

PERIPHERAL BLOOD AND BONE MARROW FINDINGS IN LYMPHOMAS: A STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Lymphomas are the common haematological malignancies encountered in clinical practice. Most of them present with enlarged lymph nodes and extra nodal presentation is a rare feature. All the lymphoma cases require peripheral blood and bone marrow studies to stage the disease before chemotherapy. Peripheral blood and bone marrow involvement play a major role in the prognosis of these patients. We had studied various haematological parameters in diagnosed cases of lymphomas, in which bone marrow aspiration was also done as a part of staging of the disease.

METHODS

This is a three-year retrospective study conducted in the department of pathology of a tertiary care hospital. Material for the study included lymphoma cases that underwent bone marrow aspiration also for staging of the disease. Clinical details, haematological parameters and bone marrow findings were collected from the files and recorded.

RESULTS

A total of 63 cases of lymphomas were included in the study that comprised of 15 (23.8%) and 48 (76.2%) cases of Hodgkin lymphoma (HL) and non-Hodgkin lymphomas (NHL) respectively. Anaemia was the prominent feature in cases that showed bone marrow infiltration and accounted for 94.2% of these cases.

CONCLUSIONS

Anaemia alone or in combination with other abnormal blood counts is common finding in patients of lymphoma, more frequently in non-Hodgkin lymphoma showing bone marrow infiltration. A detailed study of peripheral blood smear showed atypical lymphoid cells in 41.6% of patients with marrow infiltration.

KEYWORDS

Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Bone Marrow, Anaemia, Atypical Lymphocytes.

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BACKGROUND

Lymphomas are most common haematological malignancies which are characterized by the clonal proliferation of lymphoid cells and account for 5% of all malignancies. These are broadly classified as Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphomas have the propensity to infiltrate extranodal tissues, of which bone marrow is the most common site. Abnormalities in peripheral blood counts are also a frequent finding in NHLs. Studies have reported that NHLs had one or more haematological abnormalities; in the levels of haemoglobin, both in numbers and morphology of leucocytes or platelets counts. Anaemia was the most

prevalent abnormality in these patients.^{1,2} In lymphomas peripheral blood counts are a part of workup before therapy along with bone marrow examination as they reflect the prognosis even more when these were not normal.³

METHODS

This was a retrospective study conducted in the department of Pathology of a tertiary care hospital. Duration of the study was 3 years. This retrospective study included newly diagnosed cases of lymphomas which underwent bone marrow aspiration. Clinical findings, haematological parameters and bone marrow findings were collected from the files and recorded. Lymphoma patients who were already on treatment were excluded from the study. Haemoglobin level of less than 13.0 g/dl and 12.0 g/dl in males and females respectively was considered as Anaemia.⁴ The full blood counts (consisting of haemoglobin level, total white blood cell count and platelet count) of all patients at the time of diagnosis were recorded and findings such as the presence of anaemia, leucopenia or leucocytosis, and thrombocytopenia or thrombocytosis noted as per the age-specific normal ranges in the 9th edition of Practical Haematology by Dacie and Lewis.⁵ Manual differential count

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findings of each case were performed on peripheral blood smear. Presence of atypical cells was also noted. The absolute counts were calculated using the manually obtained differential counts, and the presence of lymphocytosis and eosinophilia were determined by comparing with the normal ranges outlined in the 9th edition of Practical Haematology by Dacie and Lewis.⁵ In bone marrow smears presence of more than 20% lymphocytes was taken as marrow lymphocytosis and presence of more than 6% eosinophils and eosinophilic precursors was considered as bone marrow eosinophilia.⁶

RESULTS

A total of 63 cases were studied which were diagnosed during study period of 3 years. There were 48 cases (76.2%) of Non-Hodgkin Lymphoma (NHL) and 15 cases (23.8%) of Hodgkin lymphoma (HL).

