Evaluation of Patients with Lymphadenopathy in Hematology Unit in Baghdad Teaching Hospital

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ABSTRACT:

BACKGROUND:

Lymphadenopathy is defined as abnormality in the size or character of lymph nodes, is caused by the invasion or propagation of either inflammatory cells or neoplastic cells into the nodes.

OBJECTIVE:

To determine the etiological and clinical characteristics of Lymphadenopathy in adults.

PATIENTS AND METHODS:

Sixty patients with Lymphadenopathy attended Hematology department/Baghdad Teaching Hospital for the period between December 2011 and April 2012. Diagnostic procedures included clinical history and examination, complete blood count, lymph node, bone marrow studies and immunohistochemistry studies.

RESULTS:

Thirty six male and 24 female patients were included, with mean age of 36.2 ±16.3 years. Malignant causes were found in 55(92%), mainly lymphomas 40(66.7%), while benign causes constituted only 8 %(5 patients). Size, consistency and systemic symptoms were important parameters in differentiation between both, and immunohistochemistry was important in reaching a diagnosis in one patient and in solving the discrepancy between lymph node and bone marrow results in other patient.

CONCLUSION:

Lymph node and bone marrow examination, in addition to immunohistochemistry were important investigation to reach a diagnosis in patients with Lymphadenopathy. High malignant etiology is attributed to being the study done in tertiary hospital.

KEY WORDS: lymphadenopathy, immunohistochemistry, baghdad teaching hospital.

INTRODUCTION:

Lymphadenopathy (LAP) is a common problem in clinical practice; the causes are variable from trivial benign causes that need no treatment to serious malignant invariably fatal causes that require rapid treatment [(1)].

Lymphadenopathy can be primary or secondary to wide range of disorders including infections with any type of organisms, immunological disorders, malignant diseases whether hematological or metastatic solid tumors, and other numerous less common diseases such as lipid storage diseases, and histeocytosis [(2-4)], some drugs such as sulfonamides, penicillin, allopurinol, isoniazid, and phenytoin are also known to cause LAP [(3,4)].

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One study in adult population showed that they have 0.6% annual incidence of LAP, 10% of these are referred to a specialist ,lymph node(LN) biopsy is performed for only 3.2 % of these, and in biopsied patients, malignancy was found as a cause in 3.2% of them [(5)].

There are a lot of factors that may predict malignant diagnosis, and thus indicate biopsy, among these factors are: age > 40 Year [(6)], size > 1cm, [(7-10)], long/short axis ratio < 2 [(11)] and hard consistency [(12)]. Other factors are also associated with higher risk of malignancy but to a lesser extend such as male gender, family history of malignant disease [(13,14)].The duration of LAP of < 2 weeks, or > 1year is highly suggestive of benign causes [(15)].Presence of generalized pruritus, with fever may suggest Hodgkin disease, or NHL, and makes biopsy mandatory [(15)].

Fine-needle aspiration (FNA) biopsy is a quick, cost-effective, and safe diagnostic modality that provides answers to guide treatment and management in patients with LAP. But although FNA may be useful in the differentiation of benign and malignant LAP, inability of the diagnosis is often encountered in specific diagnosis of malignant diseases. In addition, an excision biopsy is needed for the diagnosis of lymphoma. Excision biopsy is a diagnostic procedure that can be applied safely with minimal morbidity and mortality [16].

Immunohistochemistry (IHC) brought about a diagnostic and prognostic revolution in the evaluation of primary neoplasm of the hematopoietic system. The classification and identification of lymphomas was positively impacted, and it is added as a method to daily diagnostic routine, which is presently a mandatory item in pathology reports [17].

PATIENTS AND METHODS:

This study is a cohort one, included 60 patients attended hematological clinic in Baghdad teaching hospital with LAP, whether biopsied or not. It was conducted from December 2011 to April 2012.

Full history was obtained from all patients, including age, gender, residency, the duration of LAP, systemic symptoms (loss of >10Kg of the body weight during 6 months, drenching sweating and fever).

Complete physical examination was performed for all patients, with special concentration on site of LAP, number and size of LN at presentation, LN characteristics, and drained area.

Lymph node and/or bone marrow (BM) biopsy were studied for all patients.

Immunohistochemistry using DAKO kits (Denmark made) was performed in some cases for sub typing of lymphomas, and to assess its compatibility with the results of LN and BM biopsy.

RESULTS:

Sixty patients with LAP (36 male, and 24 female) were studied, mean of age was 36.2 ± 16.3 years. According to LN and/or BM biopsy, malignant cause of LAP was found in 55(92%) of all patients (table 1, and 2), including 34(95%) out of 36 male patients, and 21(88%) out of 26 females.

Out of 30 patients ≤30 years old, a malignant diagnosis was made in 26(87%), compared to 15 out of 16 patients (94%) in patients 31-50 years old, and all of the 14 (100%) patients >50 years old (tab. 1).

