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Original Research Paper

Clinico-hematological profile of multiple myeloma in a teaching hospital - A 2 year study

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ABSTRACT

Introduction: Multiple myeloma accounts for 1% of all cancers and 10-15% of all hematologic malignancies. It is characterized by bone marrow infiltration with clonal plasma cells, production of monoclonal immunoglobulin, and associated end-organ damage. The study aims to find out the incidence of multiple myeloma and to study the clinico-hematological profile along with radiological features.
Materials and Methods: The present study was done both retrospectively and prospectively in 26 patients of multiple myeloma diagnosed over a period of 2 years from June 2017 to June 2019 in our teaching hospital. Data from hematological, biochemical, and radiological investigations were collected. For evaluation of each case, revised International Myeloma Working Group criteria were applied.
Results: 26 patients were diagnosed during the study period, with the majority of them in the 6^{th} decade with age range was 41-74 years. The male to female ratio was 1.3:1. Most common clinical feature was fever (50%) followed by bone pains (42%) and generalized weakness (42 %). Anemia was the most common hematological manifestation. All the patients had 'M band' on serum electrophoresis, and 27% of patients had urinary Bence Jones proteins. Among the skeletal system, the spine (63%) is the most common site of involvement.
Conclusion: Among the 26 patients, various clinical presentations observed were pathological fracture, infections, renal impairment, generalized weakness in addition to anemia, and bone pains. Multiple myeloma should be considered as a differential diagnosis in old age patients presenting with such complaints.

1. Introduction

Multiple myeloma is a clonal malignant neoplasm of plasma cells originating in the bone marrow along with the presence of monoclonal immunoglobulin in the blood and or urine associated with end-organ damage. It accounts for 1% of all malignant tumors, 10 -15% of all hematologic malignancies, and 20% of deaths from hematological malignancies.[1] Multiple myeloma is a disease of the elderly, with a peak age of 60-70 years at presentation.[2] It is more common in males when compared to females.[3] 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.[4]There is marked variability in the clinical features seen in patients with multiple myeloma from healthy patients to those presenting with generalized weakness, bone pains, fever, infections, anemia. In some patients, complications like renal failure, pathological fractures, and lytic bone lesions may lead to significant morbidity and mortality. The study aims to find out the incidence of multiple myeloma and to study the clinico-hematological profile along with radiological features.

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2. Materials and Methods

The present study was done both retrospectively and prospectively in 26 patients of multiple myeloma diagnosed over a period of 2 years from June 2017 to June 2019 in our teaching hospital. All newly diagnosed patients of Multiple Myeloma with relevant data during the above mentioned period were collected from the records and included in the study. Patients under remission were excluded from the study. A detailed history was taken, and clinical examination was performed. Hematological investigations like Hemoglobin estimation (Hb), Total and differential counts, Erythrocyte sedimentation rate (ESR), platelet count, peripheral blood smear, and bone marrow examination were done. Serum protein electrophoresis was done, and urine was examined for Bence Jones Proteinuria. Radiological investigations included X-ray, imaging studies like magnetic resonance imaging, and data was noted. For evaluation of each case, Revised International Myeloma Working Group criteria were 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 $\geq$ 60%, serum-free light chain ratio $\geq$ 100and more than one focal lesion on magnetic resonance imaging (MRI).[5]

Out of 26 patients,15 were males (57%), and 11 were females (43%) with male preponderance, as shown in Table 1. The sixth decade was the most common age group at presentation in both the genders. The mean age at presentation in our study population was 60 years with a range of 41-74 years as shown in Table 1 .

Table 1: Age and Gender wise distribution of patients

Age group(years)	Male (%)	Female (%)	Total (%)
<40	0	0	0
41-50	2(33%)	4(66%)	6(23%)
51-60	4(66%)	2(33%)	6(23%)
61-70	8(66%)	4(33%)	12(46%)
>70	1(50%)	1(50%)	2(8%)
Total	15(57%)	11(43%)	26

Common clinical presentations were fever (50%), bone pains (42%), and generalized weakness (42%), as shown in Table 2.

