Hodgkin's Lymphoma with Special Emphasis on Bone Marrow Involvement: A Six Year Report from King Hussein Medical Center

Raida I. Oudat,[*1] *William J. Haddadin* [2]

Abstract

Objective: To determine the frequency and the histopatholgic type of Hodgkin's Lymphoma (HL) in newly diagnosed patients and to determine the frequency of Bone Marrow (BM) involvement by the disease at King Hussein Medical Center (KHMC) over 6 years.

Methods: A total of 150 HL patients were diagnosed at the department of pathology KHMC and classified according to the WHO classification of hematological malignancies between January 2001 and December 2006. All cases were reviewed histologically. The available BM Trephine Biopsy (TB) and BM Aspirate Smears (AS) for 98 patients were also reviewed and analyzed.

Results: Patients ranged in age from 3 to 64 years with a mean of 31.1. They were 80 males and 70 females. Of the 150 HL patients, nodular sclerosis variant was the commonest subtype 36%, followed by mixed cellularity HL 25.3%, the lymphocytic rich classic subtype 5.3%, and the lymphocytic depleted subtype 2.7%. There were 36 cases of classic HL which could not be further subtyped. For the 98 patients who had available BMTB and BMAS from unilateral site, 12 patients (12.2%) had positive BM involvement which was picked by BMTB. All the corresponding BMAS were negative. Lymphocytic depleted HL showed the highest percentage of BM involvement 50%, followed by mixed cellularity 37.5%.

Conclusion: Nodular sclerosis HL is found to be the most common type of disease at our hospital. BMTB is a simple tool for the assessment of the disease spread and is superior to BMAS in detecting BM involvement. The need for bilateral BMTB is emphasized particularly in highly suspicious cases.

Keywords: Hodgkin's lymphoma, Bone marrow trephine biopsy, Bone marrow aspirate.

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Introduction

Hodgkin Lymphoma (HL) may involve the Bone Marrow (BM) with a reported incidence ranging from 2% to 23% of cases. [1-4] This incidence includes untreated as well as previously treated HL patients. This wide range in incidence is explained, in part, by patient selection. In untreated patients who undergo Bone Marrow Trephine Biopsy (BMTB) as part

1. **Hematopathologist, Princess Iman Research and Laboratory Sciences Center, King Hussein Medical Center, Amman, Jordan.**
2. **Histopathologist, Princess Iman Research and Laboratory Sciences Center, King Hussein Medical Center, Amman, Jordan.**

**** Correspondence should be addressed to:***
Raida I Oudat, MD.
King Hussein Medical Center.
Hematopathology Department, Amman, 11855, Jordan.
E- mail: droudat@hotmail.com

of the staging work up, a number of clinical and pathologic findings correlate with BM involvement. These findings include advanced stage nodal disease, systemic symptoms, peripheral blood cytopenia, tumor bulk, and histologic type of HL. [1-5] Patients with BM involvement are reported to have short survival times, increased sensitivity to the myelosupressive effects of chemotherapy and early relapse. [6]

In this study, we examined the frequency and the histopathologic type of HL in 150 newly diagnosed patients and we determined the frequency of BM involvement by disease in 98 patients at King Hussein Medical Center (KHMC) over six years.

Methods

One hundred fifty newly diagnosed HL patients were selected from the computer records of the pathology department at Princess Iman Research and Laboratory Science Center KHMC, during the period from January 2001 to December 2006. The incidence of BM involvement by the disease was assessed in 98 patients who had available BMTB and BMAS from unilateral site only. BMTB and BMAS were identified from the records of the pathology department and reviewed. All BMAS were stained with Wright - Giemsa stain, and at least 3 smears were reexamined. All tissue sections from paraffin embedded lymph nodes and decalcified BM specimens were re-examined by standard hematoxylin and eosin stain. A panel of immunohistochemical markers using the streptavidin biotin peroxidase method was applied on lymph nodes tissue section and on selected BMTB sections when needed to confirm the diagnosis. The panel included antibodies against Leukocyte Common Antigen (LCA; CD45), the T-cell antigen CD3, the B-cell antigen CD20 (L26) and Hodgkin's markers CD15 (Leu-M1) and CD30 (BerH2).