A malignant diagnosis was made in all 36 (100%) of patients with one or more of systemic symptoms, compared to 19 (95%) out of 24 of those without these symptoms. (Table 1)

Regarding the size of lymph nodes, a benign cause was found in 5(84%) out of six patients whose largest LN ≤2cm in size, compared to none of the 54 patients whose largest LN is >2 cm. the frequency of specific diagnosis of malignant disease in relation to size of the largest LN is shown table 2.

Painful LN were benign in 2 (40%) out of 5 patients, compared to 3(5%) out of 55 patients with painless LAP. None of patients had hard LAP, only 5 patients had soft LAP, 4(80%) of them were benign, compared to 55 patients with rubbery LAP only one (2%) of whom was benign. (Table 2)

Table 1 : Causes of LAP in relation to gender, age, and presence of B symptoms .

Patients characteristics	HL No.(%)	NHL No.(%)	AML No.(%)	ALL No.(%)	CLL No. (%)	Benign No. (%)	Total No.
Male	8 (22)	14 (39)	4 (11)	6 (17)	2 (6)	2 (6)	36 (100)
Female	6 (25)	12 (50)	1 (4)	1 (4)	1 (4)	3 (13)	24 (100)
Age<30 years	9 (30)	8 (27)	3 (30)	6 (20)	0 (0)	4 (13)	30 (100)
Age 30-50	5 (31)	8 (50)	1 (6)	1 (6)	0 (0)	1 (6)	16 (100)
Age > 50	0 (0)	10 (71)	1 (7)	0 (0)	3(21)	0 (0)	14 (100)
No B symptoms	6 (25)	8 (33)	1(4)	4 (16)	0 (0)	5 (21)	24 (100)
With B symptom	8 (22)	18 (50)	4 (11)	3 (8)	3 (8)	0 (0)	36 (100)
total	14 (23)	26 (43)	5 (8)	7 (12)	3 (5)	5 (8)	60 (100)

Table 2: Causes of LAP in relation to LN characteristics.

LN characteristics	HL No. (%)	NHL No. (%)	AML No.(%)	ALL No. (%)	CLL No. (%)	Benign No. (%)	Total No.(%)
size≤2cm	0 (0)	0 (0)	0 (0)	1 (17)	0 (0)	5 (83)	6 (100)
Size 2-10 cm	11 (22)	25 (51)	5 (10)	5 (10)	3 (6)	(0)	49 (100)
Size ≥10 cm	3 (60)	1 (20)	0 (0)	1 (20)	0 (0)	0 (0)	5 (100)
Painless LAP	13 (24)	26 (47)	5 (9)	5 (9)	3 (5)	3 (5)	55 (100)
Painful LAP	1 (20)	0 (0)	0 (0)	2 (40)	0 (0)	2 (40)	5 (100)
Constancy rubbery	14 (25)	26 (47)	5 (9)	6 (11)	3 (5)	1 (2)	55 (100)
Constancy soft	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	4 (80)	5 (100)
Constancy hard	0 (NA)	0 (NA)	0 (NA)	0 (NA)	0 (NA)	0 (NA)	0 (100)
total	14 (23)	26 (43)	5 (8)	7(12)	3 (5)	5 (8)	60 (100)

Lymph node biopsy was performed for 45 patients, in 25 patients of them BM aspiration and biopsy was also performed for staging or confirming the diagnosis. In other 15 patients BM examination without LN biopsy was studied (Table 3). In those 25 patients whose LN biopsy as well as BM was studied, the diagnoses were compatible with each other except for only one patient (4%) (Pat. No. 18 in tab. 4) whose LN biopsy supported by IHC changed the diagnosis from NHL low-intermediate grade made by BM biopsy into NHL diffuse, large B-cell high grade lymphoma. (Table 3).

Immunohistochemistry was performed in 25 patients, in 12 patients of them (48%) some details had been got from IHC but no influence had been achieved on management, on the other hand in 6 patients (24%) IHC added details to the diagnosis and gave idea about prognosis without influencing treatment, and in other 5 patients (20%) IHC dramatically influenced the management by aiding in selecting chemotherapy protocol through determining more specific diagnosis of the disease and hence predict responsiveness to molecular targeted therapy. In one patient (4%) (Pat. No. 7 in tab. 4) the diagnosis obtained with LN biopsy had been changed according to IHC, and in another patient (pat, No. 18 in tab 4) IHC helped in solving the discrepancy between results of LN, and BM examination (tab 4).

Table 3: Results of LN, and BM biopsies in LAP.

Source of biopsy	HL No.	NHL No.	AML No.	ALL No.	CLL No.	Begin No.	Total No.
Lymph node only	11	4	0	0	0	5	20
Bone marrow only	0	1	4	7	3	0	15
Both	3	21	1	0	0	0	25
Total	14	26	5	7	3	5	60

Tab le 4:The results of LN, and BM biopsies, and IHC study in 25 patients :- (Dx: diagnosis, HG; High grade, In.G. intermediate grade, LG: Low grade).