Other rare presentations include decreased urine output, fractures, backache, shortness of breath and motor weakness of lower limbs. Clinical examination revealed pallor, bony tenderness and swelling, hepatomegaly, splenomegaly, and pedal edema. Hematological features were anemia in 18 patients (70%) as shown in Table 2. The mean hemoglobin concentration was 7.8g/dl with a range of 4.7-13.9 g/dl. ESR was elevated in 19 patients (73%). Rouleaux formation was observed in 15 patients (57%) Figure 1.

Table 2: Clinico-hematological manifestations

Clinico-hematological manifestation	No. of patients	Percentage
Anaemia	18	70%
Fever	13	50%
Bone pains	11	42%
Generalised weakness	11	42%
Renal impairment	9	35%
Pathological fracture	1	4%

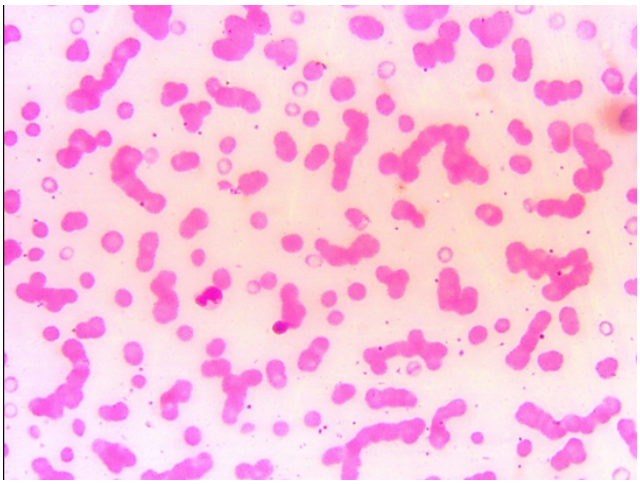

Fig. 1: P.S showing rouleaux formation, Leishman stain, 400x

White blood cell count was less than 5000 cells/mm^3 in 9 patients (35%), platelet count was less than 1 lakh/mm^3 in 7 patients(27%) and more than 4 lakh/mm3 in 1 patient(4%). Serum creatinine of more than 2 mg/dl was seen in 9 patients (35%) at presentation and hypercalcemia was observed 32% of patients. All patients had the presence of M band in the gamma region on serum electrophoresis. 27% of patients had urinary Bence Jones protein -positive as shown in Table 3.

Table 3: Investigations

Investigations	Result	Percentage
E.S.R	elevated	73%
Peripheral smear	Rouleaux formation	57%
Serum Creatinine	>2 mg/ dl	35%
Serum Calcium	>12 mg/dl	32%
Serum electrophoresis	M band in gamma region	100%
Urine Bence Jones Protein	Positive	27%

3. Result

Among skeletal involvement, 19 patients had osteolytic lesions (73%) on radiological investigations, and one patient had a pathological fracture (4%). Spine was the most frequent site of involvement (63%) Figure 2 followed by ribs and pelvis(27%) and skull(10%), as shown in Table 4.

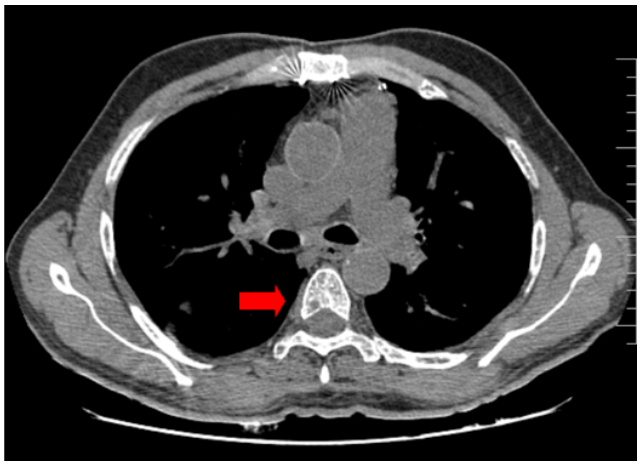

Fig. 2: CT Chest showing lytic lesions in the vertebral body

Table 4: Radiological survey

Osteolytic lesions	No. of patients	Percentage
Spine	12	63%
Ribs and pelvis	5	27%
Skull	2	10%
Total	19	73%

On bone marrow examination, more than 70% of plasma cells in 6 patients (23%), 1 patient (4%) had 50% of plasma cells, 10 patients (38%) had plasma cells in the range of 30-50%, 9 patients (35%) had plasma cells in the range of 10-30% as shown in Table 5.

