ORIGINAL ARTICLE

HEMATOLOGICAL PRESENTATION OF MULTIPLE MYELOMA IN KHYBER PAKHTUNKHWA

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ABSTRACT

Background: Being a B-cell malignancy, multiple myeloma is characterized by clonal expansion and accumulation of abnormal plasma cells in the bone marrow compartment. This study was conducted to determine the frequency and hematological presentation of multiple myeloma in Khyber Pakhtunkhwa.

Methodology: This descriptive cross-sectional study was carried out at Khyber Teaching Hospital and Fazle Raziq Laboratory Peshawar over a period of three years from March 2003 to April 2006. A total number of 3085 bone marrow aspirates were done during this period. Among these aspirates, 57 cases were diagnosed as multiple myeloma on the basis bone marrow cytology and results analyzed.

Results: The results of the study revealed that male: female ratio was 2.56:1, median age was: males 60 years and females 56 years. Frequency of multiple myeloma in all hematological malignancies was 5.3%, while the frequency of the same among all aspirates was 1.85%. The hematological findings showed anemia in 91% cases, thrombocytopenia in 29%, leucopenia in 10% and pancytopenia in 8.1%. Percentage of plasma cells in B.M arrow was 78.1 % of the bone marrow nucleated cells.

Conclusion: In Khyber Pakhtunkhwa province, males are affected more frequently than females by multiple myeloma. The percentage of MM among all hematological malignancies and the median age are lesser in this part of the world. Majority of patients present with anemia, MM should be included in the workup of anemia in patients above 50 years age.

KEY WORDS: Multiple myeloma, Plasma cells, Khyber Pakhtunkhwa.

INTRODUCTION

Being a B-cell malignancy, multiple myeloma (MM) is characterized by clonal expansion and accumulation of abnormal plasma cells in the bone marrow compartment.[1-3] The plasma cell proliferation usually results in extensive skeletal destruction with osteolytic lesions, hypercalcemia, anemia, and, occasionally, plasma cell infiltration in different organs. The excessive production of a monoclonal (M) protein can lead to renal failure, hyperviscosity syndrome or recurrent bacterial infections.[4]

Probably, MM has been present for centuries.[5] The first documented case of MM was that of Mr. Thomas Alexander McBean 45, who was treated by Dr. Thomas Watson in 1844, followed by that of 39 year old Sara Newbury described by Solly, the same year.[6] Sir Otto Kahler reported the third documented case of MM in 1889 which was that of Dr. Loos, whose urine showed a unique protein which was named as Bence Jones Protein (BJP) after Henery Bence Jones.[4] The standard staging system for diagnosis and prognosis has been that of Salmon-Durie.[2]

MM is part of a spectrum of diseases ranging from monoclonal gammopathy of unknown significance (MGUS) to plasma cell leukemia.

The proliferation of plasma cells interferes with the normal production of blood cells.[7] MM is commonly associated with anemia[8] which is normocytic and normochromic and is present in about two-thirds of patients at diagnosis. The anemia may result from chronic disease, relative erythropoietin deficiency and myelosuppressive effects of chemotherapy.[9] Thrombocytopenia is present in approximately 15% of patients but leukopenia may or may not be present at diagnosis.[4] Increased levels of immunoglobulins in the blood (M Spikes) and /or light chains in urine (Bence Jones Proteins) are seen in 99% of MM patients.[1,10] The characteristic osteolytic lesions and bone destruction results from the increased activity of osteoclasts and suppressed osteoblastic differentiation and activity.[11]

The annual incidence of MM in United States is 3-4 cases per 100,000 population. It represents 1% of all cancers diagnosed in the United States.[12]

It accounts for approximately 10% of all hematological malignancies[4,10,13] and 20% of all hematological malignancies in American blacks.[14] Median age at onset is 71 years. Mortality is more in males than females and in blacks than whites. The frequency of MM in young age is increasing.[15,16] Connective tissue disorders, chronic infections and skeletal metastasis, and other causes of monoclonal gammopathies should be differentiated from MM.[12]

The workup for MM includes:

a) Laboratory studies like complete blood count (to determine if patient has anemia, leukopenia or thrombocytopenia), bone marrow aspiration for cytology and cytogenetics, a comprehensive metabolic profile including urea/creatinine, uric acid, protein and globulin levels, serum protein electrophoresis for M band, Beta 2 microglobulins and c-reactive proteins.

b) Imaging studies including serial skeletal X-Rays for osteopenia or lytic lesions. MRI (magnetic resonance Imaging) and PET (positron emmision tomography).[7] Serum protein electrophoresis is performed for characteristic M spike of MM.[17] Salmon Durie staging system is the standard staging system for MM.[2]

This study was conducted to assess the frequency and hematological presentation of MM in Khyber Pakhtun Khwa (KPK) province.

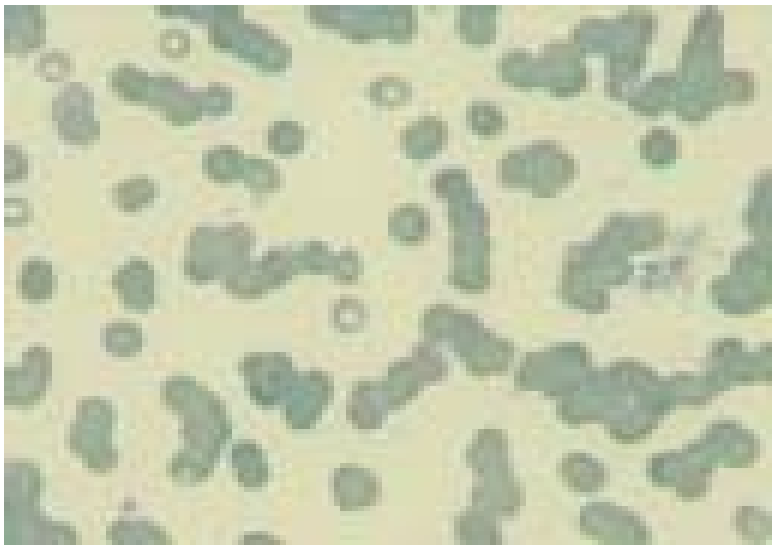

Fig. 1: Perpheral blood picture showing rouleoux formation.

