CLINICAL STUDY OF MALIGNANT LYMPHOMAS IN DUHOK: A CASE SERIES STUDY DURING 2007-2013

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ABSTRACT

Background and Objectives Earlier studies have addressed the pathological classification of malignant lymphomas in Duhok, while no studies have addressed the clinical aspects and outcome of treatment.

Aim to identify clinical features, diagnostic procedures, standard treatment and outcome of malignant lymphomas in Duhok

Material and Methods This is a case series study of 108 initially untreated patients with malignant lymphoma who were followed during the period 2007 to 2013.

Results The 108 enrolled patients included 61 patients with Non-Hodgkin's Lymphoma (NHL) and 47 with Hodgkin's Lymphoma (HL).The median age of patients with NHL was 52 (48.4±22.5) years while that of patients with HL was 29 (34.4±16.4) years. The principal clinical presentation was cervical lymphadenopathy; 38% in NHL and 70% in HL. B-symptoms were present in 20% of NHL patients and 32% of HL patients. The staging of patients with NHL showed that they were mostly in stages III and IV, while patients with HL were mostly in stage II. Bone marrow involvement was found in 35% of patients with NHL and in 3% of patients with HL. The standard treatment for NHL was protocol R-CHOP, given every 21 days; each patient received an average of 8 cycles. For HL, the standard treatment was the ABVD protocol given in an average of 6 cycles. Of all the patients with NHL, eight had relapse and were put on second line therapy (ICE protocol) while four died from infections. Of the patients with HL, two had relapsed and one died from infection.

Conclusion The NHL in the studied patients was characterized by a severe course and multiorgan involvement, and stage III and IV were the main presenting stages at diagnosis. The high rates of marrow involvement, extranodal involvement and advanced clinical stages in NHL as compared to HL, which are shared by previous studies worldwide, explain its less favourable outcomes as shown by the current study.

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Keywords: Malignant lymphomas, clinical aspects, Duhok

Malignant lymphomas are tumors of the immune system which represent a heterogeneous group of tumors with clinical courses ranging from very aggressive and rapidly fatal tumors to an indolent, well tolerated malignancies of man.[1-3]

Malignant lymphoma can arise in any site. Organs with large concentration of lymphatic tissue for example lymph nodes, tonsils, spleen or bone marrow are principally involved.[4] Monoclonal antibodies to cell surface antigens permit the identification of B or T lymphocyte proliferation.[5]

Malignant lymphoma is the third most common reported malignancy in Iraq, but there are few published Iraqi studies on the subject. [6-9]

The main two components of malignant lymphomas are the Hodgkin Lymphoma (HL) and the Non-Hodgkin's lymphoma (NHL).

HL is a neoplasm of the lymphoid tissue that primarily affects the lymph nodes. The disease is localized initially to

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a single peripheral lymph node region and the mode of progression is by contiguity within the lymphatic system.[10] The characteristic giant cell, the Reed Sternberg cell (RS) in the appropriate cytological framework is required for the diagnosis of HL.11 HL can be classified histologically into classical HL and nodular lymphocyte predominant HL .

NHL is the single largest group of tumors of the immune system, characteristized by monoclonal expansion of malignant B or T cell. Non-Hodgkin's lymphoma may originate in any organ and shows disparate histological features, clinical behavior and prognosis.[11]

The etiology of NHL remains unclear; however, there is evidence that some infectious agents like Epstein Barr and Human Immune deficiency viruses and Helicobacter pylori, are involved in the pathogenesis of some NHL.[5, 11-13]

NHL forms about 5.9% of all cancers in Iraq and has the fourth place (6.3%) among the commonest ten cancer in males and the third place (5.4%) among the commonest ten cancer in females.[14]

The aim of this study is to identify the characteristic clinical features, diagnostic procedures, standard treatment and outcome of malignant lymphomas in Duhok governorate for the period 2007-2013.

METHODS

This case series study included 108 initially untreated patients with malignant lymphomas who were attending the Hematology-oncology Department at Azadi Teaching Hospital in Duhok, which provides services for Duhok governorate. They were evaluated retrospectively and prospectively using hospital records, over the period from 2007 to 2013.

