The Pattern of Bone Marrow Infiltration in Non-Hodgkin's Lymphornas

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Abstract

The pattern of bone marrow infiltration in 40 consecutive cases of non-Hodgkin's lymphomas (NHLs) having marrow involvement is presented. For histological break-up, working formulation of NHLs was used. Low grade NHLs (50%) were the commonest, followed by intermediate (32.5%) and high grade NHLs (17.5%), respectively. Histologically, small lymphocytic type (323%) was the commonest, followed by diffuse small cleaved cell (15%) type; follicle small cleaved cell, diffuse mixed small and large cell as well as lymphoblastic types were equally frequent (12.5% each). Other histological types were less common, The pattern of infiltration of the bone marrow was diffuse in 76,7% of intermediate, 70% of low and 100% of high grade NHLs, It was focal random (non-paratrabecular) in 15% of low grade and 15.4% of intermediate grade NHLs. Focal paratrabecular pattern was evident in 15% of low grade and 7.7% of intermediate grade NHLs (JPMA 45:173, 1995).

Introduction

In Northern Pakistan, lymphomas (Non-Hodgkin's lymphomas and Hodgkin's disease) constitute the commonest malignancies in the adult males and sixth commonest group in the females[1]. In age group < 15 years , lymphomas aiongwith leukemias present as the most common malignant tumours in both sexes[1]. Although, for non- Hodgkin's lymphomas (NHLs) no universally accepted classification exists, however, a working formulation[2] has been adopted in most of the laboratories. In a study at Armed Forces Institute of Pathology (AF[P), Rawalpindi, it was shown that in Pakistan follicular lymphomas are seen less frequently, presumably because most of the patients present for medical advice with a considerable delay[3]. In this study, the commonest type of NHLs belonged to intermediate group (55.56%), followed by low grade (26.46%) and high grade (17.98%) NHLs, respectively. Histologically, diffuse large cell type was the most frequent among the intermediate grade and immunoblastic among the high grade NHLs. In case of NHL, bone marrow infiltration by the tumour indicates stage IV and has a profound effect on prognosis as well response to treatment[4,6]. Therefore, bone marrow biopsy is an important part of diagnostic workup before the treatment is instituted. The present study was aimed at studying the morphological pattern of bone marrow infiltration in patients who were diagnosed to have marrow involvement by NHL.

Materials and Methods

A total of 40 consecutive cases of biopsy-proven NI-IL who were diagnosed to have bone marrow infiltration by lymphomatous tissue were included mthis study. Histological typing was done according to working formulation of NHLs[2]. In eveiy patient, detailed clinical notes were recorded, with special reference to age, sex, duration of symptoms, lymphadenopathy, fever, symptoms related to anaemia, bleeding manifestations, weight loss, night sweats, abdominal masses, hepatosplenomegaly. The following investigations were perfonned on EDTA-blood samples collected after a clean venepuncture: Haemoglobin estimation by cyanmet-haemoglobin method, total leucocyte count and platelet count by

visual methods, using improved neubauer chamber, reticulocyte count after staining with 1% brilliant cresyl blue stain and differential leucocyte count after staining with May- Grunwald-Giemsa stain. Bone marrow aspiration was perfonned at posterior superior iliac spine; however, in children <2 years age, it was performed at upper end of tibia. The marrow smears were stained with May- Grunwald-Giemsa stain. Bone marrow trephine biopsy was performed at posterior supenor iliac spine, using Islam's needle. The biopsy material was fixed in 10% formal-saline, decalcified in 8% nitric acid, dehydrated in ascending grades of alcohol, cleared in xyline and embedded in paraffin wax. Multiple 3-4 micron thick sections were cut, mounted and stained with haemotoxylin and eosin stains. The bone marrow smears and, trephine sections were examined under the microscope for evidence of bone marrow infiltration by NHL, the pattern of infiltration in the trephine sections by NT-IL, especially as regards the diffuse, focal random (non-paratrabecular and focal para-trabecular) distribution of the infiltrate and cytological features of the lymphoma cells, in order to correlate these features with the primary site of NHL.

Results

In this series of 40 cases of NHLs the age ranged from 7 months to 72 years, with a mean±SD of 31.2±21.3 years. Disease was more frequent in males with a male :female ratio of 1.9: 1. The duration of illness ranged from 2 weeks to 7 years, with a mean of 6.3 months. The commonest clinical feature was pallor, followed by superficial lymphadenopathy, fever, splenomegaly, hepatomegaly, abdominal pain, feeling of weakness, abdominal mass, exertional dyspnoea and bleeding manifestations (Table I).

Table I. Clinical features in 40 Cases of NHL.

Clinical features	Percentage
Pallor	87.5
Lymphadenopathy (superficial)	67.5
Fever	62.5
Splenomegaly	47.5
Hepatomegaly	45.0
Pain in abdomen	37.5
Weakness	32.5
Abdominal mass	20.0
Exertional dyspnoea	17.5
Bleeding manifestations	15.0
Epistaxis	12.5
Ecchymoses	7.5
Bleeding P/R	5.0
Melaena	2.5
Haemetemesis	2.5
Haemeturia	2.5
Night sweats	10.0
Anorexia	10.0
Backache	7.5
Weight loss	7.5
Dysphagia	5.0
Testicular swelling	2.5

Table II. Primary sites of NHL.

Sites of NHL	Number of cases	Percentage
Superficial lymph nodes	28	70
Mediastinal lymph nodes	2	5
Abdominal lymph nodes	4	10
GIT	4	10
Testes	1	2.5
Retroperitoneum	1	2.5

Table II shows the primary sites of NHL. In majority of cases (85%), lymphoma was nodal in origin. Amongst extra-nodal lymphomas (15%), the commonest sites was G.I.T The ranges and means±SD values of haemoglobin level', white cell count, platelet count and reticulocyte are shown in Table III.