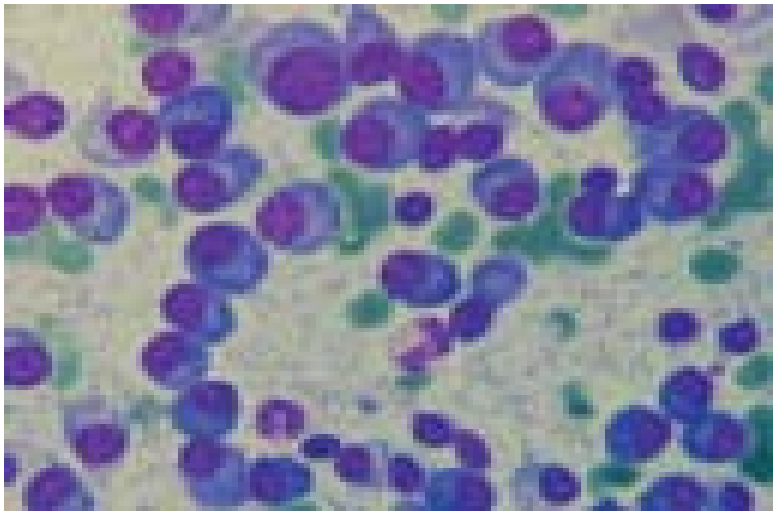

Fig. 2: Bone marrow aspirate of same patient showing plasma cells almost completely replacing the normal marrow elements.

MATERIAL AND METHODS

This was descriptive cross-sectional study. The study duration extended from March 2003 to April 2006 with patients belonging to different areas of KPK. The patients included those admitted at Khyber Teaching Hospital Peshawar and those diagnosed at Fazle Raziq Laboratory Peshawar.

The total number of bone marrow aspirates during the period was 3085. Data of all the hematological malignancies among the aspirates was recorded. The diagnosis was confirmed on bone marrow cytology. Protein electrophoresis for M band was also performed. The ages of the patients and hematological findings including Hb%, total leukocyte count, platelets count and the percentage of plasma cells in bone marrow were recorded and analyzed.

RESULTS

The total number of aspirates in the study period was 3085. Total hematological malignancies among these numbered 1073. Out of these Multiple Myeloma patients were 57. This constituted 5.3% of all the hematological malignancies and 1.85% of all the aspirates.

Among them, 41 were males and 16 females with male to female ratio of 2.5:1. Median age for males was 60 years and females was 56 years with combined median age being 58 years.

The results of hematological parameters are given in the Table 1 below.

Table 1: Hematological findings of patients.

Anemia		34 (91%)
Thrombocytopenia		14 (24.6%)
Leukopenia		5 (8.8%)
Pancytopenia		4 (7%)
Percentage of plasma cells:	Rang 40-90%	Average (78.14%)

DISCUSSION

The median age for plasma cell dyscrasia is 71 year in the US,[14] although Ghazala Ashraf et al[16] have recorded MM in a 25 years old patient. The median age in our study was 60 year in males, 56 years in females and combined age was 58 years. The mean age reported by Shaheen. H et al is also 58 years which matches with our study.[18] Multiple Myeloma in Pakistan tends to occur at younger age and is more common in males. The young age here might be due to earlier exposure to chemicals, agricultural fertilizers and probably the low socioeconomic status which has an inverse relation with MM.

The male to female ratio in developed world is 1.4: 1[14] where as in our study it is 2.5: 1. The cause may again be due to relatively increased exposure to chemicals and agricultural toxins as well as smaller attendance of females to hospitals. Majority of the patients in our study belonged to low socioeconomic group. Most of the patients presented with severe body aches due to advanced lytic lesions or pathological fractures while other had renal insufficiency, fever of uncertain origin or anemia.

MM is commonly associated with anemia[8] which is normocytic and normochromic and is present in about two-thirds of patients at diagnosis with an Hb <12 g/dl.[9] The most common hematological presentation in our study was anemia (91%). whereas thrombocytopenia ranked second to anemia (24.6%), leucopenia ranked 3rd (8.8%) and pancytopenia 4th (7.0%). The mean Hb. Level was 8.05 g/dl. The study of Shaheen et al also showed Hb. level of <8.5g/dl.[18] The anemia in MM may result from relative erythropoietin deficiency myelosuppressive effect of chemotherapy and MM acting as chronic disease.[9] There are many causes of anemia in KPK including dietary deficiency of hematinics and worm infestation leading to blood loss. MM must be kept in mind in their differential diagnosis especially in workup for anemias above 50 years of age.

In US thrombocytopenia is present in approximately 15% of patients but leukopenia may or may not be present at diagnosis[4] where as thrombocytopenia occurred in 24.6% and leucopenia in 8.8 % of patients in our study.

Plasma cells in marrow aspirates numbered 40-90% with an average of 78.14% which was higher than the minimum number of plasma cells required (i.e. 30%) in the criteria for diagnosis of MM.[2]

CONCLUSION

In Khyber Pakhtun Kwa province, males are affected more frequently than females by MM. The percentage of MM among all hematological malignancies and the median age are lesser in this part of the world. Majority of patients present with anemia, MM should be included in the workup of anemia in patients above 50 years age.

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