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Case Report

A rare cause of anaemia in multiple myeloma

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ABSTRACT

Multiple myeloma is a neoplastic plasma cell dyscrasia. Anaemia in multiple myeloma is usually related to many factors, of which the commonest cause being anaemia of chronic disease. We reported a 67 years old hypertensive male presented with low back pain and loss of appetite. Investigations revealed severe anaemia and elevated total serum protein with albumin/globulin (A/G) reversal (1:4). Bone marrow aspiration revealed plasma cell dyscrasia. Skeletal survey evaluation showed multiple osteolytic lesions. Serum protein electrophoresis revealed M spike in gamma globulin region with immunofixation suggestive of IgG and kappa monoclonal gammopathy. He was diagnosed as a case of multiple myeloma.. On evaluating the cause of severe anaemia, interestingly various findings suggestive of Autoimmune hemolytic anaemia (AIHA) were found. Packed red blood cell transfusion along with steroids was done for correction of severe anaemia. Review of literature showed that only about 4% of AIHA patients had multiple myeloma. We reported a rare case of multiple myeloma who presented with AIHA.

Keywords: Multiple myeloma, Anaemia, Autoimmune, AIHA

INTRODUCTION

Multiple myeloma is a neoplastic plasma cell dyscrasia. Plasma cell dyscrasias are a group of disorders characterised by uncontrolled proliferation and accumulation of a single clone of Immunoglobulin (Ig) secreting cells (plasma cell) and secretion of a structurally homogeneous Ig or its polypeptide chains.[2] Clinical presentation is highly variable and related to sites of infiltration by neoplastic cells and biochemical properties of the protein being overproduced.

Hypercalcemia, renal failure, anaemia, pathologic fractures are commonly seen in multiple myeloma. Anaemia in multiple myeloma is usually related to the inhibition of hematopoiesis by tumour factors, anaemia of chronic disease, erythropoietin deficiency due to renal impairment, iron deficiency anaemia, megaloblastic anaemia.[3] In our case, the cause of anaemia is autoimmune haemolytic anaemia. Autoimmune haemolytic anaemia is usually seen in B-cell lymphoproliferative disorders. Association of autoimmune haemolytic anaemia with multiple myeloma is rare, it has been reported only in few cases.

CASE REPORT

A 67 years old male known hypertensive came with complaints of back pain and loss of appetite. On examination he was pale, spinal and sternal tenderness were present. Other examination was unremarkable. He was evaluated for anaemia and simultaneously for bony tenderness. Blood investigations revealed Hb of 3.9 g/dl and total serum protein of 13.4 g/dl with albumin 3.6 g/dl (A:G reversal- 1:4). Peripheral smear showed few elliptocytes, teardrop cells and burr cells. Iron studies and vitamin B12 levels were normal. Interestingly various findings suggestive of autoimmune hemolytic anaemia - indirect hyperbilirubinemia, elevated LDH- 440 U/l (120-246 U/l), positive direct coombs test with presence of

warm IgG autoantibody were seen and cause of anaemia was found to be due to Autoimmune hemolytic anaemia (AIHA).

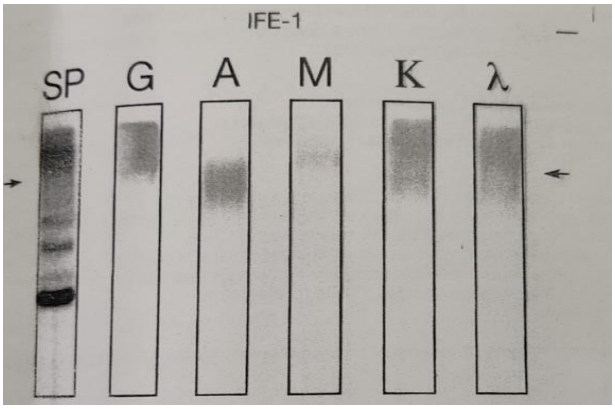

Figure 1: Faint monoclonal band seen in SP lane corresponding to this bands seen in IgG and kappa lanes. Suggestive of IgG and kappa monoclonalgammopathy serum IgG- 22.85 g/l, serum IgA- 7.83 g/l, serum IgM- 2.79 g/l, serum free kappa (light chain)- 4.81 g/l, serum free lambda (light chain)- 4.33 g/l, serum free kappa/lambda ratio- 1.11. Total protein-7.70 g/dl, total gamma-globulin- 4.40 g/dl, albumin fraction- 3.3 g/dl, A/G ratio- 0.75.