Age and Gender

Patients were in the age range of 5 to 79 years with a mean age of 34.6 and 54.6 years for HL and NHL respectively. Median age was 36 years in HL and 55 years in NHL. Out of 63 cases 31 (49.1%) were males and 32 (50.9%) were females with male to female ratio of 1:1.03 showing only a slight female preponderance. In Non-Hodgkin lymphoma, female preponderance was noted whereas in HL, there was male preponderance with male to female ratio of 1: 1.3 and 2.7: 1 respectively. Incidence of HL cases was high in the second decade whereas in case of NHL, it was seen to be in the sixth decade (Table 1).

Clinical Characteristics

In 59 (93.7%) out of 63 cases diagnosis was made on lymph node biopsy. Five cases (7.9%) were diagnosed at extra nodal sites, 2 cases from stomach and one each from testis, maxillary sinus and soft tissue that being a popliteal fossa swelling, all were NHLs. Most common clinical presentation was fever (36.5% cases) besides lymph node enlargement. B symptoms (fever, weight loss, night sweats) either singly or in combination were present in 73.3% and 47.9% of HL and NHL cases respectively. Fever was frequently seen in HL (66.6%) as compared to NHL (27%). Loss of weight was present in 16.6% and 6.7% cases of NHL and HL respectively. Hepatosplenomegaly was present in 8 cases (12.6%), only hepatomegaly in 4 (6.3%) and only splenomegaly in 5 (7.9%) cases respectively. Splenomegaly was more common in HL (20%) in comparison to NHL (4.1%). Hepatomegaly was not present in HL cases. (Table 2)

Peripheral Blood and Bone Marrow Findings

Mean haemoglobin was 10.7±2.2 g/dl (7.2-13.8 g/dl). Of the total lymphoma cases Anaemia was seen in 48 cases (76.2%). Anaemia was present in 11 out of 15 cases (73.2%) and 37 out of 48 cases (77.3%) of cases of HL and NHL respectively. Most of these cases had mild to moderate degree of Anaemia. (Table 3)

Morphologically Anaemia was normocytic normochromic in 30 (62.5%), microcytic hypochromic in 11 (22.9%), macrocytic in 2 (4.2%) and dimorphic in 5 (10.4%) cases. Mean leucocyte count was 9.8±8.4 x10⁹/l. Leucocytosis was seen 11 cases of NHL, leucopenia was seen in 2 cases of NHL and in a lone case of HL. Blood eosinophilia was seen in 2 out of 15 cases (13.4%) of HL and 14 out of 48 cases (29.2%) of NHL. Peripheral blood lymphocytosis was noted in 7 cases of NHL and atypical lymphocytes were seen in 7 cases (14.6%) and 5 cases (10.4%) of NHL respectively. Mean platelet count was 258.1 ±128.1 x 10⁹/l and 314.5 ± 123.7 x 10⁹/l in HL and NHL respectively. Thrombocytopenia was seen in 5 cases of NHL and in a single case of HL.

Among NHLs, 44 (91.7%) were B cell lymphomas and 4 (8.3%) were T- cell lymphomas. T-cell lymphomas comprised of four cases of peripheral T cell lymphoma - unspecified and single case each of lymphoblastic lymphoma (LBL) and anaplastic large cell lymphoma (ALCL). Out of 44 B-NHLs there were 16 cases of diffuse large B cell lymphoma (DLBCL), 5 cases of small lymphocytic lymphoma/ chronic lymphocytic leukemia (SLL/CLL), 3 cases of follicular lymphoma, 2 cases of lymphoblastic lymphoma and 2 cases of T-cell rich B cell lymphoma. In remaining B-cell lymphomas details of subtypes were not available.

Haematological Abnormalities in NHLs with Bone Marrow Involvement

Bone marrow infiltration was seen in 12 out of 48 cases (25%) of NHL, out of which five cases were DLBCL. Six out of twelve cases showed peripheral blood involvement as well. Trepchine biopsy was not done in any of these cases. Eleven out of twelve cases (92.8%) with bone marrow infiltration showed Anaemia. Thrombocytopenia and leucopenia were less frequent than Anaemia accounting for 21.4% and 7.1% cases respectively. Leucocytosis, lymphocytosis and atypical lymphocytes present in 66.6%, 58.3% and 41.6% cases respectively. Peripheral blood involvement was seen in 6 cases (50%), 3 cases of DLBCL, 1 case each of B-LBL, SLL/CLL and anaplastic large cell lymphoma. (Table 4)

Among 15 cases of HL there were four each of nodular sclerosis and mixed cellularity types; and one case of nodular lymphocyte predominant Hodgkin lymphoma (NLPHL). In the remaining 6 cases, subtype could not be specified due to lack of further details. Bone marrow aspiration was normal in all the HL cases.

