

Role of Bone Marrow Biopsy in Hodgkin's Lymphoma – A Study At Tertiary Care Centre Of Northern India

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Abstract

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Introduction

Average Incidence of marrow involvement in Hodgkin's disease (HD) is 10%¹ with range of 3-18%

The different histological types of HL can be identified on BM biopsy with mixed cellularity being most common and rarest is lymphocyte depleted²

BM involvement indicates vascular dissemination and hence upstages patient's disease to stage IV which further^{2,3} influences treatment plans, prognosis and obviates the need for other investigations required to stage the patient

Extra nodal primary HL is rare and isolated BM lymphoma is even extremely rare. So we should correlate clinically to rule out for primary marrow involvement or any systemic manifestation^{3,4,5}

We present here a study of 35 cases of HL to assess frequency of BM involvement in HL & to determine morphological changes in BM.

Materials and Methods

This study is a Retrospective analysis of 35 cases - over a period of 4 years.

BMB was routinely processed & stained with haematoxylin & eosin for all cases. Special stains & immunohistochemistry (IHC) was done wherever possible. Relevant clinical details were recorded in all

cases. Criteria for BM involvement in HD (McKenna & Kroft, 2001)⁶ -

CERTAIN- Typical RS cells or mononuclear variants in characteristic cellular environment

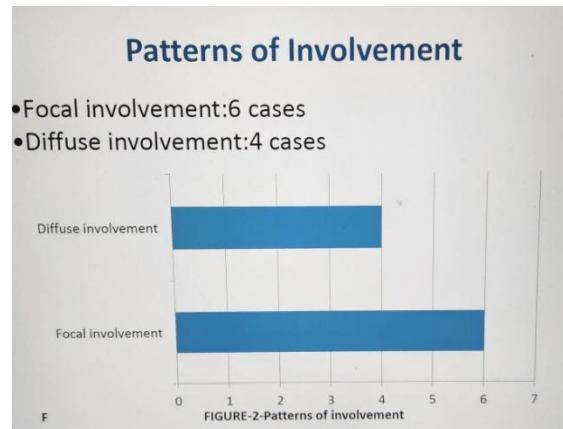
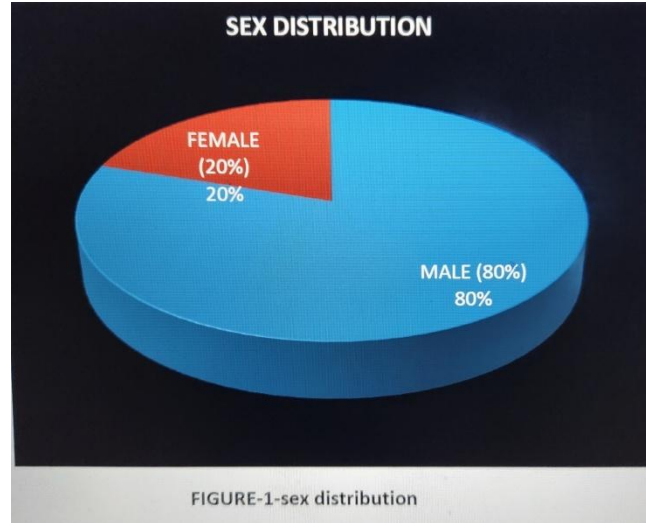
SUGGESTIVE- Atypical Histiocytes or characteristic cellular background

SUSPICIOUS- Fibrosis/Necrosis alone.

Observations and Results

- Total no. of cases: 35
- Cases with Bone marrow involvement: 10(28.6%)
- Sex Distribution:
 - Males - 8 (80%)
 - Females - 2 (20%)
- Age Distribution: (Fig-1)
 - Range 3-55yr
 - Mean -31yr
- **Histopathological findings**
 1. Focal involvement was found in 6 cases and diffuse pattern in 4 cases.(Fig-2&3)
 2. Polymorphous infiltrate of lymphocytes, eosinophils, plasma cells, neutrophils and histiocytes in all cases

