



Hemolytic Anemia as Initial Presentation of Multiple Myeloma

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Abstract

Though AIHA is a common association with lymphoproliferative diseases its association with Myeloma appears to be very rare. However it is not clear if the true prevalence is under-estimated. Also, the only small case series and the many case reports from literature seem to suggest a possible higher prevalence among Asians, people of Black-Caribbean or Black-African descent. Hence when anemia is out of proportion or unexplained in a patient with paraproteinemia and in AIHA patients with appropriate clinical/laboratory features it is worthwhile considering this association as a possibility. Checking Ig levels, serum protein electrophoresis in patients with AIHA will help pick up both the underlying lymphoproliferative disorders and monoclonal gammopathies.

Keywords: Hemolytic anemia; Multiple myeloma; Hemoglobin

Introduction

Anemia is a common manifestation of Multiple Myeloma (MM) and is one of the clinical criteria defined by the International Myeloma Working group as a disease related end organ dysfunction [1]. The postulated pathophysiology include erythroblast maturation defect, erythroid matrix destruction due to up-regulation of apoptogenic receptors, relative erythropoietin deficiency and iron deficiency associated with an increase tumor cell burden [2]. Hemolytic anemia is a rare manifestation in MM and has mostly been documented as case reports [3-7]. Here, we report a case of hemolytic anemia that was a presenting manifestation of MM.

Case Presentation

A 56 year old Indian Male with background of chronic sinusitis presented to emergency department with 2 weeks history of shortness of breath on exertion associated with loss of appetite without significant loss of weight. Conjunctival pallor and slight scleral icterus were noted on physical examination.

Laboratory investigation showed hemoglobin 8.6 g/dL with signs of hemolysis including raised LDH, low haptoglobin, raised total and indirect bilirubin and elevated reticulocyte count (Retic Index 4.25). Peripheral blood film showed moderate polychromasia, rouleaux formation and auto-agglutination of red blood cells. Direct coombs test was strongly positive with both IgG(4+) and C3d(3+). The autoantibody eluted from erythrocyte surfaces was a warm IgG antibody. Serum protein electrophoresis and immunofixation revealed 14 grams of monoclonal IgG kappa paraprotein. There was no renal impairment or hypercalcaemia and though the skeletal survey was negative, MRI scan of the Spine revealed 2 lytic lesions on L3/L4 vertebral bodies. Bone marrow aspiration showed 48% atypical plasma cells which were CD38+, CD138+ and CD56+ with cytoplasmic kappa light chain restriction with no abnormal lymphoid population. FISH on bone marrow plasma cells showed 1q21 amplification, t(4;14) and RB1 gene deletion.

A diagnosis of autoimmune hemolytic anemia and multiple myeloma was made and the patient was started on Carfilzomib based chemotherapy after initial treatment with Steroids. He required blood transfusion every 10 days or so initially, but after the first cycle of treatment he became transfusion independent. However, his disease progressed after 3 cycles of this regime with huge increase in serum free light chains and new soft tissue masses and he was treated with salvage chemotherapy followed by high dose Melphalan and Autologous Stem Cell Transplant (ASCT). AIHA was in remission after salvage therapy with near normalization of his Hb. However he developed disseminated tuberculosis (proven on lymph node biopsy) and aggressive disease relapse simultaneously within 2 months of ASCT and though he received anti-tubercular treatment he succumbed to disease progression.

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Discussion

Autoimmune Hemolytic Anemia (AIHA) is often associated with indolent B cell lymphoproliferative disease especially Chronic Lymphocytic leukaemia and lymphoplasmacytic lymphoma. It occurs in about 5% to 10% of patients with CLL and less commonly in other indolent B and T-NHLs. However AIHA is relatively rare in MM and has been mostly reported case reports and in a recent small case series [8]. AIHA associated with lymphoproliferative disorders could be both warm and cold type but the former is much more common. In our patient it was a mixed type with presence of both IgG and C3d. When a patient presents with AIHA, in addition to working up for possible underlying auto-immune disorders, checking serum Ig levels, protein electrophoresis and immunofixation (if needed after electrophoresis) will help pick up patients with underlying monoclonal gammopathies as well as associated lymphoproliferative disorders like Waldenstrom's macroglobulinemia. True prevalence of AIHA in patients with MM could have been underestimated and careful screening and testing as part of larger prospective studies might help to elucidate the true prevalence and to understand the mechanism of hemolysis in multiple myeloma.

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