No.	Result of LN biopsy	Result of BM biopsy	IHC	Influence of IHC
1	NHL, H.G.	NHL	CD 20 (-)	None
2	NHL, plasmablastic lymphoma	NHL- leukemic phase	CD180(+) CD 20,3,10,30,15 (-)	None
3	AML	AML-M3	Mpo (++), CD15(+) CD 20,3,34,117,TdT (-)	None
4	NHL, small cell- L.G.	NHL	CD 20 (+), CD 3,5,23 (-)	prognosis
5	NHL, In.G.-H.G.	NHL, H.G.	CD 20 (+)	None
6	NHL, H.G.	NHL, H.G.	CD 20 (+)	prognosis
7	NHL, L.G.	No involvement	CD 30 (+), CD 15 (-)*	Changed Dx.
8	NHL, H.G.	T-cell lymphoma	CD 3,TDT (+), CD20 (-)	None
9	HL, Nodular sclerosis	No involvement	CD 45, 15 (+)	none
10	NHL, lymphoblastic lymphoma	NHL	CD30,15,3,8,TdT (+), CD 20,4,79a (-)	prognosis
11	NHL, large cell	NHL, H.G.	CD 45,20 (+), CD3(-)	None
12	NHL, large cell In.G.	NHL, In.G.	CD 45,20 (+),	Select Protocol
13	NHL, Diffuse Large B-cell	NHL, H.G.	CD 20,10(+), CD 3,5,bcl 6(-)	Select protocol
14	NHL	NHL, inG, T-cell	CD 20 (-)	Select protocol
15	NHL	NHL,H.G,T-cell	CD3 (+), CD20,10,34,117,TdT (-)	None
16	NHL	NHL, In.G.	CD 20 (+)	prognosis
17	NHL, L.G.	NHL, L.G.	CD 20 (+)	Select protocol
18	NHL diffuse, Large B-cell, H.G.	NHL, L.G-In.G.	CD 20,5 (+), CD3,10,23,cyclin (+)*	Determine Dx
19	HL, mixed cellularity	Not Involved	CD 30,15 (+), CD20,3(-)	Prognosis
20	NHL, LG., B-cell	Not Involved	CD 20 (+),	None
21	NHL, Diffuse, Large B-cell	Not Involved	CD45,20 (+),CD3,CK,EMA (-)	None
22	NHL, Diffuse, Large B-cell	Not Involved	CD20 (+),CD3,10,5,30,bcl 6(-)	None
23	HL, Mixed cellularity	Not Involved	CD3,5,8 (+), CD20,79(-)	None
24	NHL, High grade	Not Involved	CD20,19 (+), CD3 (-)	Prognosis
25	HL, Mixed cellularity	Not Involved	CD 45,20 (+), CD15,TdT (-)	Select protocol

*These results show the importance of performing IHC study for these patients

DISCUSSION:

In our study, 60 patients referred to hematological clinic in Baghdad teaching hospital with LAP were evaluated.

Malignant diagnosis were made in 92% of the studied patients, and benign diagnosis were made to the remaining 8%, these results showed a markedly higher incidence of malignancy compared to results of a study performed by Fijtin GH, in family practice, who showed that malignant causes were found in only 1.1% of the biopsied patients[18]. This difference is attributable to the difference of the population studied since our study included referred cases to a specialized center of hematology.

Concerning age groups our study showed that benign diseases were the cause of LAP in 13% in patients under 30 years, 6.3% in those 30-50, and 0% in older than 50 years, compared to 79%,59%, and 40% respectively obtained by Lee et al who analyzed LN biopsy results done at Los Angeles country Hospital from 1973-1977 [19]. These differences are caused by inclusion of patients managed in general clinical work in Lee's study and not only in a specialized center of hematology like ours.

We found that malignant diagnosis were more frequent in males compared to female (95% Vs 88%), this is comparable to results of a study performed by Chau I. et al on 550 in Great Britain which found a relative risk factor for male gender of 2.72 [20].

Regarding LN size (length of largest LN), our study showed benign cause in 83% of patients whose LN size $\leq$ 2cm, and none in those > 2Cm

size, compared to a study performed by Pangalis who found a benign cause in all LAP <1 cm, and in 92% in those 1- 1.5 cm, and in 62% in those with > 1.5cm diameter[13].

Because of difficulty in availability, we studied IHC in only 46% of patients, it confirmed the diagnosis in (92%), and made no influence on management of (44%) of patients,

but it did determine chemotherapy protocol selection in 20%, and determined prognosis in other 24%, IHC also changed diagnosis in one (4%) patient, and determined diagnosis in another one (4%) by solving the discrepancy between LN., and BM, biopsies. these findings show the importance of IHC study in management of LAP.

CONCLUSIONS AND RECOMMENDATIONS:

1. Both LN biopsy and BM biopsy may be required for proper diagnosis and management of LAP.
2. Immunohistochemistry is important tool for management of LAP.
3. The above tools are increasingly indicated with larger size of LAP because of increasing risk of malignancy
4. Male gender also increases risk of malignancy.

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