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FREQUENCY OF BONE MARROW INVOLVEMENT IN CASES OF LYMPHOMA: A HOSPITAL BASED OBSERVATIONAL STUDY

Pathology

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ABSTRACT

Background: In patients with lymphoma, bone marrow involvement is definite evidence of disseminated disease and hence assessment of bone marrow status in these patients provides important information for decisions regarding treatment. **Aim:** To determine frequency of bone marrow involvement in cases of lymphoma. **Results:** Out of 60 histologically confirmed lymphoma patients, 51(85%) patients were of Non Hodgkin's lymphoma and 9 (15%) patients were of Hodgkin's lymphoma. International working formulation was followed to classify Non Hodgkin Lymphoma into low, intermediate and high grade. The low grade Non Hodgkin lymphoma cases comprised of 41.18% (21/51), high grade 39.21% (20/51) and intermediate grade 19.61% (10/51) cases. Out of 9 Hodgkin lymphoma (HL) cases, 8 (88.9%) were of classical type and there was a single case (11.1%) of lymphocytic predominant Hodgkin's lymphoma. 25 (41.7%) cases showed bone marrow infiltration by the atypical lymphomatous cells. Bone marrow involvement was seen in 47.05% (24/51) cases of NHL. Among Non Hodgkin lymphoma cases, maximum involvement was seen in low grade NHL 57.14% (12/21) followed by intermediate grade NHL 50% (5/10) & minimum was seen in high grade NHL 35% (7/20). **Conclusion:** Thorough examination of bone marrow in lymphoma patients can increase the diagnostic accuracy as it may be the single most important finding in a patient with an otherwise localized disease there by contributing to the prognosis and appropriate treatment modalities.

KEYWORDS

Bone marrow, Infiltration, Lymphoma

INTRODUCTION:

In patients with malignant lymphoma, trephine bone marrow (BM) biopsy is an important diagnostic tool [1]. Assessment of bone marrow is a crucial part of the Ann Arbor system which is the commonly used staging tool in lymphoma and in which bone marrow involvement implies the highest disease stage (Stage 4). Also, the presence of bone marrow involvement may change the choice of therapy. Bone marrow involvement has been reported to be an important predictor of occurrence of infusion-related reaction following rituximab administration [2]. Trephine imprints becomes very useful, especially if aspiration has manifested a blood/dry tap. Sometimes, the biopsy may demonstrate lymphoma when no abnormal cells have been detected in blood and bone marrow smears. It permits an assessment of pattern and extent of infiltration, both of which have diagnostic and prognostic relevance [3]. The incidence of marrow involvement in non-Hodgkin in aggregate for all Histopathological subtypes ranges from 40% to 55%. The incidence is higher in low-grade lymphomas than in many of the high-grade lymphomas. It is approximately 10% in classical Hodgkin mixed cellularity and approximately 1% in lymphocyte predominant Hodgkin and lymphocyte-rich classical Hodgkin disease. The histopathological pattern of B.M infiltration which is observed on trephine biopsy comprises of diffuse, focal paratrabecular, focal nonparatrabecular, interstitial, intrasinusoidal, and rarely intravascular [4]. In Indian perspective, limited studies on bone marrow involvement in lymphomas are available. So the study was performed to avail more data on bone marrow involvement in lymphomas for increasing the diagnostic yield and staging purpose.

MATERIALS AND METHODS:

The present observational study with both prospective and retrospective component extending over a period of 2 years was conducted in Department of pathology, Government Medical College, Jammu. The study was approved by Institutional ethics committee. During the study period, a total of 60 cases with confirmed histological diagnosis of lymphoma, referred to the Haematology section of the Department of Pathology were studied. All the patients of lymphoma, who were part of the prospective study were subjected to unilateral bone marrow trephine biopsy under local anesthesia using the conventional technique with a Jamshidi needle from the posterior superior iliac spines, fixed in 10% formalin solution and decalcified using 10% formal - formic acid for 4 - 6 h followed by routine processing and paraffin embedding. For retrospective study, the H&E as well as Reticulin stained sections of the bone marrow trephine biopsy and Giemsa stained imprint smears were retrieved from the archives of the department. Imprint smears were studied in detail for cellularity & presence of any atypical cells. Bone marrow trephine biopsy in addition was studied for infiltration, pattern of infiltration, if present and marrow fibrosis. Sections with at least five well preserved marrow spaces were studied for cellularity, normal hematological elements, presence of infiltration if any, the extent, histologic pattern and morphology of infiltration, reticulin fibrosis and other secondary changes. Reticulin was graded from 0 to 4. Data was analyzed using the Statistical Package for the Social Sciences. The results were expressed as mean for quantitative variables and presented as frequency & percentages for qualitative parameters.

RESULTS:

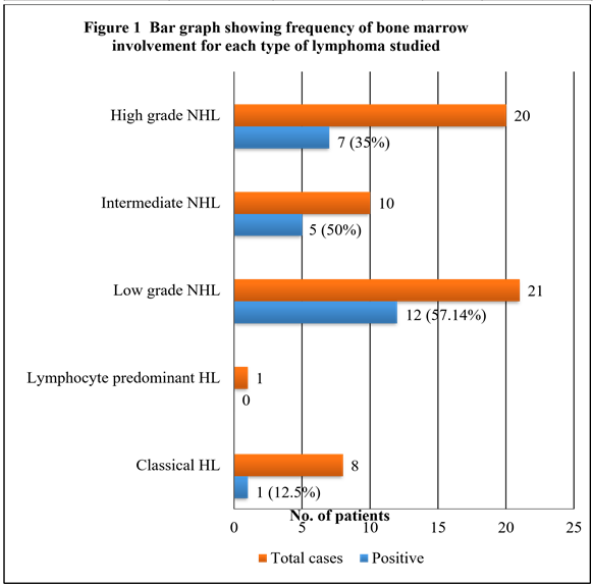
Out of sixty histologically confirmed lymphoma patients, 51(85%) patients were of Non Hodgkin's lymphoma and 9 (15%) patients were of Hodgkin's lymphoma. International working formulation was followed to classify Non Hodgkin Lymphoma as low, intermediate and high grade. The low grade Non Hodgkin lymphoma cases comprised of 41.18% (21/51), high grade 39.21% (20/51) and intermediate grade 19.61% (10/51) cases (Table 1). Out of 9 Hodgkin lymphoma (HL) cases, 8 (88.9%) were of classical type and there was a single case (11.1%) of lymphocytic predominant Hodgkin's lymphoma .Out of 60 cases, 25 (41.7%) cases showed bone marrow infiltration by the atypical lymphomatous cells (Table 2). Bone marrow involvement was seen in 47.05% (24/51) cases of NHL. Among Non Hodgkin lymphoma cases, maximum involvement was seen in low grade NHL 57.14% (12/21) followed by intermediate grade NHL 50% (5/10) & minimum was seen in high grade NHL 35% (7/20). Bone marrow involvement in Hodgkin lymphoma was seen in 11.11% (1/9) cases. Bone marrow involvement was seen in 47.05% (24/51) cases of NHL. Among Non Hodgkin lymphoma cases, maximum involvement was seen in low grade NHL 57.14% (12/21) followed by intermediate grade NHL 50% (5/10) & minimum was seen in high grade NHL 35% (7/20). Bone marrow involvement in Hodgkin lymphoma was seen in 11.11% (1/9) cases. Maximum number of cases were seen in the age group of 51 to 60 years (mean age 52.1 years and median age 59.5 years). Maximum number of patients (12) with bone marrow involvement also belonged to the age group of 51 to 60 years (median 60 years). Male preponderance was seen and constituted 66.7% cases and females constituted 33.3% with male to female ratio of 2:1. Similar preponderance was seen in patients (25) with bone marrow involvement with male to female ratio of 1.8:1. 25 (41.7%) cases showed bone marrow infiltration by the atypical lymphomatous cells.