The following data were recorded for the studied patients:

History: Included the age, sex, occupation, residence, date of presentation, history of other medical problems, family history of previous hematological malignancies and/or immunodeficiency, history of exposure to chemicals or pesticides, history of celiac disease, presenting symptoms and presence of "B-symptoms" which are unexplained fever of more than 38.5o C, weight loss of more than 10% of body weight in the last 6 months and drenching night sweating.

Physical Examination: Full clinical examination was carried out.

Investigations: Hematological tests including full blood counts and morphology, and erythrocyte sedimentation rate (ESR), were done for all patients. Bone marrow aspirate and/or biopsy were done for some patients. Imaging investigations included chest X-ray, Computed tomography scan, Magnetic resonance imaging Ultrasound examination and PET scan whenever this was appropriate. The histopathological methods used to reach the histological diagnosis were pathological biopsy, fine needle aspiration, cytology, appropriate endoscopic techniques or through major surgical operation.

Clinical Staging: Staging was done for the patients according to Ann -Arbor classification for HL and NHL, as shown below:

Ann-Arbor Staging

Stage 1	Involvement of a single lymph node region or single extra lymphatic site.
Stage 11	Involvement of two or more lymph node regions on the same side of diaphragm. Localized contiguous involvement of only one extra lymphatic site and lymph node region(stage 11E).
Stage 111	Involvement of lymph node region or structures on both sides of the diaphragm.
Stage 1V	Disseminated involvement of one or more extralymphatic organs with or without lymph node involvement.

A= If there are no B – symptoms, B= If there are B - symptoms

The standard treatment used in this study for NHL and HL is summarized below:

NHL = CHOP±R		HL =ABVD	
C	Cyclophosphamide	A	Doxorubicin Hydroxide
H	Doxorubicin Hydroxide	B	Bleomycin
O	Oncovin (Vincristine)	V	Vinblastine
P	Prednisolone	D	Dacarbazine
R	Rituximab		

RESULTS

This is a case series study of 108 patients with malignant lymphoma. It included 61 NHL patients with a median age of 52 (48.4±22.5) years and 47 HL patients with a median age of 29 (34.4±16.4) years (age range 13-75 years) as shown in figure 1.

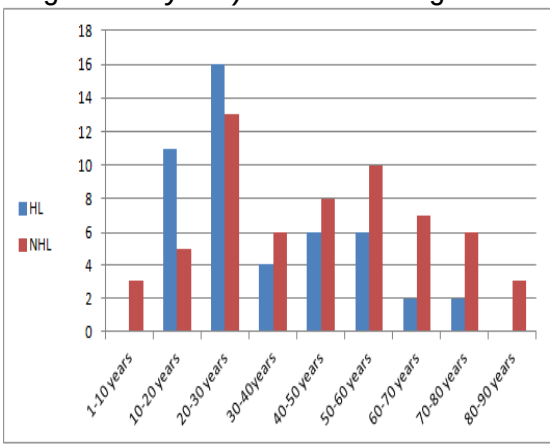

Figure 1. age distribution of enrolled Hodgkin's and non-Hodgkin's lymphoma patients

Table 1 demonstrates that cervical lymphadenopathy was encountered in 23 patients (38%) with NHL, while abdominal pain and distention were present in seven (11%) of them; features of intestinal obstruction was present in another three (5%). B-symptoms were present among 12 patients (20%) with NHL. Cervical lymphadenopathy was encountered in 33 patients (70%) with HL, while abdominal pain and distention were present in two (4%), none had features of intestinal obstruction. B-symptoms were present among 15 patients (32%) with HL.

The diagnostic procedures used for the studied patients are shown in Table 2. A positive pathological finding was obtained from lymph node biopsy in 30 patients (49%) and from laperotomy in 20 patients (33%), and the result of endoscopy was positive in three (5%) patients with NHL. On the other hand, HL patients had a positive pathological finding from lymph nodes in 43 of them (91%) and from laparotomy with splenectomy in two of them (4%).

The staging of patients with NHL is shown in Table 3.Twenty-nine patients (48%) had stage IV at diagnosis, while only three patients (5%) had stage I A, which was the least frequent. Table 4 shows the staging of patients with HL. Only two patients (4%) had stage IV at diagnosis, while 31 patients (66%) had stage II, which was the highest group.