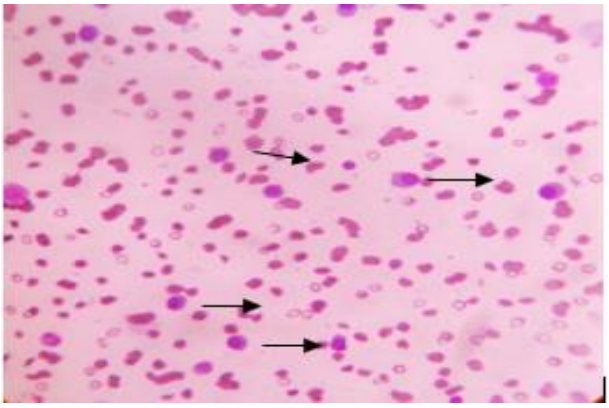

Figure 2: Bone marrow aspiration- markedly suppressed marrow with normoblastic maturation. Plasma cells- 56%, normoblasts- 10%, myelocytes- 1%, metamyelocytes- 02%, neutrophils- 18%, lymphocytes- 12%, eosinophils- 1%.

Serum protein electrophoresis revealed M spike in gamma globulin region with immunofixation (Figure 1) suggestive of IgG and kappa monoclonalgammopathy. Bone marrow aspiration (Figure 2) revealed plasma cell dyscrasia with 56% plasma cells and skeletal survey revealed multiple osteolytic lesions in sternum, clavicle, humerus, ribs, vertebral bodies. He was started on intravenous dexamethasone 4 mg twice a day for pain management after bone marrow aspiration sample was taken. He was diagnosed as a case of multiple myeloma with autoimmune hemolytic anaemia. Patient was initiated on steroids along with packed red blood cell transfusions were done for correction of severe anaemia. His haemoglobin improved (7 g/dl) and his bone pain reduced, and first cycle of chemotherapy with subcutaneous bortezomib- 2 mg stat, and subcutaneous denosumab- 120 mg stat, tablet lenalidomide 10 mg once a day was given and discharged.

DISCUSSION

Multiple myeloma usually presents with non-specific symotoms and signs and include fatigue, bony pain, easy bruisability and bleeding, recurrent infections, manifestations of anaemia, hypercalcemia, renal insufficiency, lytic bone lesions, hyperviscosity, thrombocytopenia, and hyper- or hypogammaglobulinemia.[4] The anaemia is normochromic, normocytic in most patients, but macrocytosis can be observed as well. The anaemia is related partially to direct infiltration and replacement of the bone marrow. Hemoglobin concentration is also correlated directly with the percentage of MM cells in S phase, suggesting that the bone marrow cytokine milieu- permissive for MM cell proliferation, is not conducive to efficient erythropoiesis.[5] Cytokines, like tumour necrosis factor-α and Interleukin (IL-1), may inhibit erythropoiesis.[6] Fas ligand-mediated erythroid apoptosis is also increased in patients with MM.[7] Relative erythropoietin deficiency from MM-induced renal insufficiency also contributes to the observed anaemia. The diagnosis of MM is made from constellation of findings, including anaemia, monoclonal proteins, bone lesions, renal complications, hypercalcemia and bone marrow plasmacytosis.

AIHA is usually seen in B-cell lymphoproliferative disorders. AIHA is rare in Multiple myeloma. Yi et al reported IgG mediated AIHA in a patient of multiple myeloma with IgA kappa M-protein which shows AIHA was independent of multiple myeloma.[8] It is not known whether AIHA is a complication of multiple myeloma or just a coincidence. Further studies are necessary to understand mechanism of hemolysis in multiple myeloma.

Conventional AIHA treatment is with steroids, but patients may become refractory. In such cases Bortezomib can be effective for steroid resistant AIHA in multiple myeloma which is reported in few cases.[9] Hamdan et al reported a case of multiple myeloma with initial presentation as AIHA which is refractory to steroid therapy and responded to Bortezomib.[10]

CONCLUSION

Association of AIHA with multiple myeloma is rare and only few cases has been reported. Although rare, AIHA should be considered while evaluating for the cause of anaemia in multiple myeloma. Prompt treatment is the need of the hour as it responds well to steroids.

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