Table 5: Bone Marrow Examination (% of plasma cells)

% of plasma cells	No.of patients	% of patients
10-30	9	35%
30-50	10	38%
50-70	1	4%
>70	6	23%

Bone marrow aspiration smear characteristically showed a high percentage of plasma cells with binucleation, Russell bodies and Mott cells Figures 3, 4 and 5.

Bone marrow biopsy showed sheets of plasma cells also with binucleation and multinucleation Figure 6.

4. Discussion

Multiple myeloma is a bone marrow based, multifocal neoplastic proliferation of plasma cells, usually associated

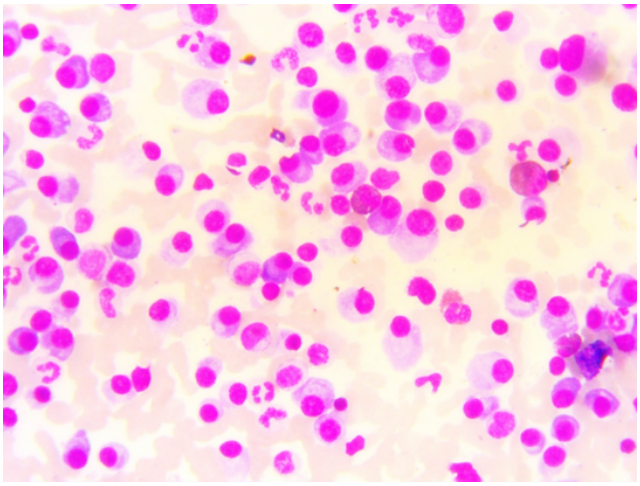

Fig. 3: B.M.A showing plasma cells, Leishman stain, 400x

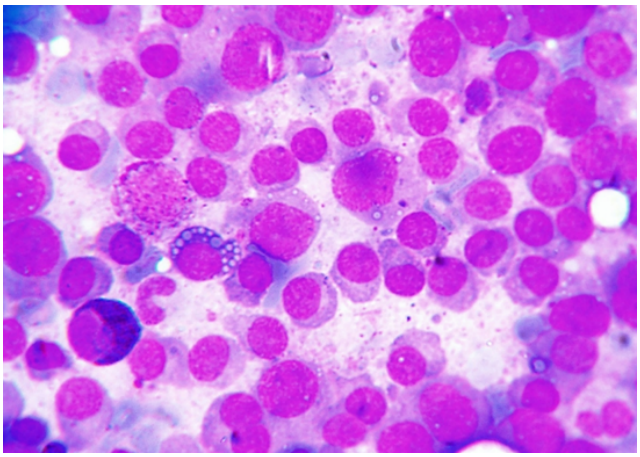

Fig. 4: B.M.A showing plasma cells and mott cell, Leishman stain, Oil immersion

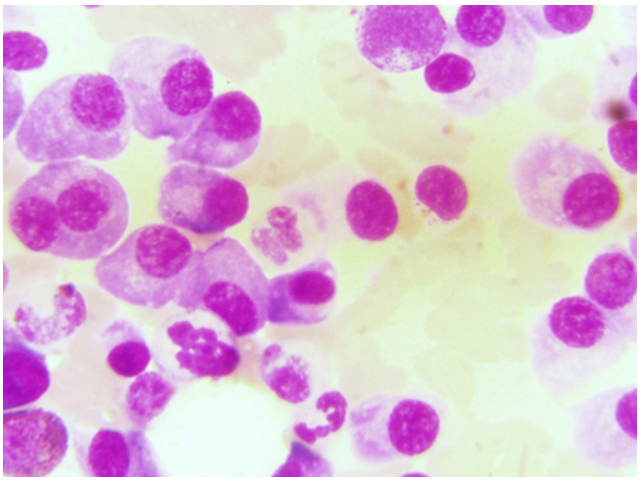

Fig. 5: B.M.A showing binucleated plasma cell, Leishman stain, oil immersion

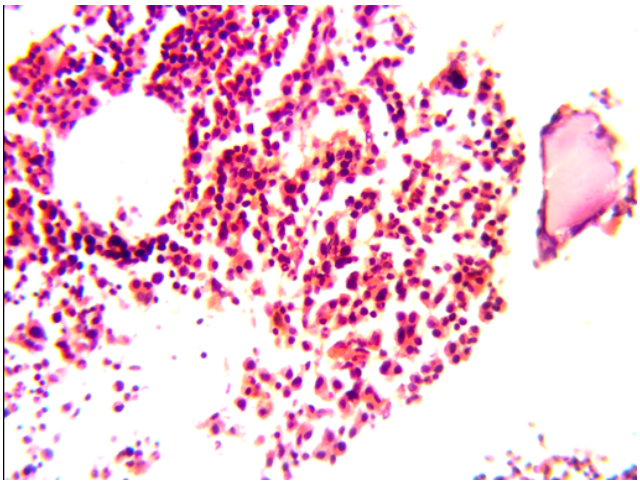

Fig. 6: B.M.B showing sheets of plasma cells, H & E stain, 400x

with an M protein in serum and urine or either one and evidence of organ damage related to the plasma cell neoplasm. Multiple myeloma is mainly seen in people over the age of 60 years. The age group included in our study ranged from 41-74 years, with a mean age of 60 years. The commonest age group at presentation was the 6^{th} decade, which is similar to studies done by Diwan et al.[2] and Mohanty et al.[6]

The majority of the patients in our study were males with a Male to Female ratio of 1.3:1. Similarly, Sagale et al.[3] Sultan et al.[7] and Odunukwe et al.[8] found that multiple myeloma is more common in males. This finding is in discordance with a study done by Vahini et al., which showed female preponderance.[9]

The most common clinical manifestation at the time of presentation was fever (50%), followed by bone pains (42%) and generalized weakness (42%) in our study. This finding is in discordance with other studies where bone pains are the most common clinical manifestation.[2,3,9]

The majority of the patients were anemic (73%). This finding is comparable to other studies.[2,3,9,10] In our study, nine patients (35%) had hemoglobin below 7g/dl, which is similar to the study done by Mohanty et al.[6] and Kyle et al.[11] The proposed mechanism of anemia in most is inadequate red blood cell production due to either erythropoietin deficiency from the accompanying renal failure or replacement of the marrow by myeloma cells.