Diagnosis of HL was made by lymph node biopsy. BM involvement was diagnosed when typical Reed-Sternberg (RS) cells or mononuclear variants were found in a cellular background characteristic of HL. [7]

Results

Of the 150 untreated HL patients, 80 (53.3%) were males and 70 (46.7) were females with age ranging from 3 to 64 years and a mean of 31.1. Nodular sclerosis variant was the most common subtype (54 cases, 36%); of thoser, 40 cases were of grade 1 and 14 were of grade 2 subvariants. Mixed cellularity HL was the second most frequent (38 cases, 25.3%), followed by the lymphocytic predominant subtype (10 cases, 6.7%), the lymphocytic rich classic subtype (8 cases, 5.3%) and the lymphocytic depleted subtype (4 cases, 2.7%). There were 36 cases, 24% of the classic HL which could not be further subtyped due to the small nature of the specimens. Of the 150 patients, 98 had available BMTB and BMAS from unilateral site only. Among these patients, 10 cases (10.2%) were lymphocytic predominant HL, 8 (8.1%) were lympocytic rich classic HL, 16 (16.3%) were mixed cellularity, 30 (30.6%) were nodular sclerosis, and 4 (4%) were lymphocytic depleted HL. The remaining 30 cases (30.6%) were classic HL not otherwise specified (Table 1).

BM involvement as evidenced on BMTB was seen in 12 patients of the 98 (12.2%). None of the corresponding BMAS was positive for involvement. 6 of the 16 (37.5%) mixed cellularity cases, 2 of the 4 (50%) lymphocytic depleted patients and 4 of the 30 (13.3%) classic HL not otherwise specified (Table 1).

Immunohistochemical studies done on tissue sections showed RS cells to be positive for CD15 and CD30 (with a paranuclear and membranous pattern of staining). RS cells were negative for CD3, CD20, and LCA; CD45. These results supported the diagnosis of HL.

Table (1): Distribution of 150 patients with HL according to WHO classification.

HL Type	*No of cases*	*Mean age (± 1 S.D)*	*Gender (M/F)*	*No. of available BMTB & BMAS*	*%Marrow Involved*
Mixed cellularity	*38*	*31.3(17.5)*	*24/14*	*16*	*37.5*
Nodular sclerosis grade 1	*40*	*27.9(14.5)*	*14/26*	*18*	*0*
grade 2	*14*	*33.1(20.7)*	*8/6*	*12*	*0*
Lymphocytic predominant	*10*	*22.6(4.7)*	*6/4*	*10*	*0*
Lymphocytic rich classic	*8*	*31.3(20.5)*	*6/2*	*8*	*0*
Lymphocytic depleted	*4*	*49 (15.6)*	*2/2*	*4*	*50*
Classic HL (NOS)	*36*	*34.2(17.7)*	*20/16*	*30*	*13.3*
Total	*150*	*31.1(16.6)*	*80/70*	*98*	*12.2*

Discussion

The results of our study showed that nodular sclerosis variant was found to be the most common subtype of HL followed by the mixed cellularity variant. This result is similar to the result of the study carried out on malignant lymphoma in Jordan. [8] However, it differs from another study carried out in Jordan [9] in which mixed cellularity was slightly more common than nodular sclerosis variant. These differences might be explained by geographical differences as our study represents patients from all regions of the country in contrast to their study which selected patients form one region in the North of Jordan.

The results of this study are similar to results from other countries in the region such as Kuwait, [10] UAE, [11] and Saudi Arabia. [12, 13] No important difference was found in the percentage of various subtypes of HL in the west. [14, 15]

In our study, 12 (12.2%) patients showed BM involvement by the disease. Previous studies report an incidence of HL involving BM in a range between 5% to 20% in untreated patients undergoing BMTB as part of routine staging. [2- 5, 16, 17]

It is well-known that histopathologic type of HL correlated with BM involvement. In our study, we found that lymphocytic depleted HL showed the highest incidence of BM involvement followed by mixed cellularity with similar results from the literature. [3, 5, 18]

Biopsy is more sensitive than aspiration in the assessment of BM in patients with HL. All the 12 positive BM involvement patients showed positive BMTB but negative BMAS. Others have reported similar results. [1, 19] The most likely explanation for the discrepancy between aspiration and biopsy is that fibrosis associated with HL in BM precludes aspiration of the neoplastic RS cells.

