MULTIPLE MYELOMA: CLINICOHAEMATOLOGICAL STUDY OF 3 YEARS AT A TERTIARY CARE CENTRE

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ABSTRACT

BACKGROUND

Multiple myeloma is also called as plasma cell myeloma or myelomatosis. It is a malignant clonal proliferation of neoplastic plasma cells within the bone marrow. Its incidence increases with age. Multiple Myeloma accounts for 1% of all human cancers and 10% of all haematological malignancies. We wanted to study clinical presentation of multiple myeloma and haematological parameters along with bone marrow aspiration with biopsy interpretations.

METHODS

This is descriptive, analytical study. The total 212 bone marrow aspirations were done during study period at Department of Pathology and evaluated for MM. The Study period was 3 years from January 2016 to December 2018 at our tertiary care hospital. Detailed clinical data including all biochemical investigations, routine and specific haematological investigations were done. The imaging findings, serum electrophoresis, urine analysis etc were considered. The bone marrow aspiration and biopsy study were done.

RESULTS

In data analysis for 3 years, total 12 cases of multiple myeloma were diagnosed. The male: female ratio was 2:1. The age range was 55-79 years, with mean age 67 years. The common clinical presentation was bony pain (66%), followed by renal failure (25%), neurological symptom (pain) (41.7%), easy fatigability (66.7%), infection (6%), etc. On investigation, it was observed that anaemia (75%), lymphocytosis (33.3%), elevated ESR (66.7%), increased serum creatinine (83.3%), increased serum calcium (91.7%), BJ proteinuria (50%) were seen in various cases. On serum electrophoresis, M-band was noted in all patients. Bone marrow plasmacytosis was noted in 100% cases with mean count was 41%. On radio imaging 75% showed bony lytic lesions.

CONCLUSIONS

Elderly patients with unexplained anaemia, bony pain and renal manifestations should be investigated for multiple myeloma. Bone marrow aspiration, electrophoresis, and related investigations. It plays an important role in diagnosis and management of multiple myeloma cases.

KEYWORDS

Plasma Cell Neoplasm, Myeloma, Bone Marrow, M-Band Electrophoresis

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BACKGROUND

Plasma cell dyscrasias are a group of disorders that arise from clonal proliferation of neoplastic plasma cells or associated B cells with production of immunoglobulins. These cells produce large quantities of myeloma protein. These individuals are prone infection. The cases of multiple myeloma are on rise, so haematological diagnosis on bone marrow aspiration study play important role in patient early detection and management of patients. MM is seen worldwide and in all races. MM is the most prevalent haematological malignancy after non-Hodgkin's lymphoma.[1] It is account for 1% of all human cancers and 10% of all haematological malignancies.[2] In different geographic areas there is considerable variation is recorded related to its incidence and survival. There are many advancements have been made in the pathogenesis and aetiology of this disease. But still there has not made its way into the category of curable diseases.

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METHODS

Study Design

This is descriptive, analytic data study carried out in Krishna Institute of Medical Sciences Deemed University, Karad.

Total 212 cases of bone marrow aspiration were done at pathology department and evaluated for MM. Out of which total 12 cases of multiple myeloma were diagnosed. The Study period was 3 year from January 2016 to December 2018, at our tertiary care hospital.

Inclusion Criteria

All cases of bone marrow aspiration clinically suspected of multiple myeloma.

Exclusion Criteria

Known cases of multiple myeloma on treatment and other plasma cell dyscrasia cases.

Ethical Considerations

The study is approved by Ethic Committee of Institute.

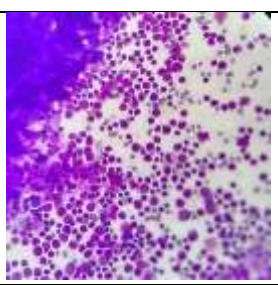

Figure 1. Bone Marrow Aspiration Study Showed Plasma Cells- Mature and Immature Forms (Leishman's Stain, 100x)

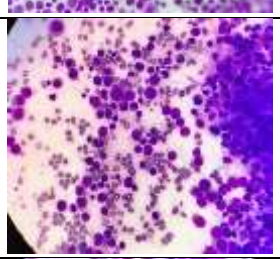

Figure 2. Bone Marrow Aspiration Study Showed Hypercellularity with Increased Plasma Cells (Leishman's Stain, 100x)

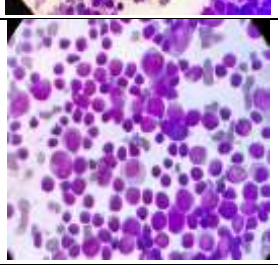

Figure 3. Bone Marrow Aspiration Study Showed Plasma Cells- Mature and Immature Forms, Various Binucleate Forms, Dutcher Bodies, Flame Cells (Leishman's Stain, 1000x)

RESULTS

Detailed clinical data, all biochemical investigations, routine and specific haematological investigations were done of all 12 cases. The imaging findings, serum electrophoresis, urine analysis etc were considered. The criteria for the diagnosis of multiple myeloma were fulfilled in our study.[3] The bone marrow aspiration study showed plasma cells- mature and immature forms ranging from 12 to 90%. The aspiration showed various binucleate forms, Dutcher bodies, Russel's body, flame cells, etc.