3. Classical RS cells - 1 case
4. Mononuclear cells - 7 cases (Fig-4)
5. Focal necrosis - 3 cases(Fig-5)
6. Granulomas - 2 cases(Fig-6)
7. Gelatinous marrow transformation - 1 case
8. Reticulin – Increased in all cases to Grade 3-4 (Fig-7)



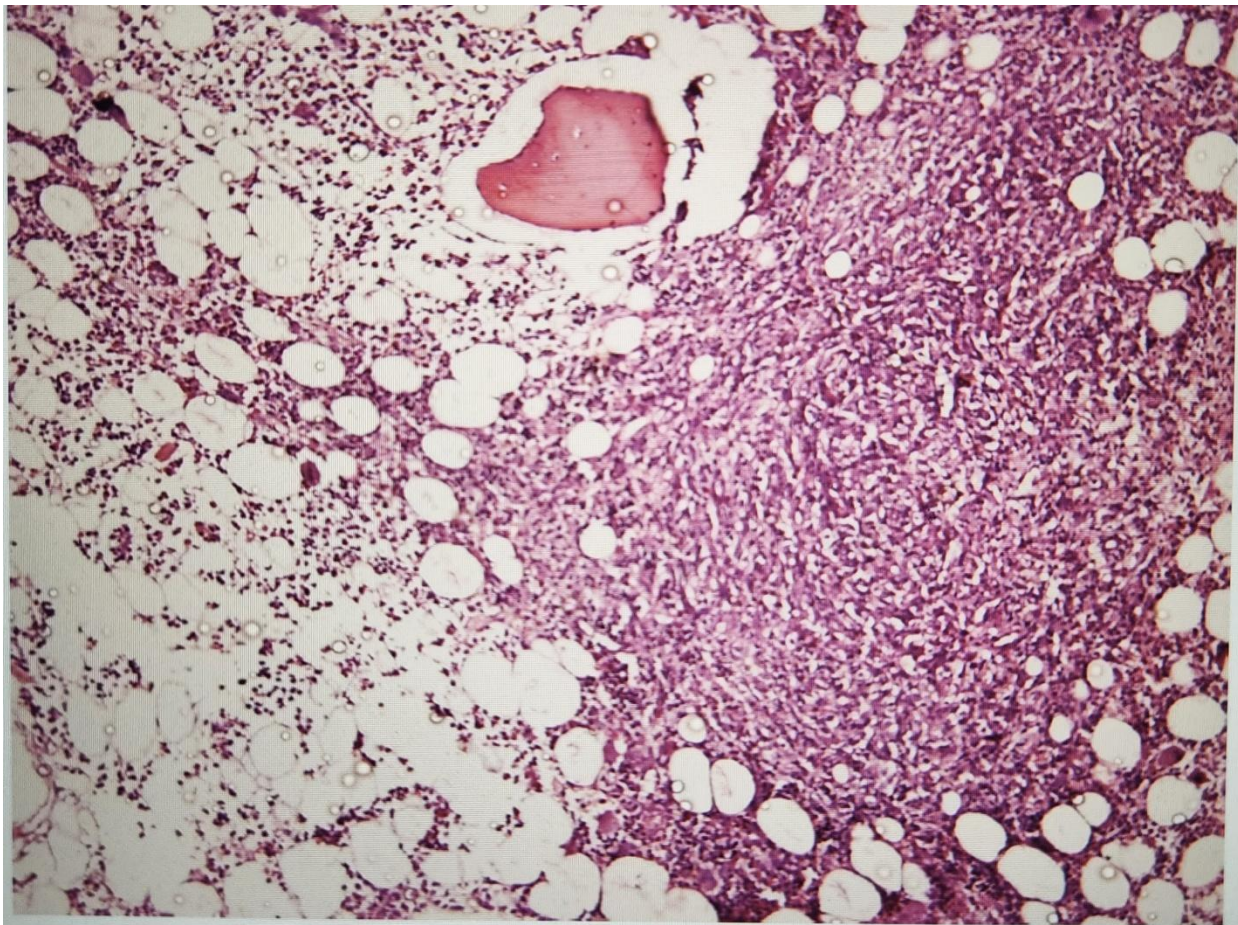


Figure 3-BMB shows focal HD deposit in marrow, intervening marrow is normal

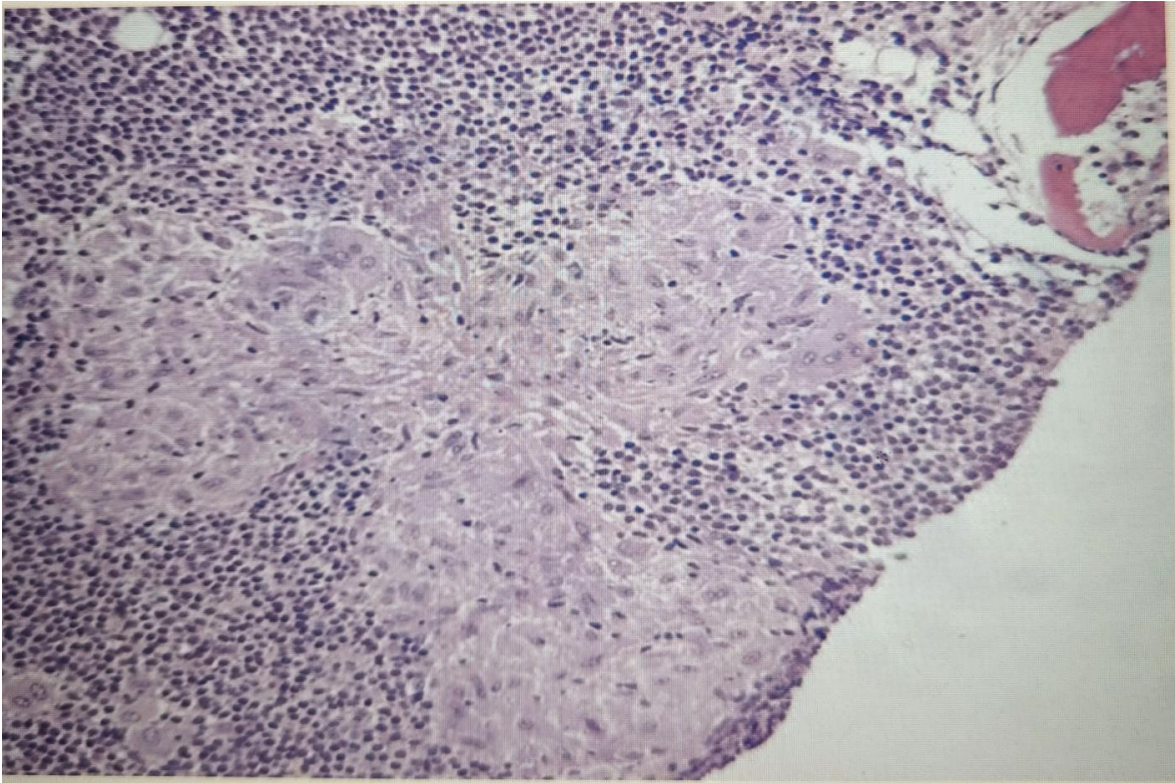


Figure 6-BMB showing granuloma in a patient of HD

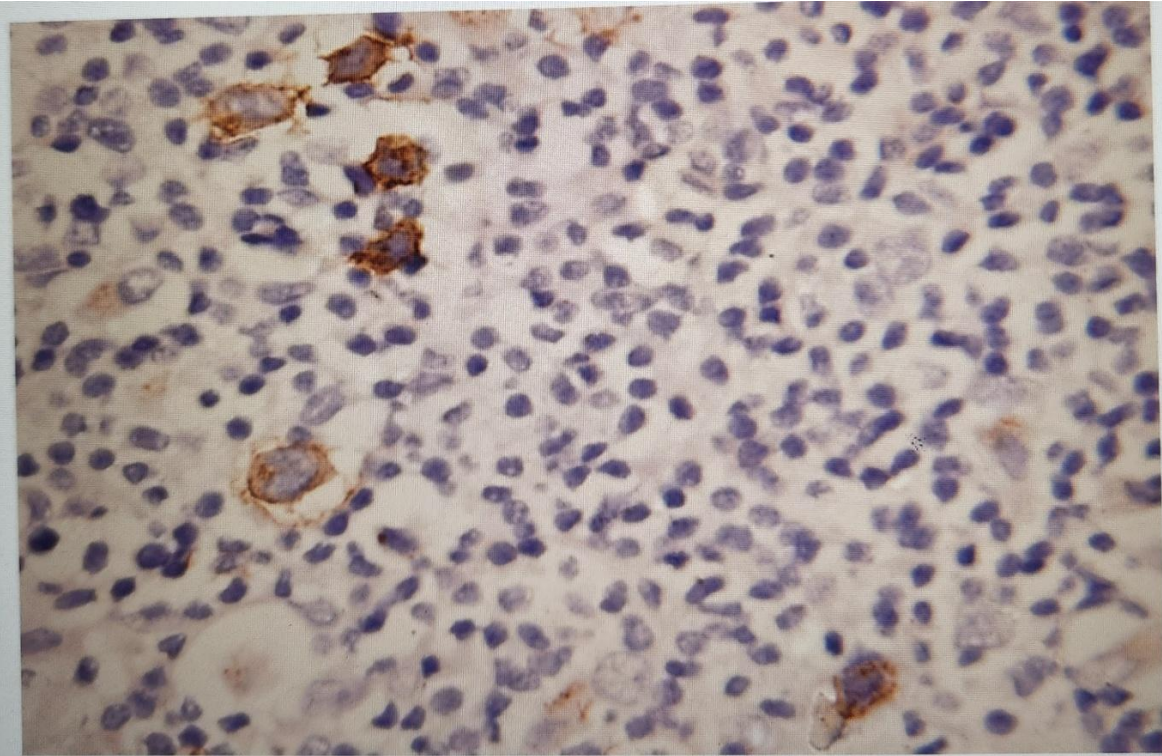


Figure 8-Mononuclear RS cells showing CD 30 positivity

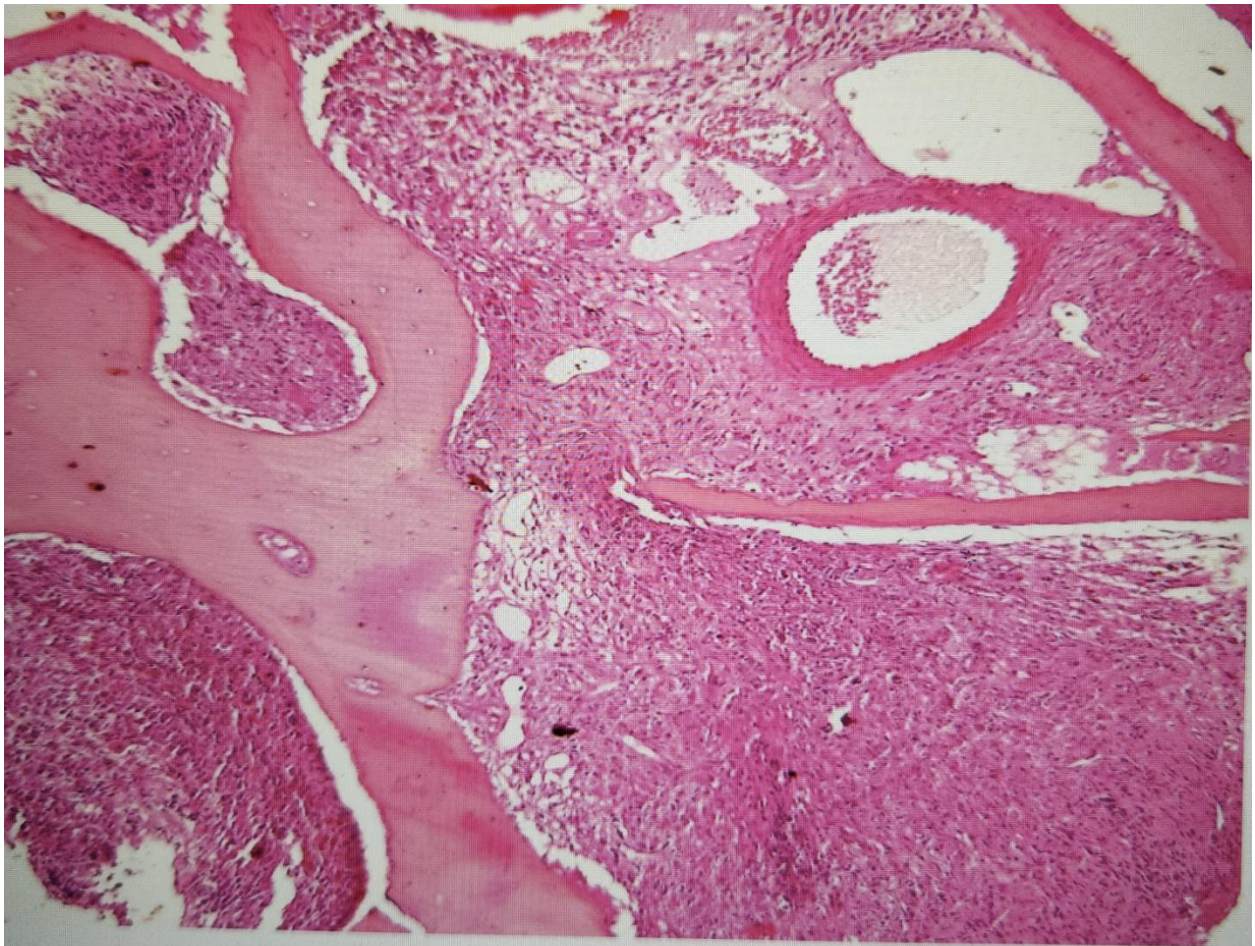


Figure 7-BMB showing diffuse fibrosis in HD

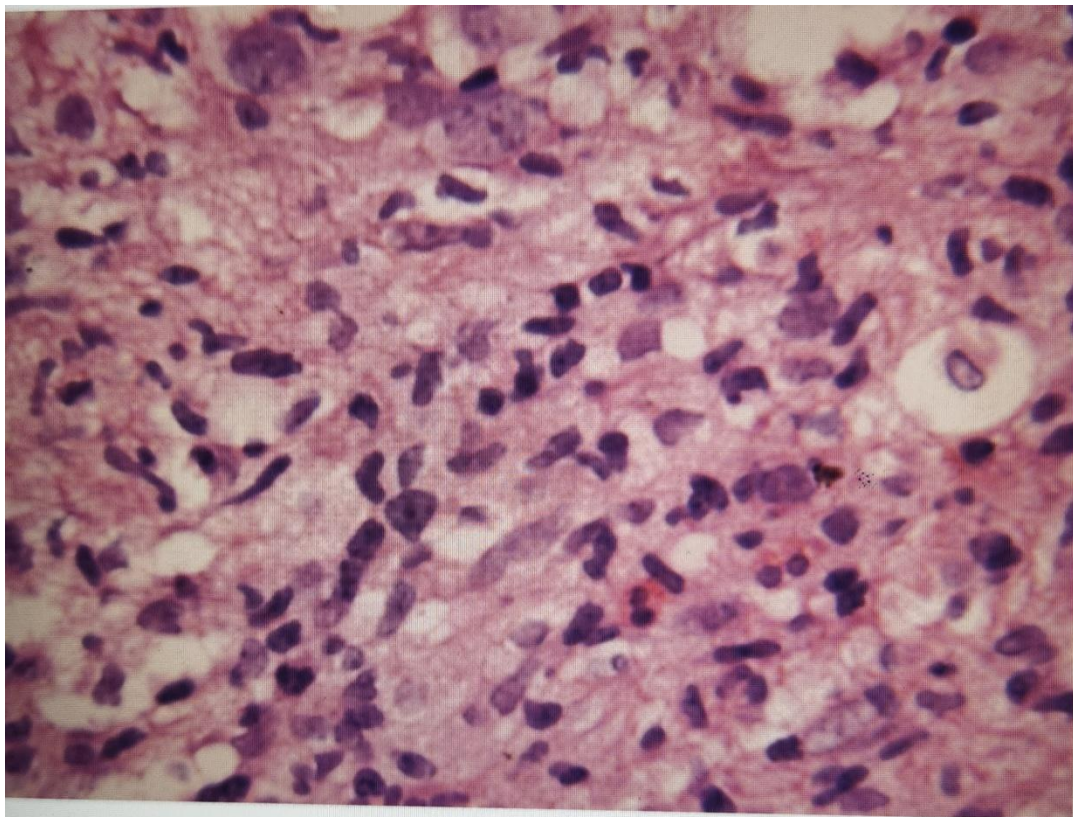


Figure 4-BMB showing mononuclear cells in polymorphous background

Discussion

Incidence of infiltration of BM in HL varies in different studies. Subramanian *et al*⁷ has reported infiltration in 18% cases out of a total of 76 cases.