Persistent kidney dysfunction in multiple myeloma was most commonly caused by tubular nephropathy due to monoclonal immunoglobulin secreted by plasma cells.[12] Renal impairment was present in 35% of cases in our study. The incidence of renal involvement is slightly higher in studies conducted by Dawson et al. and Kyle et al., who have found an incidence of 45% and 55%, respectively.[13]

Hypercalcemia was found in 32% of patients in our study, which is comparable to the study done by Vahini et al.[9] and Todaro et al.[14]

In our study, 73% of patients had osteolytic lesions showing varied skeletal involvement in radiological investigations. Bone disease in multiple myeloma results in severe bone pain, pathological fractures, and hypercalcemia. Multiple myeloma bone lesions arise from altered bone remodeling due to both increased osteoclast activation and decreased osteoblast differentiation.[15] Bone involvement in our study is in concurrence with the study conducted by Todaro et al,[14] who found 74% of patients of multiple myeloma had osteolytic lesions.

In our study, all cases demonstrated M band on serum electrophoresis in the gamma region similar to the study done by Vahini et al.[9]

27% of patients in our study had urinary Bence Jones protein -positive, which is comparable to the study done by Diwan et al.[2]

5. Conclusion

Multiple myeloma is a disease with variable clinical presentation with the involvement of various organ systems. The clinico-hematological features are comparable to previously published data. It is most common in the 6^{th} decade with slight male preponderance. The most frequent clinical presentation in our study is fever, followed by bone pains and generalized weakness with anemia as the most frequent hematological manifestation. Multiple myeloma should be considered as a differential diagnosis in an elderly patient presenting with various clinical presentations like infections, pathological fracture, generalized weakness, back ache, renal impairment, and unexplained anemia.

6. Conflict of interest

None

7. Source of funding

None

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