Original article

Clinico – hematological profile of multiple myeloma in tertiary care Hospital, Pune

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Abstract:

Introduction: Multiple myeloma accounts for 1% of all cancers and 10% of all hematologic malignancies. It is characterized by bone marrow infiltration with clonal plasma cells, production of monoclonal immunoglobulin and associated end organ damage.

Objective: The study was carried out to find out the frequency of multiple myeloma and to study clinico-hematological profile and radiological features.

Materials and methods: Patients of multiple myeloma encountered over a period of four and half years from January 2011 to June 2015 were evaluated clinically, hematologically and with pertinent laboratory and radiological investigations. The data collected was analyzed and clinic-hematological correlation attempted.

Observations and conclusion: 13 patients were diagnosed during the study period with the mean age of 50 years with age range was 36-74 years. Male to female ratio was 1.1:1. Most common clinical feature was bone pain and osteolytic lesion (77 %) followed by renal failure. Anemia was the most common hematological manifestation.

Keywords: Multiple myeloma, renal failure, anemia

Introduction:

Multiple myeloma is a clonal malignant neoplasm of plasma cells originating in the bone marrow with usually presence of monoclonal immunoglobulin in the blood and or urine associated with end organ damage. Multiple myeloma accounts for 1% of overall malignancies and 10% of all hematologic malignancies.[1] Overall incidence of myeloma increases with age. Median age at diagnosis is 70 years.[2] The etiology of the disease remains poorly understood. Certain etiological risk factors like ionizing radiation, pesticides, benzene, arsenic, carbon monoxide have been mentioned in the literature. [3]

Almost all patients with multiple myeloma evolve from asymptomatic premalignant stage termed monoclonal gammopathy of undetermined significance (MGUS). In some of the patients, an intermediate asymptomatic but more advanced premalignant stage referred to as smoldering multiple myeloma (SMM) can be recognized.[4] There is marked variability in the clinical features seen in patients with multiple myeloma from the apparently healthy patients to debilitated ones with anemia and pathological fractures with or without renal impairment. Objective of the study was to find out the frequency of multiple myeloma and to study clinico-hematologic profile and radiological features.

Materials and methods:

Present study was done retrospectively in patients of multiple myeloma over a period of four and half years from January 2011 to June 2015 in B.J. Govt. Medical college and Sassoon General

hospital Pune.. All the cases were evaluated clinically, hematologically with pertinent biochemical and radiological investigations. Peripheral venous blood samples were determined by automated hematology cell counter ERMA. Biochemical tests were done on fully automated biochemistry analyzerErba. Biochemical tests analyzedwere Sr. Creatinine, Urea, Calcium, Total Protein, Albumin. M protein was determined by serum protein electrophoresis. Bone marrow aspirate and trephine biopsy was done from posterior superior iliac spine with Jamshidi needle. Bone marrow aspirate slides were stained with Leishman stain. Bone marrow biopsy was received in Bouin's fluid. It was processed and stained with hematoxylin and eosin. Urinary Bence Jones proteins was performed. X ray and M.R.I. findings were reviewed.

For evaluation of each case revised International Myeloma Working Group criteria was applied. As per the revised International Myeloma Working Group criteria the diagnosis of multiple myeloma requires, the presence of one or more myeloma defining events (MDE) in addition to evidence of 10% or more clonal plasma cells on bone marrow examination or biopsy proven plasmacytoma. MDE consist of established CRAB features (hypercalcemia, renal failure, anemia or lytic bone lesions) as well as three specific biomarkers: clonal bone marrow plasma cells ≥ 60%, serum free light chain ratio ≥ 100 and more than one focal lesion on magnetic resonance Imaging (MRI).[5] Anemia was classified according to hemoglobin level into mild (< 11 g/dl Hb) moderate (8 – 11 g/dl Hb) and severe anemia (< 8 g/dl Hb) in adult males and adult nonpregnant females. Renal impairment was defined as elevated serum creatinine > 2 g/dl.

Observations:

13 cases of multiple myeloma were detected during the study period. The ratio of multiple myeloma to leukemia was 1:8. Of the 13 patients studied 7 were males and 6 were females. Male to female ratio was 1.1:1. Mean age at presentation was 50 years. The age range was 36 - 74 years. Majorityof the patients were in the 4th and 5th decade of life. Age distributionis shown in table no. 1.

Table 1: Age distribution of multiple myeloma

Age group	No. of cases
31- 40 yr	1
41-60 yr	8
61-70 yr	2
71 – 80 yr	2
Total	13

The most common clinical presentation was bone pain and osteolytic lesion (77%) followed by renal impairment (62%). Anemia (85%) was the most common hematological manifestation Table no. 2)

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Table no. 2: Clinico – hematological manifestation in multiple myeloma

Clinico-hematological manifestations	No. of cases
Anemia	85%
Osteolytic lesions	77%
Renal impairment	62%

Mean hemoglobin level was 7.6 gm/dl ranging from 3.7 to 12.5 gm/dl. Severity of anemia is shown in table no 2. Majority of the patients presented with severe anemia. It was seen in 8 cases (62%).