Table 1: Clinical presentation of patients with NHL and HD

Clinical Presentation	NHL (N=61)		HD (N=47)	
	No.	%	No.	%
Cervical lymphadenopathy	23	38	33	70
Axillary lymphadenopathy	11	18	5	11
Inguinal lymphadenopathy	5	8	2	4
Tonsil	1	2	0	0
Abdominal pain and distention	7	11	2	4
Abdominal mass	5	8	2	4
Intestinal obstruction	3	5	0	0
Superior vena cava obstruction	2	3	0	0
Dyspnea	4	7	3	6
B-symptoms	12	20	15	32
Fever	10	16	8	17
Weight loss	7	11	5	11
Sweating	4	6	2	4
Bone marrow involvement	21	35	1	3

Table 2. Diagnostic procedures used in the studied patients

Diagnostic Procedures	NHL (N=61)		HL (N=47)	
	No.	%	No.	%
Lymph node biopsy	30	49	43	91
Fine needle aspiration	3	5	0	0
Laparotomy	20	33	0	0
Laparotomy with splenectomy	1	1.6	2	4
Endoscopy	3	5	0	0
Bronchoscopy	1	1.6	0	0
Tonsillectomy	1	1.6	0	0
Pleural biopsy	1	1.6	0	0
Thoracotomy	1	1.6	1	2
Lung biopsy	0	0	1	2

Table 3. Staging of 61 patients with NHL

Stage	IA	IB	IIA	IIB	IIIA	IIIB	IVA	IVB
No.	3	-	12	2	12	3	25	4
Total	3		14		15		29	
%	5		23		25		48	

Table 4. Staging of 47 patients with HL

Stage	IA	IB	IIA	IIB	IIIA	IIIB	IVA	IVB
No.	0	0	24	7	7	7	0	2
Total	0		31		14		2	
%	0		66		30		4	

DISCUSSION

This study shows that the age distribution of both HL and NHL patients had a peak in the third decades of life, and patients with NHL had a second peak in the six decades which is attributed to patients with low grade NHL. NHL was more frequent in the current series as compared to HL (1.3:1) and these findings are to some extent consistent with other studies,[14,15] though it is lower than previously reported from Iraq and from the USA where the ratios was 3:1 and 5:1 respectively[9,16]

The clinical presentation in NHL patients involved various systems, which reflects its multicentric nature like cervical lymphadenopathy, abdominal pain and distention and intestinal obstruction. Bone marrow involvement amongst patients with NHL was high on initial presentation and forms up to 35% (compared to 3% in HL). This finding also affirms the aggressiveness and the severity of illness in the studied group and these results are consistent with other studies in the Middle East.[6, 9, 17,18]

Owing to the fact that HL is a nodal disease, therefore the value of surgical biopsy in HL is evident (91%) in this study compared to its use in NHL (51%), where by the illness is multicentric and might require a variety of ways to confirm the diagnosis. Fine needle aspiration for the diagnosis of patients with malignant lymphoma contributed to 5%, which reflects its low use and unreliability as a sole diagnostic tool.

The staging of the patients with NHL showed that 48% had stage IV A and B, and only 5% had stage I A, which was the least. Such findings support the aggressive and severe nature of NHL, as well as its multicentric involvement in the studied group. This result was supported by a previous study in Iraq.[6-9]

The standard treatment for NHL was protocol R-CHOP, which is given every 21 days; each patient received eight cycles. For HL, the standard treatment was the ABVD protocol, which given six cycles (dose at day 1 and day 14, means one cycle).[19]

Of all the patients with NHL, eight had relapse and were put on second line therapy, (ICE protocol): ifosfamide 5 g/m2 on day 2 plus carboplatin AUC 5 plus etoposide 100 mg/ m2 daily on days 1-3; every 14 days, while four died from infections. Of the patients with HL,

two had relapsed and one died from infection after one year from the diagnosis.

The NHL in the studied patients was characterized by a severe course and multiorgan involvement.and stage III and IV were the main presenting stages at diagnosis. The high rates of marrow involvement, extranodal involvement and advanced clinical stages in NHL as compared to HL, which are shared by previous studies worldwide, explain its less favorable outcomes as shown by the current study.

