An atypical presentation of multiple myeloma in a young patient with pathological fracture

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ABSTRACT

We report a case of a 34-year-old male with a history of pulmonary tuberculosis and pathological fracture of shaft of long bone presented with symptoms of lower respiratory tract infection. The patient did not have any typical symptoms of multiple myeloma or hypercalcemia on presentation. Throughout his hospitalization, his serum globulin level was very high along with mild normocytic normochromic anemia and mild renal function derangement without apparent cause. Acute phase markers of inflammation, for example, erythrocyte sedimentation rate (ESR) were not elevated in this patient and there was no lytic lesion in bone radiographs. He was eventually diagnosed as a case of stage 3 multiple myeloma by immuno-fixation electrophoresis and bone marrow study. Multiple myeloma represents a pathology of diverse distribution and has varied unusual presenting symptoms. We consider it an underdiagnosed disease often missed especially in young because it is not considered by clinicians.

Keywords: Hypercalcemia, multiple myeloma, plasma cells, β2 microglobulin

Introduction

Multiple myeloma (MM) (myelo-marrow and –oma mass in Greek) is characterized by the clonal proliferation of plasma cells associated with the secretion of monoclonal immunoglobulins.¹ It is the most common bone marrow malignancy, with 10% of all blood cancers being attributed to MM.² Occurrence of MM in Asia in general and India, in particular, is less as compared to the West.³ As per a recent study collected cases during 2012–2014 from various cancer registries in India, MM is approximately 1.9% of all malignancies in India with male-to-female ratio of 1.4:1.⁴ At diagnosis, less than 2% of patients are under 40 years of age and it is very scarce in less than 30 years old.⁵ MM usually presents with anemia, bone pain, hypercalcemia, and high erythrocyte sedimentation rate (ESR) but sometimes patients can be asymptomatic or present with uncommon clinical findings.⁶ Here, we report an atypical presentation of MM in a young male.

Case Summary

A 34-year-old male presented in medicine outdoor with complain of fever and productive mucoid cough for 3 days. The patient also complained of decreased appetite, fatigability, and generalized body pain for a long time. He had suffered from pulmonary tuberculosis 4 years ago for which he took 6 months of anti-tubercular treatment (WHO category 1). He also had a fracture of shaft of right femur following trivial trauma 6 months ago and underwent intramedullary nailing [Figure 1]. There was no history of hemoptysis, weight loss, polyuria, polydipsia, pain abdomen, or any neurological symptoms. Systemic examination was unremarkable except crepitation in the left infra‑scapular region. Based on these findings, a presumptive diagnosis of lower respiratory tract infection or reactivation of pulmonary tuberculosis was made.
Laboratory investigations showed mild anemia (9.7 gm/dL), normal white and differential cell count (5460/µL, 52% neutrophils and 37% lymphocytes), and platelets (2.07 lakh/µL). ESR and highly sensitive C-reactive protein were within normal limits (11 mm AEFH and 3.38 mg/dL). He had mild renal dysfunction (B urea 38 mg/dL; serum creatinine 1.79 mg/dL; eGFR – 46 ml/min/1.73 m2). RBC morphology was suggestive of normocytic normochromic anemia. Reticulocyte count was 2.60%. Other parameters were within normal limits (serum vitamin B12 levels > 2000 pg/mL, serum iron 36 ug/dL, TIBC 198 µg/dL, ferritin 262.7 ng/mL, serum calcium levels –9.7 mg/dL, serum alkaline phosphatase –46 U/L, and intact PTH –27.1 pg/mL). Liver function showed a marked reversal of albumin-to-globulin ratio (albumin 2.03 gm/dL and globulin 10 gm/dL). Skull X-ray showed no lytic lesions.

Because of raised globulin, serum protein electrophoresis (SPEP) was performed which showed monoclonal gammopathy (M spike in gamma globulin region) [Figure 2]. Immuno-fixation electrophoresis (IFE) identified M spike in IgG and Kappa region [Figure 3] with serum β2 micro-globulin levels 9988 ng/mL (normal 0–3 ug/mL), kappa light chain 693 mg/L (normal 3.3–19.4 mg/L), and kappa/lambda ratio was 58.729 (normal reference range, 0.26–1.65). Bone marrow examination [Figures 4a and b] was suggestive of plasma cell dyscrasia with 61% plasma cells suggesting MM. The patient was classified as stage 3 MM according to the international scaling score.

**Discussion**

MM is a B-cell disorder characterized by unchecked clonal proliferation of plasma cells and the accumulation of these malignant cells in the bone marrow. It usually presents with anemia, infections, lytic or osteopenic bone disease, or renal failure. It can be asymptomatic sometimes and diagnosis may be made incidentally, which was present in our case. The diagnosis of MM needs the presence of at least one (MDE) myeloma defining events along with the presence of at least 10% clonal plasma cells on bone marrow study or a biopsy-proven plasmacytoma. MDE consists of hypercalcemia, renal failure, anemia, or lytic bone lesions as well as three specific biomarkers: clonal bone marrow plasma cells ≥60%, serum free light chain (FLC) ratio ≥100 (provided involved FLC level is ≥100 mg/L), and more than one focal lesion on MRI.

Clinical suspicion of MM should be confirmed by M band on protein electrophoresis, immune fixation, and bone marrow examination. Risk stratification can be done by a revised international staging...
system that incorporates components of tumor burden and disease biology (presence of high-risk cytogenetic abnormalities or raised LDH level) to create a unified prognostic index.

MM is rare in individuals younger than 35 years. In 1996, Blade et al. conducted a study in Mayo clinic and the frequency of MM in patients younger than 30 years was found to be 0.4%. They also found that clinical presentation and response to therapy was similar among patients of all ages.

Our case was having quite an unusual presentation as a case of mild respiratory infection. This patient lacks the classical symptoms of low backache, weight loss or symptoms of hypercalcemia present in most patients with MM. He also had normal ESR, normal serum calcium level and without any lytic lesions on spinal or skull bones and is only 34 year old. This type of patient can be easily missed by the clinician and usually presents in late stages with complications. In our case diagnosis was suspected only by abnormal high globulin level and history of pathological fracture of long bone. On evaluation, the patient had anemia, mild renal dysfunction, classical M spike and >60% plasma cells on bone marrow examination. Diagnosis would often be missed by a local doctor at the primary health center in this type of patient as MM is rarely kept in differentials for pathological fracture at such a young age. A high degree of clinical suspicion is necessary to diagnose MM patients at an early stage.

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Conflicts of interest
There are no conflicts of interest.

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