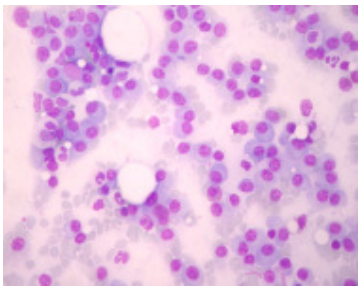
Table no. 3: Severity of anemia in multiple myeloma

Anemia	No. of cases
Mild (<11 g/dl)	0
Moderate (8 -11 g/dl)	3
Severe (<8g/dl)	8

Erythrocyte sedimentation rate was in the range of 5-80 mm/hr.In 10 cases (77%) E.S.R. was raised. Total protein ranged from 4.2 to 8.8 mg/dl. Hypoalbunemia was seen in 62% of cases and hyperglobulinemia in 46% of cases. Reversal of albumin to globulin ratio was seen in 77% of cases. Serum electrophoresis was performed in 5 cases. Out of 5 cases 4 showed presence of M protein. Bence Jone's protein was detected in one case. 23% of cases showed hypercalcemia and renal impairment was seen in 8 cases (62%).

Radiological survey revealed multiple osteolytic lesions and pathological fractures in 10 cases (77%). Percentage of plasma cells in the bone marrow ranged from 25-90%. (Figure 1,2)

Fig. 1 Photomicrograph showing increased number of plasma cells in bone marrow aspiration 40X



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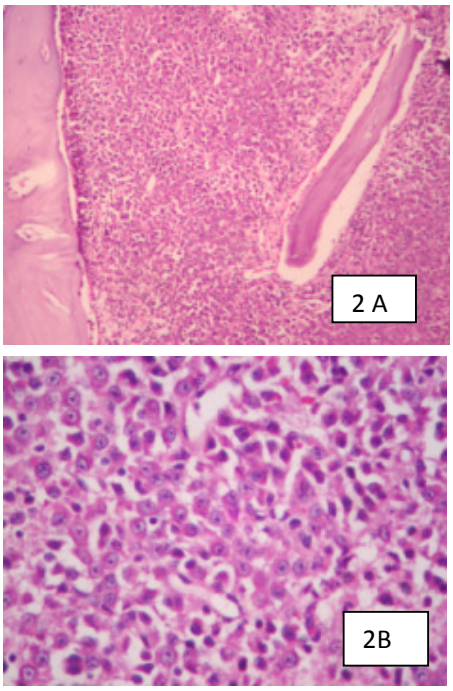

Fig. 2 Bone marrow biopsy: Plasma cells in sheets (2A). Plasma cells have relatively uniform eccentrically located nuclei with dispersed nuclear chromatin and prominent centrally located eosinophilic located nucleolus (2B)

Discussion:

Multiple myeloma is a plasma cell dyscrasia characterized by infiltration of bone marrow with clonal plasma cells, production of monoclonal protein and associated with features of end organ damage. Multiple myeloma mainly seen in people over the age of 60 years.[6] The age group of the patients included in the study group ranged from 36-74 years.Mean age was 50 years. This could be due to less sample size in our study. Majority of the patients in our study were males.Male to female ratio was 1.1:1. Similarly Odunukwe N N et al[6] and Sadia S et al found that multiple myeloma was common in males.

Among the diagnostic data evaluated most of the patients presented with anemia as hematological manifestation. In our study 85% of patients presented with anemia. This finding is in comparison with data collected from Federal University of Minas Gerais where 81.2% patients had anemia as hematological manifestation.[7]

Various mechanisms have been explained in the pathogenesis of anemia such as deficiency of erythropoietin, inadequate utilization of iron and bone marrow infiltration by clonal plasma cells. Similarly Noorwati Sutandyo et al[8] found anemia was the most common hematological manifestation in patients with multiple myeloma.

In our study 77% of the patients were presented with bone pain and osteolytic lesions. Bone disease in multiple myeloma results in severe bone pain, pathological fractures and hypercalcemia. Multiple myeloma bone lesions arise from the altered

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bone remodeling due to both increased osteoclast activation and decreased osteoblast differentiation.[9]

Myeloma lytic bone lesions are in agreement with Paget's concept of seed and soil theory where neoplastic plasma cells (Seed) have tropism for certain microenvironment (Soil : bones).[10]Bone involvement in our study is in concurrence with study conducted by Juliana et al[7] who found74% of patients of multiple myeloma presented with osteolytic lesions in their 5 year retrospective study period.

Persistent kidney dysfunction in multiple myeloma was most commonly caused by tubular nephropathy due to monoclonal immunoglobulin secreted by plasma cells.[11] Renal impairment was present in 62% of cases in our study. Incidence of renal involvement is slightly higher in our study as compared to study conducted by Dawson et al and Kyle et al who have found incidence of 45%and 55% respectively,[12]as bone marrow aspiration and biopsy wereperformed in all the cases of patients requiring renal dialysis under government funded scheme Rajiv Gandhi Yojna in our study period. However a study conducted by Prakash J et al[13] found higher incidence of renal disease in 84% patients of multiple myeloma. Hypercalcemia was found in 23% of cases in our study. Juliana T et al[7] found incidence of hypercalcemia in 32% of patients with multiple myeloma. In our study serum electrophoresis was performed in 5 cases,out of which M protein was present in 4 cases.

To conclude multiple myeloma is a disease with variable clinical presentation with involvement of multiple organ systems. Clinicopathological features are comparable to previously published data. Most frequent clinical presentation in our study was bone pain and osteolytic lesions followed by renal failure.

Multiple myeloma should be considered as the differential diagnosis in old age patients requiring frequent renal dialysis. Hence in such cases bone marrow aspiration and biopsy should be performed to rule out multiple myeloma.

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