Table III. Ranges and Means±SD values of haemoglobin levels, white cell counts, platelet counts and reticulocyte counts.

Haematological parameter	Range	Mean±SD
Haemoglobin level (G/dl)	3.5-13.2	8.0±2.6
White cell count ($x10^9$/l)	0.75-15.3	3.63±2.63
Platelet count ($x10^9$/l)	10-390	98.6±53.2
Reticulocyte count (%)	0.2-2.6	0.8±0.40

The histological types of NHL have been elaborated in Table IV.

Table V. Pattern of infiltration in cases of NHL (Percentage in Parenthesis).

Type of NHL	Pattern of Infiltration		
	Focal Random Non-paratrabecular	Diffuse	Focal Paratrabecular
Low grade	3	14	3
20 cases	(15)	(70)	(15)
Intermediate grade	2	10	1
13 cases	(15.4)	(76.7)	(7.7)
High grade	-	7	-
7 cases	-	(100)	-
Total	5	31	4
40 cases	(12.5)	(77.5)	(10)

Low-grade NI-ILs were the commonest, followed by intermediate and high grade NHLs, respectively.

Small lymphocytic was the commonest histological type. Follicle small cleaved cell, diffuse mixed small and large cell and lymphoblastic NHLs were equally frequent.

Table V. Pattern of infiltration in cases of NHL (Percentage in Parenthesis).

Type of NHL	Pattern of Infiltration		
	Focal Random Non-paratrabecular	Diffuse	Focal Paratrabecular
Low grade 20 cases	3 (15)	14 (70)	3 (15)
Intermediate grade 13 cases	2 (15.4)	10 (76.7)	1 (7.7)
High grade 7 cases	- -	7 (100)	- -
Total 40 cases	5 (12.5)	31 (77.5)	4 (10)

Table V shows the pattern of infiltration as seen in the trephine biopsies. In majority of cases (77.5%), the pattern of' infiltration was diffuse, without intervening areas of normal marrow. This pattern was observed invariably in high grade NHLs and was slightly morn frequent in intennediate grade as compared to low grade NHLs. Focal random (Non-trabecular) pattern with intervening areas of preserved marrow was observed in 12.5%cases and was equally represented in low as well as intermediate grade NHLs. This pattern was not observed in high grade NHL cases. Focal paratrabecular pattern was encountered in only 10% cases. None of the high grade NHL cases manifested this pattern. A disparity between cytology at the prunaiy site of NHL and the cytology of marrow infiltrate was observed in six cases (15%). Amongst these patients, three had diffuse mixed small and large cell type, two had lymphoblastic and one had diffuse large cell type of NHL at the primary site. However, in the trephine sections, cytology of small lymphocytic NHL was observed in four and of diffuse small cleaved cell NHL in two cases.

Discussion

Bone marrow trephine biopsy is superior to bone marrow aspiration in determining the bone marrow involvement by non-Hodgkin's lymphoma[6-8]. The, procedure is essential as a pre-treatinent protocol of non-Hodgkin's ly mphomas and the patients found to have marrow infiltration are labelled as having stage IV disease[7]. The pattern of marrow infiltration by NHL can be classified as follows, in order of frequency: well defined focal aggregates, poorly defined focal aggregates with spread to adjacent tissue and diffuse pattern with or without focal aggregates[9,10]. The paratrabecular streaming of cells is regarded as a supportive evidence of infiltration by NHL[7,10] and correlates strongly with follicular lymphoma[11]. Whereas all types of NHL have a prediliction for marrow involvement[12,13] the low grade NHLs, especially small cell type, have a greater tendency of such infiltration, as compared to high grade and intermediate grade NHLs[14].

A search of literature from within the country has shown only one published study regarding marrow infiltration by NHLs[15]. According to this report, inpatients manifesting such infiltration, the lymphoma

tissue in the marrow presented as focal aggregates in 12.5% of low grade NHLs only. Diffuse infiltration was reported in 46.3% and paratra becular distribution in 19.5% of all types of lymphoma. In the present study, low grade NHL was the commonest (50%), followed by intermediate grade (32.5%) and high grade NHLs (17.5%), respectively. The commonest histological type was small lymphocytic NHL (32.5%). This high incidence of small lymphocytic NHL in our cases can be explained on the basis of a previous observation that this type of lymphoma has a greater prediliction for marrow involvement as compared to other histological types[14]. In our series, marrow infiltration was diffuse in 77.5% and focal in 22.5% cases; amongst the latter, focal random (non- paratrabecular) pattern was observed in 12.5% and focal paratrabecular in 10% cases. The percentage of diffuse infiltration in our cases was higher and of focal paratrabecular pattern was lower than the previous local series[15]. However, in both series, the percentage of focal random (non-paratrabecular) aggregates was comparable. A bilateral trephine biopsy should be performed before ruling out infiltration of bone marrow by NHL[7]; it is especially important because focal infiltrates may otherwise be missed, particularly if trephine biopsies am small. An appropriate sized trephine biopsy in this context is important. In four of NHL (3 focal and one diffuse), diagnosis could be established on bilateral trephine biopsy. In all the patients, trephine biopsies were taken by Islam's needle which is believed to make it possible to obtain a long uniform core of marrow containing bone without the marrow architecture being distorted[16]. The commonest pattern of lymphomatous infiltration of bone marrow is of diffuse type, followed by focal random (non-paratrabecular) and focal paratrabecular varieties, respectively. A high percentage of diffuse pattern is probably due to a delay by the patients in presenting for examination. The diffuse pattern is more frequent in high grade lymphomas (100%) as compared to low grade and intermediate lym phomas; in the latter two grades, the diffuse pattern is comparable.

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