Hamid *et al*² reported an incidence of 30% out of 50 cases. In a study of Pakistan by Siddiqui *et al*⁸ infiltration by HL in BM was seen to the range of 53.4%. In our study, we found BM infiltration in 28.6% of cases out of total of 35 cases which is in concordance with other studies. High incidence in Pakistan studies may have been due the fact that higher percentage of patients presented in late stages (III&IV) as concluded by Siddiqui *et al*⁸.

Study done by Khan *et al*⁹ observed 10:1 male to female ratio. In studies done by Cheema *et al*¹⁰ and Siddiqui *et al*⁸, this bias towards male child is explained by economic status and more importance given to male child. Our study also shows male preponderance which correlated with above mentioned studies.

Diagnosis of HL involvement in BM is very challenging and according to Ann Arbor (1977) conference, criteria for diagnosis on marrow differ if a tissue diagnosis has already been made (Kar R Dutta S¹¹ and Dholaria B *et al*¹²). When the tissue biopsy is already done, as was the cases in our study the criteria for diagnosis are less stringent. There should be atypical mononuclear cells in a polymorphous background. If only few atypical cells with fibrosis and inflammatory cells or necrosis is seen then it is suggestive, not diagnostic. In these cases, IHC is needed to confirm the diagnosis (Lukes *et al*¹³). We did CD30 (Fig-8) in all suspicious cases. Extra caution was taken during decalcification as it affects antigen retrieval (Vangla *et al*³). We found polymorphous infiltrate of lymphocytes, eosinophils, plasma cells, neutrophils and histiocytes in all cases. Classical RS cell in only one case and mononuclear cell in seven cases.

Necrosis is more commonly seen in bone marrow in HL after initiation of therapy (Brunner RD *et*

