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Original Research Paper

Pathology

BONE MARROW BIOPSY IN MULTIPLE MYELOMA: AN IMPORTANT DIAGNOSTIC TOOL IN CASES WITH FIBROSIS, HYPOCELLULAR MARROW AND FOCAL DEPOSITS

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ABSTRACT

Introduction:MM is commonest hematologic malignancy of old age. Diagnosis requires demonstration of increased monoclonal plasma cells in bone marrow. We aim to highlight role of BMB in diagnosis of MM.

Methods: Bone marrow Biopsy (BMB) and Bone Marrow Aspirate of 50 patients of multiple myeloma were examined thoroughly for different parameters. IHC using CD38, CD138, kappa, lambda antibodies was performed for assessment of tumor load and clonality.

Results: Of 8 cases with unsatisfactory bone marrow aspirate (BMA), 4 cases showed significant fibrosis. In other 4 cases, marrow cellularity was low (20-30%) and tumor deposit was focal, thus, BMA was inadequate. 8 of 14 cases with focal deposits on BMB couldn't be picked up on BMA. Monoclonality was demonstrable using CD38, CD138, kappa, lambda. Two cases with non-specific symptoms were diagnosed Smoldering Myeloma on basis of >10% clonal plasma cells on BMB.

Conclusion: Bone Marrow Biopsy is particularly useful for diagnosis of MM in cases with low cellularity and marrow fibrosis where BMA is inadequate.

KEYWORDS : Multiple Meloma, BoneMarrow Biopsy, Diagnosis

INTRODUCTION

Although commonest haematological malignancy of old age, Multiple myeloma poses a diagnostic challenge often.[1] A battery of tests are required including Skeletal survey, Serum calcium, Creatinine, Free light chain assay, haemoglobin levels and other tests are required. One of the most important criteria remains percentage of plasma cells in Bone Marrow, for which Bone Marrow Aspiration (BMA) is done.[1,2] However, there are many shortcomings of doing BMA examination alone. We used Bone Marrow biopsy (BMB) as a routine procedure in such cases with aim to highlight its diagnostic importance.

MATERIAL AND METHODS

Study group included 50 patients of multiple myeloma diagnosed over a period of 3yrs based on criteria of International Myeloma working Group.[2]

Along with detailed analysis of clinical parameters and various investigations including radiological survey, Serum calcium, BMA; Bone Marrow Biopsy was performed with consent of patient.

After fixation in 10% Neutral buffered formalin, it was decalcified using 2% Calcium EDTA and routinely processed in histokinette. Paraffin embedded blocks were prepared and slides were stained using HE stain, Reticulin stain and Iron stain. They were examined for pattern of infiltration, cellularity, differentiation of plasma cells, residual haematopoiesis and fibrosis. CD38, CD138, kappa and lambda antibodies were used to determine percentage of plasma cells helping with diagnosis of borderline cases and assessment of clonality.

OBSERVATION AND RESULTS

Study group included 50 patients of multiple myeloma diagnosed according to criteria of International Myeloma working Group.[2] Age of patients ranged from 30-82 years with 19 patients(42%) less than 50 years of age. The study group included 15 Females and 35 Male patients.

BMA was assessed for Morphology of plasma cells was classified as mature in 23, immature in 9, intermediate in 8 and plasmablastic in 10 according to classification by Griepp et al.[1]

Table 1: **Comparison of Plasma cell percentage yield on BMA and BMB**

Percentage of Plasma cells	BMA	BMB
<20%	15	2
20-50%	18	24
>50%	13	20

On BMB, most of the marrow were hypercellular (86%), but there were 2 hypocellular and 4 normcellular marrow for age. The pattern of involvement of marrow by plasma cells was diffuse in 9, focal in 14, interstitial in 7 cases. Residual Haematopoiesis was adequate in 70%(35) cases. Fibrosis of different grades was observed in 12 cases. Plasma cell yield was higher in Two cases with non-specific symptoms were diagnosed Smoldering Myeloma on basis of >10% clonal plasma cells on BMB. Clonality of plasma cells was demonstrated by use of kappa and lambda antibodies.

DISCUSSION

Mean Age of patients was 58.3yrs., comparable to Rana et al and Griepp et al.[3,4] Male to Female ratio was 2:1 similar to other Indian studies[3,5] but higher than western literature.[1]

Infiltration Pattern of Marrow was interstitial in 13 (26%) nodular/focal in 19(40%) and diffuse in 18(36%). Results are comparable to other studies.[4,6]

A total of 13 cases (26%) showed higher yield of plasma cells on BMB compared to BMA. Among these were 7 out of 19 cases (38%) of focal/nodular involvement of marrow. Four cases were associated with fibrosis and 2 case had hypocellular marrow.

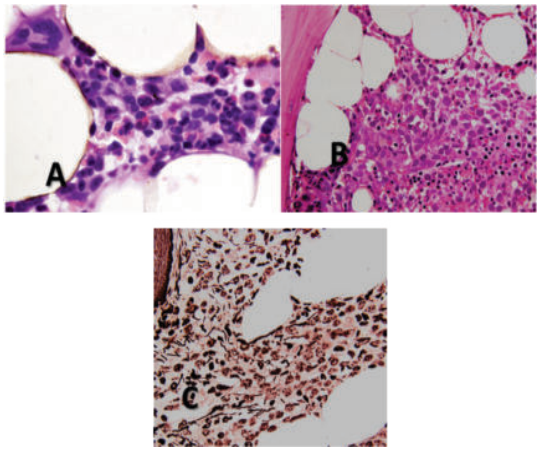

Fig. A- Hypocellular marrow in a case With raised plasma cells **(400X HE) Fig. B**- Nodular infiltrate of plasma Cells on marrow **(100X HE) Fig. C**- Prominent fibrosis in a case of Plasmablastic Myeloma**(100X Reticulin)**

Our findings are similar to Terpestra et al, Subramaniam et al,etc [6-10] who found Biopsy to be a better tool for evaluation of plasma cell fraction. The causes listed by them for the same were fibrosis and focal/nodular involvement . *We also found that hypocellularity of marrow contributed to the discrepancy in results.*

Use of IHC (CD38,CD138) on biopsy was also helpful in determining the exact tumor load and thus, raised the yield on biopsy.

In cases of Smoldering myeloma, where demonstration of monoclonality is essential, BMB becomes a must. Monoclonality was proven by use of kappa and lambda antibodies on BMB which showed positivity with either one in such cases.

CONCLUSION

Bone Marrow Biopsy is particularly useful in diagnosis of Multiple Myeloma in

- Focal/Nodular pattern of infiltration by plasma cells
- Bone Marrow Fibrosis
- Hypocellular Bone Marrow
- Smoldering Myeloma

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