Age in Years	Hodgkin Lymphoma (n=15)	Non-Hodgkin Lymphoma (n=48)	Total (n=63)
0-10	2 (13.3%)	1 (2.1%)	3
11-20	4 (26.7%)	0	4
21-30	0	1 (2.1%)	1
31-40	3 (20%)	2 (4.2%)	5
41-50	1 (6.7%)	5 (10.4%)	6
51-60	3 (20%)	19 (39.6%)	22
61-70	1 (6.7%)	9 (18.7%)	10
71 and above	1 (6.7%)	5 (10.4%)	6

Table 1. Age Incidence of Hodgkin and Non-Hodgkin Lymphomas

Clinical Characteristics	HL (15 Cases)	NHL (48 Cases)
Symptoms (fever, weight loss, night sweats)	11 (73.3%)	23 (47.9%)
Splenomegaly	03 (20%)	02 (4.1%)
Hepatomegaly	-	05 (10.4%)
Hepatosplenomegaly	01 (2.1%)	07 (14.6%)

Table 2. Clinical Characteristics of Lymphomas

Characteristics	Hodgkin Lymphoma (N=15)	Non-Hodgkin Lymphoma (N=48)
Anaemia	11 (73.3%)	37(77.1%)
Leucocytosis	-	11(22.9%)
Leucopenia	1(6.7%)	2(4.2%)
Thrombocytosis	-	5(10.4%)
Thrombocytopenia	1(6.7%)	5(10.4%)
Eosinophilia	2(13.4%)	14(29.2%)
Lymphocytosis	-	7(14.6%)
Pancytopenia	1(6.7%)	1(2.1%)
Peripheral blood involvement	-	6(12.5%)
Atypical lymphocytes	-	5(10.4%)
Bone marrow lymphocytosis	-	15(31.2%)
Bone marrow eosinophilia	3(20%)	13(27.1%)
Bone marrow infiltration	-	12(25%)

Table 3. Peripheral Blood and Bone Marrow Findings in Lymphomas

Haematological Findings	B-CELL				T-CELL		Total N=12
	DLBCL (n=5)	LBL (n=1)	SLL /CLL (n=1)	others (n=2)	LBL (n=1)	ALCL (n=1)	
Anaemia	5	1	2	2	-	1	11 (91.6%)
Leucocytosis	4	1	1	-	1	1	8 (66.6%)
Lymphocytosis	4	1	1	-	-	1	7 (58.3%)
Leucopenia	1	-	-	-	-	-	1 (7.1%)
Thrombocytopenia	1	1	-	1	-	--	3 (21.4%)
Atypical lymphocytes	3	-	1	-	1	1	5 (41.6%)
Peripheral blood involvement	3	1	1	-	-	1	6 (28.6%)

Table 4. Haematological Abnormalities in NHLs with Bone Marrow Involvement (n=12)

DISCUSSION

Lymphomas are commonly encountered haematological malignancies. Zeggaia et al studied 526 Hodgkin lymphoma patients, among whom 51.9% were male and 48.1% were female, with a male to female ratio of 1.1:1 indicating a slight male preponderance. The mean age of the patients in their series was 33.33 years, ranging from 14 to 86 years. Hodgkin lymphoma was common in young adults.⁶ In the present study also, Hodgkin lymphoma showed a male preponderance with an M:F ratio of 2.7:1 and 40% of the HL cases were seen in patients less than 20 years of age. These findings are in consonance with the study by Zeggaia et al.⁶

In various studies on NHL, a slight male predominance was reported with a male to female ratio of 1.4:1 to 1.7:1 to whereas in this present study a slight female preponderance was observed with a male to female ratio of 1: 1.3 which is a contrast.^{7,8} In Lim EJ et al and Jamila et al studies of NHLs mean age was 34.2 years and 42.7 years respectively.^{2,9} In the present study mean age for NHLs was 54.6 years and

majority (58%) of the cases were seen above 50 years of age.