al¹⁴). However, three of our cases showed necrosis at the time of presentation.

Granulomas are noted in two of our cases. This corresponds to a large study by Pease GL¹⁵ discussing granulomatous lesion in bone marrow biopsy in 150 cases in which he found six cases of HL.

Gelatinous marrow transformation or serous atrophy of bone marrow is a rare disorder which is mainly seen in immunocompromised patients. It is also seen in one of our cases, similar findings reported by Das et al¹⁶.

It has been reported in literature and in a study done by Shi et al¹⁷ that bone marrow by HL involves fibrosis. This was corroborated by our study in which fibrosis was seen in all cases (Reticulin grade 3 to 4).

Infiltration in HL has a focal pattern which may be a cause for negative bone marrow aspiration. In our study also six had focal involvement and four had diffuse involvement. It has been studied by A. Voltin et al¹ that PET CT is more sensitive in detecting infiltration of BM by HL with sensitivity reaching upto 95%. But it has been advocated by Hammid S J et al² and Subramanian et al that in developing countries like India PET is not available everywhere, Hence, trephine biopsy is the main stay for staging HL.

Conclusion

- HD in marrow is associated with fibrosis & therefore is not aspirable
- Characteristic morphological features & IHC on BMB are useful in clinching the diagnosis¹⁰
- Bone marrow infiltration in clinical stage IA and IIA upstages them to stage IV. so, Bone marrow biopsy should be performed for prognostic significance, early implementation of therapy and better survival of patients.¹¹

Contributor's Statement

All authors have made substantial contributions to idea and design, acquisition of data, analysis and interpretation of findings.

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