

HISTOPATHOLOGIC FINDINGS OF LYMPH NODE BIOPSY CASES IN COMPARISON WITH CLINICAL FEATURES

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ABSTRACT

Objective: To determine useful and important clinical signs and symptoms for evaluation of lymphadenopathy with consideration of histopathologic findings of biopsy.

Methodology: This retrospective case-series study was done on patients hospital folders who came with lymphadenopathy, Informations was collected about clinical signs, symptoms, age, gender and histopathologic findings. It was then analyzed by SPSS version 13 with chi-square test.

Results: There were 208 specimens, 98 women (47.1%) and 110 men (52.9%). Mean age was 32.94 years. There were 45 cases (21.6%) of malignancy, 33 cases (15.9%) of infectious diseases and 130 cases (62.5%) of reactive lymphadenopathy. The most common histopathologic finding in all ages was reactive lymphadenopathy. Clinical signs and symptoms had significant relationship with pathologic findings.

Conclusion: For a decision of lymph node biopsy attention to patients symptoms and signs especially B signs, size of the lymph node >2cm, generalized lymphadenopathy, mobility of lymph node and splenomegaly seems to be the useful guide lines for physician. In this study it seems that decision to take biopsy was correct in 75% of the cases.

KEY WORDS: Lymphadenopathy, Biopsy, Malignancy.

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INTRODUCTION

Lymphadenopathy is defined as abnormal size or structure of lymph node. It is a common problem in all age groups. It is mostly caused by benign disorders and shows transient responses to the local or general infections but sometimes it is due to malignant disorders.¹ We usually consider age, location of lymphadenopathy, duration of disease, being local or generalized, other signs and symptoms like fever and splenomegaly. According to the location of lymphadenopathy we can make some differential diagnosis for example, cervical lymphadenopathy is usually due to pharyngitis, otitis, dental abscess, measles, rubella, infectious mononucleosis, CMV and other viral infections,

Kikuchi disease, lymphomas and metastatic carcinoma from pharynx.^{2,3}

In supraclavicular lymphadenopathy we should think about gastrointestinal cancers. Inguinal lymphadenopathy may indicate STDs (sexually transmitted diseases) and cancers of genitalia or anal canal. Abdominal lymphadenopathy is mostly due to malignancy and sometimes tuberculosis. There are many etiologies for generalized lymphadenopathy. Some of them are: ALL, CLL, Hodgkin's lymphoma, non Hodgkin's lymphoma, infectious mononucleosis, CMV, AIDS, toxoplasmosis, tuberculosis, rheumatoid arthritis, lupus and sarcoidosis.² Lymphadenopathy in children and young adults is usually due to benign and reactive etiologies; in contrast, in ages older than 50, prevalence of malignant etiologies increase.^{3,5} In referral centers such as hematology wards, prevalence of malignant lymphadenopathy in biopsy specimens is about 40%.⁶ Generally in primary health care we can say that patients older than 40 years with lymphadenopathy without obvious causes have the chance of malignancy about 4% and in patients under age 40 years this chance is about 0.4%.⁷

In review studies done on patients with lymphadenopathy there was 17.5% malignant etiology including, 11.4% lymphoproliferative disorders and 6.1% metastasis, 31% had reactive benign etiologies and 26% had other non malignant diseases.^{8,9}

In a study done by Nilgun Yaris et al. in 2006 on 126 lymphadenopathy cases, 98 patients had lymphadenopathy out of which 52% were local and 48% were generalized. The most common area was neck. Seventy five patients had benign etiologies, 60% of patients had reactive lymphadenopathy and 39% had lymphadenitis and lymphadenitis in comparison with lymphadenopathy was more local and had a larger size >3 cm. Twenty three patients had malignancy and were older than other patients and enlargement of supraclavicular nodes was mostly due to malignancy. The risk of malignancy was higher in patients with generalized lymphadenopathy, lymph node larger than 3cm, hepatosplenomegaly and high serum level

of LDH. This study determined important clinical clues that can be useful in differential diagnosis of lymphadenopathy.¹

In a study done by Memon W, Samad A et al. in Pakistan from year 2002 to 2006 on 498 patients with cervical lymphadenopathy, 40 patient (8%) had Hodgkin's lymphoma, 80% of them were men and 20% were women. Most of the patients were in stage 2 or 3 of disease. Patients clinical feature such as "B" symptoms, anorexia and location of lymphadenopathy was determined. Finally researchers showed that prevalence of Hodgkin's lymphoma in cervical lymphadenopathy in their country is less than western countries.¹⁰

Study done by Burns B, et al. in 1985 on 69 patients with lymphadenopathy the most common pattern of lymphadenopathy was reactive follicular hyperplasia (62%), 8 patients had Hodgkin's lymphoma and two patients had non Hodgkin's lymphoma.¹¹ Al Maghrabi J et al. study done in 2005 on 2500 lymph node biopsy specimens, they found 15 cases with Kikuchi-Fujimoto disease (0.6%), with F/M ratio = 2.7/1, mean age was 29 years and most common location was cervical area.¹²