Fever was a frequent presentation in HL (66.6% cases) as compared to NHL (27%). Fever was present in 64.5% cases and loss of weight in 37% cases of Hodgkin lymphoma in a study by Sultan S et al.¹ in the present study splenomegaly was more common in HL (20% case) than NHL (4.1% cases). Hepatomegaly was seen in 10.4% of NHLs and it was not noted in HLs at all. Extranodal presentation was very rare in HL as reported by Sadia S et al.¹ Extranodal presentation was seen in 8.3% of NHLs whereas no extra nodal presentation seen in HL group in this study. In Devi AA et al study on NHL cases hepatomegaly was noted in 44% cases, splenomegaly in 30% cases and extranodal presentation in 43% cases, which was more frequent in comparison to our study. Of the histological subtypes nodular sclerosis was the most common subtype in HL and B-cell lymphomas were common in NHL, which is in concurrence with other studies.¹⁰

Abnormalities in the peripheral blood counts are commonly encountered in NHLs. Anaemia was a common feature in patients with malignant lymphomas or lymphoproliferative disorders. Reported incidence of Anaemia in NHL was approximately 39% in Lim EJ et al study.² Yasmeen T et al in their study reported prevalence of Anaemia in HL patients as 53.2%.¹¹ In the present study Anaemia was seen in 73% of HLs and 77.3% of NHLs which is higher in comparison to the above studies. The cut off values for the above-mentioned studies were lower than that in the present study, which may be the reason for the higher prevalence in present study.

Blood eosinophilia is a common occurrence in Hodgkin lymphoma,¹² in NHL it is predominantly seen in T-cell lymphomas.¹³ In the present study blood eosinophilia was seen in both HL and NHL cases, however it was not present in T NHLs but B NHL which was in contrast to other studies. In Lim et al study marrow eosinophilia was commonly found in B NHL patients without marrow infiltration where as more frequent in TNHL patients with marrow involvement, no such correlation was found in our study.²

In Jeong SY et al and Devi AA et al study, incidence of bone marrow involvement by NHL was 12.5% and 13% respectively which is slightly less in comparison to our study which was 25%. Jeong et al had found that 35.6% of Non-Hodgkin lymphomas with bone marrow involvement also showed peripheral blood involvement in the present study it was 50%.^{10,14}

In Jamila et al study Anaemia, thrombocytopenia and leucopenia were seen in 94%, 31%, and 12% respectively and atypical cells were seen in 64% of NHL cases showing bone marrow infiltration. The findings in our study were comparable to this study. In the same study lymphocytosis was seen in 22% cases, which was less in comparison to our study.⁹ In a Philippine study it was noted that bone marrow infiltration was less frequent in NHL patients with HB >11.5 g/dl and platelet count >10 x 10⁹ /l.¹⁵ Bhatia et al had noted that haemogram of patients of NHLs did not have a

dependable predictive value for bone marrow infiltration.¹⁶ No such correlation could be established in our study.

Reported incidence of bone marrow involvement in Hodgkin lymphoma was about 5 to 27.4%.¹⁷ None of the cases of Hodgkin lymphoma showed bone marrow involvement in this study.

CONCLUSIONS

In this study anaemia alone or in combination with other abnormal blood counts was a common finding in lymphoma patients, more frequently in non-Hodgkin lymphoma showing bone marrow infiltration. Bone marrow involvement was not reported in Hodgkin lymphoma, but seen in 25% NHLs. Lymphocytosis and presence of atypical cells was frequently seen in NHL with marrow infiltration. A thorough examination of a peripheral blood smear will be useful in detecting atypical lymphoid cells in the blood.

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