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پوختە

ڤەکولینەکا کلینیکی لدور پەنجەشێرا گریکێن لمفی ل دهوك: شروڤەکرنا زنجیرەکا حالەتا ژ ٢٠٠٧–٢٠١٣

پێشەکی وئارمانج: ڤەکولینێن هاتینە ئەنجامدان لدور رێکێن دابەشکرنا جورێن پەنجەشێرا لمفی، لێ هیچ ڤەکولین نینن لدور نیشانێن نەخوشیێ و هەروەسا ئەنجامێن چارەسەریێ.

ئەنجامێن ڤەکولینێ: دەستنیشانکرنا نیشانێن نەخوشیێ و رێکێن دیارکرنا نەخوشیێ چارەسەری و ئەنجامێن چارەسەریێ، بو نەخوشیا پەنجەشیرا گرێکێن لمفی ل دهوکێ.

النتائج: ژ سەرجەمێ (١٠٨) نەخوشا (٦١) کەس توشبوین جورێ نەنهوجکن لمفوما (NHL) بون، و (٤٧) کەس توشبوین جوری هوجکن لمفوما (HL) بون. ناڤنجی ژی یی وان نەخوشێن توشی نەنهوجکن لمفوما بوین (٣٥) سال بون ، بەلێ ئەوێن توشی هوجکن لمفوما بوین (٣٠) سال بون. جورێ هەرێ بەربەلاڤی شانێن نەنهوجکن لمفوما پلەیا ناڤنجی بو وجورێ هەرە بەربەلاڤ خانێن مەزن و بەلاڤبوی بون ، بەلێ بو هوجکن لمفوما خانێن تێکەل بون

رێکێن ڤەکولینێ: ئەڤ ڤەکولینە هاتە ئەنجامدان ل سەر زنجیرەکا نەخوشێن توشبوی ب نەخوشیا پەنجەشێرا گرێکێن لمفی، و ژمارا وان

ئەنجام: (١٠٨) نەخوش بون ،ل دەستپێکێ بەری بێنە چارەسەرکرن . ل دیف چونا وان هاتە کرن دماوێ دناڤ بەرا سالێن (٢٠٠٧–٢٠١٣). نیشانێن سەرەکی وەرمینا گرێکێن لمفی یێن ستوی ب رێژا ٣٠٪ بو نەنهوجکن و٧٠٪ بو هوجکن بون. ونیشانێن B (B symptom) هە بین بـ٢٠٪ بونەخوشێن نەنهوجکن و ٣٢٪ بونەخوشێن هوجکن . پتریا نەخوشێن نەنهوجکن دقوناغا (٣) و (٤) دا بون ، بهەلێ نەخوشێن هوجکن پتریا وان دقوناغا (٢)دا بون . بەلاڤبونا نەخوشی یێ دناڤ مەژی یی هەستیدا ل دەف نەخوشێن نەنهوجکن لمفوما ٣٢٪ بو، و ل دەف نەخوشێن هوجکن لمفوما ب رێژا ٣٪ بو . چارەسەریا سەرەکی بو نەنهوجکن لمفوما (R-chop) هەر ٢١ روژا ئیك قورچ و سەرجەمێ قورچا دبنە (٨) قورچ . بەلێ بو نەخوشێن هوجکن لمفوما چارەسەریا سەرەکی (ABVD) دەست پێدکەت، و(٦) خول هاتنە پێدان هەرخولەك ژ (٢) قورچا پێك دهات ، قورچەك ل روژا ئێکێ و قورژەك ل روژا (١٤) یێ . دئەنجامدا (٨) نەخوشان نەنهوجکن لمفوما نەخوشیا وان دووبارا زڤری و دچارەسەریا دووێ هاتنە پێدان، بەلێ (٤) نەخوشا گیانێ خو ژدەستدا ژ ئەگەرێ هەودانێن ڤەگر .

هەروەسا نەخوشیا (٢) نەهخوشێن هوجکن لمفوما دوبارە زڤری و نەخوشەکی گیانێ خو ژدەستدا .