Signs and Symptoms	Number of Cases	Percentage (%)
Bone pain	10	83.3
Renal failure	03	25.0
Neurological symptom	05	41.7
Easy fatigability	08	66.0
Weight loss	09	75.0
Infection	02	16.7

Table 1. Clinical Presentation of Multiple Myeloma Cases

Laboratory Findings	Number of Cases	Percentage (%)
Hb%(<10 gms)	09	75.0
Lymphocytosis	04	33.3
Increased ESR (>80 mm at end of 1 hr)	08	66.7
Increased serum calcium (>11 mg/dl)	11	91.7
Increased serum creatinine (>2 mg/dl)	10	83.3
Urine BJ proteinuria	06	50.0
M band (serum electrophoresis)	12	100
Bone lesions (lytic /fracture)	06	50.0
Clonal bone marrow plasma cells (>10%)	12	100

Table 2. Laboratory Investigations of Multiple Myeloma Cases

DISCUSSION

Multiple myeloma is a haematological malignancy characterised by proliferation of a single clone of plasma cells derived from B-cells. These cells accumulate mainly in bone marrow and later on gives multiple organs involvement with excessive production of monoclonal protein (M Protein). Plasma cell neoplasm includes spectrum of diseases from monoclonal gammopathy of undetermined significance to plasma cell leukemia. In multiple myeloma there are variants like Symptomatic myeloma, Asymptomatic (Smoldering) myeloma, Nonsecretory myeloma and Plasma Cell Leukemia. Multiple myeloma accounts for 10-15% of all haematological malignancies.[4,5]

The aetiology of multiple myeloma not known. The various risk factors include genetic predisposition, environmental, radiation exposure, occupational exposure to agricultural, and chemical exposure to formaldehyde, epichlorohydrin, Agent orange, hair dyes, paint sprays, asbestos, Viral infection like Herpes virus 8 etc. The diagnosis is done as abnormal monoclonal plasma cells in bone marrow, serum/urine in M protein on electrophoresis, osteolytic bone lesions and other clinical and laboratory findings. Multiple myeloma shows proliferation of a clone of plasma cells that manifest by one or more lytic bone lesions. It shows varying clinical, laboratory and haematological features. In this study total of 212 cases of bone marrow aspirations were examined. The clinical manifestations of cases having unexplained anaemia, bone pain, weakness, renal abnormalities, neurological pain were studied, out of which 12 cases were diagnosed as multiple myeloma. The age ranged from 55-79 years with the median age at diagnosis is of 69 years at presentation.[6] The reported median age of 55 years in Indian National Cancer Registry Programme Statistics.[4] The male: female ratio in this study is 2:1. The reported ratio is 1.1:1 to 2:1.

The most common symptom in this study is bone pain (66.7%) followed by renal failure (25%). Diwan et al noted bone pain in 85% cases and renal failure in 30% cases.[7] In our study, the patient was presented with fracture bone or on radiological imaging showed multiple lytic lesion,

backache related with cord compression. The renal manifestations were related to acute renal failure, oliguria and one patient with polyuria having known case of diabetes mellitus. The raised creatinine>2 mg/dl was found in (83.3%) cases. Study by Diwan et al showed in 30% cases.[7] On laboratory finding, microcytic hypochromic anaemia was noted in majority of patients with significant elevated ESR. The findings were similar to study by Kaur et al.[8] BJ proteinuria was noted in 50% cases. On serum electrophoresis revealed a localised M band on cellulose acetate gel in all cases, majority of them having Ig G kappa or lambda M protein**.**

The bone marrow aspiration study showed plasma cells-mature and immature forms ranging from 12 to 90% (mean 41%). The aspiration showed various binucleate forms, Dutcher bodies, flame cells, etc. The average plasma cells in bone marrow reported by various studies were 45%, 64.3%.[7,8,9] In 2% of patients with multiple myeloma have true nonsecretory disease and have no evidence of an M protein. The serum free light chain (FLC) assay, and >1 focal lesions on magnetic resonance imaging (MRI) studies (at least 5 mm in size) are helpful for diagnosis.

For multiple myeloma the CRAB criteria- hypercalcemia, renal impairment, anaemia, bone involvement are used to assess the complications and prognostic risk during disease course. There is often a delay between symptom onset and diagnosis of myeloma.[10] In our study one case rapidly progressed to acute renal failure and showed features of plasma cell leukemia and died within 3 months of diagnosis. The various complications such as renal failure, anaemia, lytic bone lesions, organomegaly, infections, and amyloidosis lead to morbidity as well as mortality.[11,12]

Various modalities of treatment are available. The newer drugs coming up with good results with the help of better understanding regarding the pathogenesis of myeloma, and marrow micro-environment. Patients who are not transplant candidates are treated with standard alkylating agent therapy. The highly active agents like thalidomide, bortezomib, lenalidomide etc., are used in the treatment of myeloma and have emerged as important role.[13,14] Autologous hematopoietic stem-cell transplantation improves complete response rates and prolongs median overall survival . There is not curative treatment. Survival-overall median survival is 33-40 months.[15] Multivariate analysis showed age, plasma cell index, creatinine value, platelet count, serum albumin, C-reactive protein are important prognostic factors for its management. The various other prognosis factors greatly depending on stage of disease, cytogenetics abnormalities, LDH level, extra medullary disease, tumour burden, hypercalcemia. The development of novel therapies in further will improve patient outcome.

CONCLUSIONS

Elderly patients with bone pain, renal manifestations and anaemia should be properly evaluated for multiple myeloma. Diagnosing myeloma in the elderly is challenging. Early diagnosis of multiple myeloma cases with specific treatment and supportive care will be helpful for improvement of patients.

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