients aged 40–59 years, increasing to 70–75% in those aged 60–79 years and to 79–86% for those aged 80 years and above[20]. Pooled European data from six randomized trials demonstrated that 69% of patients with MM had cardiovascular comorbidities at the diagnosis[21].

Progressive myeloma and/or symptomatic patients require therapeutic intervention. The therapy of myeloma includes an initial induction regimen followed by consolidation and maintenance therapy. Therapy is partly dictated by the patient's age, other risk factors and comorbidities. In newly diagnosed patients with MM have high response rate (>80%) lenalidomide, an immunomodulatory derivative of thalidomide and bortezomib, a proteosome inhibitor combined with dexamethasone. The overall median survival is about 5–7 years, but the prognosis varies between patients: Some patients die within a few months and others survive more than 10 years[22].

CONCLUSION

This case illustrates the importance of exploring heart failure particularly heart failure with reduced ejection fraction (HFrEF) with anemia. Heart failure per se linked to anemia and renal dysfunction in low output state or aggravates each other. Indeed, serum protein electrophoresis most important test especially in the elderly even in the absence of evocative clinical signs allowing the diagnosis of myeloma and accelerating the therapeutic management. The management of cardiovascular risk factors is an emerging area of interest among the MM community. A multidisciplinary approach involving hematogist, oncologists and cardiologists can help to optimize outcomes and expand access to new treatments for cardiac comorbidities in multiple myeloma patients.

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