دەرئەنجام: نەخوشێن ژجورێ نەنهوشکن لیمفوما نەخوشیا وان یا دژوار و گەلەك ئەندامێن لەشی ڤەگرتبوون، و پرانیا وان ل قوناغێن سێ و چار بوون یێن نەخوشیێ. رێژا زێدە یا ڤەگرتنا مەژیێ هەستیکی و ئەندامێن دەرڤەی گرێکێن لمفی و دژواریا نەخوشیێ ل جورێ نەنهوشکن بەراوردی دگەل جورێ هوشکن دیاردکەت کو دەر ئەنجامێن وی دخرابن، و ئەڤە یا دیارە دڤەکولینێن دیدا.

الخلاصة

دراسة سريرية للمفوما الخبيثة في دهوك: دراسة حالات متتالية للفترة من ٢٠٠٧ - ٢٠١٣

خلفية وأهداف الدراسة: أجريت دراسات سابقة حول تقسيم أنواع اللمفوما الخبيثة في دهوك ولكن لا توجد دراسات حول الأعراض السريرية ونتائج العلاج. تهدف الدراسة إلى تحديد الأعراض السريرية وطرق التشخيص والعلاج ونتائجه للمفوما الخبيثة في دهوك.

طرق البحث: هذه الدراسة اجريت على سلسلة من الحالات المرضية المصابة بسرطان الغدد اللمفاوية وعددهم ١٠٨ حالة من البداية قبل العلاج، تم متابعتهم خلال فترة ٢٠٠٧-٢٠١٣.

النتائج: أظهرت دراسة (١٠٨) حالة من اللمفوما الخبيثة وجود ٦١ حاله كانوا مصابين بـ(ننهوجكن لمفوما) (NHL) و٤٧ حالة مصابين بهوجكن لمفوما (HL) . معدل العمر لننهوجكن لمفوما هو ٣٥ سنة ولكن لمرضى هوجكن لمفوما هو ٣٠ سنة. النوع الاكثر شائع النسيجي لننهوجكن لمفوما هو الدرجة الوسطية والأكثر شائع هو الخلايا الكبيرة المنتشرة ولكن لهوجكن لمفوما هو الخلايا المختلطة . الاعراض الرئيسية هو تضخم العقد اللمفاوية العنقية بنسبة ٣٨% لننهوجكن و٧٠%لهوجكن لمفوما. الاعراض (B-SYMPTOM) موجودة بنسبة ٢٠% لمرضى ننهوجكن و٣٢% لمرضى هوجكن لمفوما. مراحل مرضى ننهوجكن لمفوما على الاكثركانوا في المرحلة الثالثة والرابعة ولكن مرضى هوجكن لمفوما على الاكثر في المرحلة الثانية. انتشار المرض في النخاع العظمي لمرضى ننهوجكن لمفوما ٣٢ % ولكن لمرضى هوجكن كان بنسبة ٣%. العلاج الرئيسي لمرض ننهوجكن لمفوما بدأت (R-CHOP)، كل ٢١ يوما جرعة وعددالجرعات الكلية ٨ جرعة. ولكن لمرضى هوجكن لمفوما العلاج الاساسي بدأت (ABVD) وأعطيت ٦ دورات وكل دورة جرعتان، جرعة في اليوم الاول وجرعة في اليوم الرابع عشر. كانت النتيجة ٨ مرضى ننهوجكن، المرض عاد واعطيت علاج ثاني ولكن ٤ مرضى توفى نتيجة الالتهابات المعدية. أما مرضى هوجكن , عاد المرض في حالتين، واحد المرضى منهم توفي نتيجة الالتهابات.

الاستنتاجات: إن مرضى الـ(ننهوجكن ليمفوما) كانوا يعانون من شدة المرض ومن إصابة عدة أعضاء وكانت لدرجة الثالثة والرابعة أكثر الدرجات شيوعاً لدى التشخيص. إن النسبة العالية لإصابة نخاع العظم وإصابات خارج الغدد والأعراض السريرية الشديدة في مرضى الـ(ننهوجكن) مقارنة بمرضى الهوجكن كانت السبب في النتائج غير الواعدة وكما ظهر في دراسات مشابهة أخرى.