Table 1: Showing distribution of patients as per grade of Non Hodgkin lymphoma:-

Non Hodgkin lymphoma	No. of patients	%age
Low grade NHL	21	41.18
Intermediate grade NHL	10	19.61
High grade NHL	20	39.21
Total	51	100

Table 2: Showing frequency of marrow involvement in cases of lymphoma:-

Bone marrow infiltration	Hodgkin lymphoma	Non Hodgkin lymphoma	Total	Frequency (%age)
Positive	1	24	25	41.7
Negative	8	27	35	58.3
Total	9	51	60	100.0



DISCUSSION:

The diagnosis of Non Hodgkin lymphoma depends on histopathological findings on lymph node biopsy including Haematoxylin & Eosin staining and immunohistochemistry whereas other invasive and non-invasive procedures are employed to evaluate extent of the disease, also termed as Staging. Bone marrow is an important site where lymphomatous cells can reside (Figure 2). Detection of lymphomatous bone marrow involvement may be clinically relevant from several perspectives [2]. In the present study, the group of 60 patients comprised of 51 (85%) patients of Non-Hodgkin's lymphoma (NHL) and 9 (15%) patients of Hodgkin's lymphoma (HL). Similar results were observed by Hingorjo MR et al [5] in their study of 60 cases of lymphoma in which 49 (81.6%) cases were diagnosed as Non-Hodgkin's lymphoma and 11 (18.3%) cases as Hodgkin's lymphoma, with an overall male predominance. In our study, low grade Non Hodgkin Lymphoma comprised of 41.18% cases, high grade 39.21% cases (Figure 3) and intermediate grade 19.61% cases. K Kaur et al. [6] in a study of 85 patients with Non Hodgkin Lymphoma observed low grade (Figure 4) in 68.2% cases, intermediate grade in 28.2% and high grade in 3.5% cases. Different observations were seen in a study by Chakrabarti S et al. [7] who showed low grade lymphoma in 18.4%, intermediate grade lymphoma in 55.3% and high grade lymphoma in 26.3% patients of Non Hodgkin Lymphoma and by Isikdogan A et al. [8] who showed 71 (14.4%) low grade cases, 342 (69.8%) intermediate grade cases and 43 (8.7%) high grade cases of NHL. In our study, out of 60 cases, 25 (41.7%) showed bone marrow infiltration by the atypical lymphomatous cells and 35 (58.3%) showed no marrow involvement. Bone marrow involvement was seen in 47.05% (24/51) cases of Non Hodgkin lymphoma. Among Non Hodgkin lymphoma, maximum involvement was seen in low grade NHL 57.14% (12/21) followed by intermediate grade NHL 50% (5/10) & minimum was seen in high grade NHL 35% (7/20). While marrow involvement in Hodgkin lymphoma was 11.11% (1/9). A single case of lymphocyte predominant HL included did not show any marrow involvement. Shi YF et al. [9] found frequency of bone marrow involvement to be 16.1% (153/950) (NHL and HL). Among cases of Hodgkin lymphoma, 4.4% (6/138) cases showed bone marrow involvement. Lambertenghi Deliliers G et al. [10] found bone marrow infiltration in 32.14% cases (NHL and HL). Kumar S et al. [11] in a study on 49 cases of Non Hodgkin lymphoma found that the overall incidence of marrow involvement by Non Hodgkin lymphoma was 55.1%. Sultan S et al. [12] found the frequency of bone marrow infiltration in Non Hodgkin lymphoma patients to be 31.5% (58/187) . Kittivorapart J et al. [13] found the incidence of bone marrow involvement in cases of Non Hodgkin lymphoma to be 23.8% which is on the lower side when compared to our study. Marrow involvement in our study in cases of Hodgkin lymphoma was found to be 11.11% (1/9) which is in agreement with Chakrabarti S et al. [7] who showed bone marrow involvement in 4 (8.33%) cases of Hodgkin lymphoma. Franco V et al. [14] in a review analysed that in adult population the incidence of bone marrow infiltration is estimated between 2 and 32%, with an average of 10% cases of HL. Panneerselvam R et al. [15] found the 92 frequency of bone marrow involvement to be 6.6% in cases of Hodgkin lymphoma. Different results were seen in study by Chauhan K et al. [16] with the incidence of bone marrow involvement in cases of Hodgkin lymphoma to be 18.3% (9/49). Subramanian R et al. [17] showed 18% (14/76) cases of biopsy proven Hodgkin's disease.