Nowadays, immunohistochemical studies are applied routinely to all cases of HL to allow direct assessment of RS cells and to differentiate HL from other lymphomas that could involve BM. [20] In our study, we applied immunohistochemical studies using a special panel of antibodies mentioned previously which supported the diagnosis of HL.

In our study, all the BMTB were done from unilateral site only. Previous studies have shown a higher rate of detection of HL in BM with bilateral biopsies. Moreover, the diagnosis of disease in BM could be missed in 2-17% of cases by using unilateral biopsy only. [21, 22]

In conclusion, mixed cellularity HL is found to be the most common type of disease at our hospital. BMTB is a simple tool for the assessment of disease spread and is superior to BMA in detecting BM infiltration. The need for bilateral BMTB in the staging work up of patients with disease is emphasized particularly, in highly suspicious cases.

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هوتشكن ليمفوما في الأردن ومدى شمول نخاع العظم بها

رائده العودات، وليم حدادين
قسم الأنسجة، مدينة الحسين الطبية، عمان، الأردن

الملخص

الهدف: تهدف هذه الدراسة إلى تحديد نسبة هوتشكن ليمفوما ومعرفة النوع النسيجي لها، وتحديد نسبة شمول نخاع العظم بالمرض عند حالات هوتشكن ليمفوما مشخصة حديثا في مدينة الحسين الطبية خلال 6 سنوات.

الطرق: تم جمع ومراجعة 150 حالة هوتشكن ليمفوما شخصت في قسم الأمراض في مدينة الحسين الطبية وصنفت حسب تصنيف منظمة الصحة العالمية للأورام الدموية في الفترة ما بين شهري 2001/1 و 12 /2006م.

وقد تمت مراجعة وتحليل عينات خزعة وسائل نخاع العظم عند 98 حالة لمعرفة نسبة شمول نخاع العظم بالمرض.

النتائج: تراوحت أعمار المرضى ما بين 3 و 64 سنة وبمتوسط 31,1 سنة، وكان عدد الذكور80 وعدد الاناث 70. وقد تبين أن النوع المتصلب العقدي لهوتشكن ليمفوما شكّل الغالبية العظمى من 150 حالة معالجة بنسبة 36% تلاه نوع مختلط الخلايا بنسبة 25% ثم نوع هوتشكن الكلاسيكي غني الخلايا الليمفاوية بنسبة 5,3%، واخيراً هوتشكن نادر الخلايا الليمفاوية بنسبة 2,7%.

لم يتم تصنيف 36 حالة من حالات هوتشكن الكلاسيكي المتبقية لصغر حجم العينة. وقد تبين شمول نخاع العظم بالمرض عند 12 حالة (12,2%) من 98 حالة ممن توفرت لديهم عينات خزعة وسائل نخاع العظم. وقد أظهر نوع هوتشكن ليمفوما نادر الخلايا الليمفاوية أعلى نسبة شمول لنخاع العظم بنسبة 50% من الحالات، تلاه نوع مختلط الخلايا بنسبة 37,5%.

خاتمة: شكل النوع المتصلب العقدي لهوتشكن ليمفوما الغالبية العظمى للحالات المشخصة في مستشفانا. تعتبر خزعة نخاع العظم من الوسائل البسيطة لمعرفة وتقييم مدى انتشار المرض وهي في ذلك تعلو في اهميتها اهمية سائل نخاع العظم.

ويجب التركيزعلى ضرورة الحاجة لأخذ عينة خزعة نخاع العظم من جهتين، وخاصةً عند الحالات الأكثر عرضة لشمول نخاع العظم بالمرض.

الكلمات الدالة: هوتشكن ليمفوما، نخاع العظم، الأردن، الخلايا الليمفاوية.