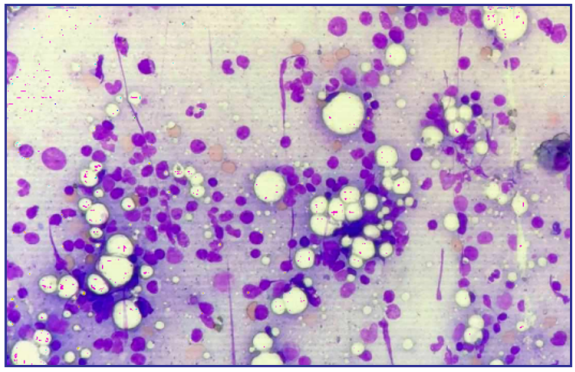


Figure 2: Photomicrograph of imprint smear showing infiltration by Non Hodgkin lymphoma (MGG 400x)

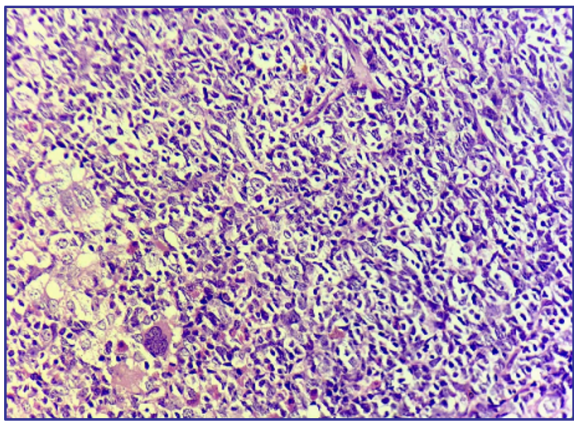


Figure 3: Photomicrograpgh of bone marrow biopsy section showing infiltration by a high grade Non Hodgkin ymphomal (H&E 400x)

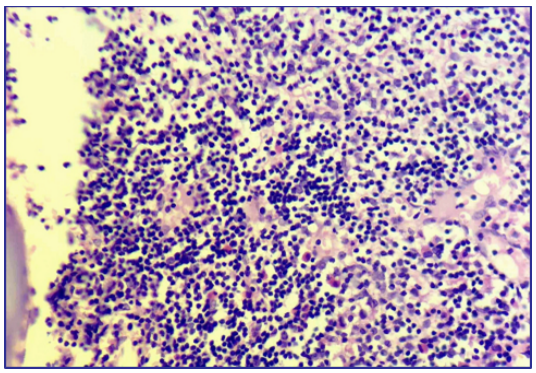


Figure 4: Photomicrograph of bone marrow biopsy section showing infiltration by low grade Non Hodgkin Lymphoma (H&E 400x)

CONCLUSION:

Marrow involvement may be the single most important finding in a patient with an otherwise localized disease as it indicates stage IV disease. Our study showed that Non Hodgkin's lymphoma is more common than Hodgkin's lymphoma. The frequency of bone marrow infiltration on trephine biopsies of lymphoma patients was 41.7%. Low grade Non Hodgkin lymphoma cases showed maximum number of cases with bone marrow involvement followed by intermediate grade Non Hodgkin lymphoma. Meanwhile, FDG-PET has become an established method for lymphoma staging as it is a non-invasive alternative or a complementary method to BMB. However in our setup and in a cost effective way, bone marrow biopsy still remains the gold standard for staging of lymphoma.

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