In yet another study made by Moor SW et al. in 2003 on 1877 cervical lymphadenopathy in cases younger than 15 years, 1.5% were normal, 48.7% had non specific reactive hyperplasia, 36.3% had chronic granulomatous changes, tuberculosis lymphadenitis was seen in 25%. 2/3 of 154 patients with neoplastic lymphadenopathy had lymphoma. In 32 cases pyogenic organisms were found and 5 cases were HIV positive. This study showed that an important cause of cervical lymphadenopathy in developing countries is tuberculosis and other infections.¹³

Another study done by Freidig EE et al. in 1986 on 419 lymph node biopsy specimens, in 113 cases the cause of lymphadenopathy was unknown, 92 cases had sarcoidosis, 86 cases had lymphoma, 17 cases were metastatic cancer, histoplasmosis was seen in 18 cases and tuberculosis in 13 cases. From 66 cases of infectious lymphadenopathy 48 cases had granulomatous or acute inflammatory lesions.¹⁴

Thus, physicians should consider level of referral and conditions of patient and epidemiologic background of that area for better approach to lymphadenopathy. Indications of lymph node biopsy is not so clear and it depends on physician opinion and it should be performed considering all patient conditions, clinical features and epidemiologic information about different causes of lymphadenopathy. On the other hand, these type of studies are rare in our country and we need more statistical informations about prevalence of reactive, infectious and malignant causes of lymphadenopathy and relationship between these causes and clinical signs and symptoms of patients, so that we can make more reliable decisions about patients with lymphadenopathy.

METHODOLOGY

This descriptive case-series study was done on patients hospitalized in Yazd Shahid Sadoughi hospital from 21 March 2006 to 22 July 2008 and lymph node biopsy was performed for them. We had 208 cases and their age ranged from 1 to 83 years. Those patients who were known cases of cancers and were hospitalized for relapse of cancer and those cases with insufficient information were excluded. Questionnaires were filled from reports of pathology ward and patients hospital folders. These information included age, gender, date of hospitalization, signs, symptoms and histopathology results of biopsy.

Table-I: Frequency distribution of pathologic findings by age groups

Pathologic findings	Age Groups		Total No.(%)
	<40 year No.(%)	>40 year No.(%)	
Reactive	92(64.8)	38(57.6)	130(62.5)
Infectious	25(17.6)	8(12.1)	33(15.9)
Malignant	25(17.6)	20(30.3)	45(21.6)
Total	142(100)	66(100)	208(100)

P. value = 0.10

Clinical signs and symptoms included in our study were: cough, fever, night sweat, weight loss, pain and tenderness of lymph node, anatomic site of lymphadenopathy, being localized or generalized, size of lymphadenopathy, consistency, mobility of lymph node and presence of splenomegaly. Finally information were analyzed by SPSS program (version13) and Chi-square test. We consider the significant P. value < 0.05 was considered significant.

RESULTS

We had 208 cases with age range 82 (from 1 to 83 years) and mean age was 32.94 years with SD 19.08 years. There were 98 (47.1%) female and 110 (52.9%) male. One hundred thirty (62.5%) cases were reactive lymphadenopathy, 33 (15.9%) cases were infectious and 45 (21.6%) cases had malignancy. We had one case of angioimmunoblastic lymphadenopathy, three cases of Castleman disease, four cases of Kikuchi-Fujimoto disease and 25 cases of granulomatous lymphadenopathy. We divided the cases into two age groups: <15 years and >15 years. We divided them into two age groups: <40 years and >40 years. The most common pathologic finding in all ages was reactive lymphadenopathy, but in ages older than 40 years malignancy was in second place. Pathologic findings had no significant statistic relationship with age groups (P.value=0.051) (Table-I). There was no significant relationship between gender and pathologic findings (Table-II). The most frequent malignant lymphadenopathy

Table-II: Frequency distribution of pathologic findings by gender

Pathologic findings	Gender		Total No.(%)
	Male No. (%)	Female No. (%)	
Reactive	66(60)	64(65.3)	130(62.5)
Infectious	17(15.5)	16(16.3)	33(15.9)
Malignant	27(24.5)	18(18.4)	45(21.6)
Total	110(100)	98(100)	208(100)

P. value = 0.55

Table-III: Frequency distribution of positive clinical signs and symptoms by pathologic findings

ClinicalFeatures	Pathologic Finding			Total No.(%)	P. value
	ReactiveNo.(%)	InfectiousNo.(%)	MalignantNo.(%)		
Cough	9 (6.9)	9 (27.3)	14 (31.3)	32 (15.4)	<0.001
Fever	17 (13.1)	29 (87.9)	16 (35.6)	62 (29.8)	<0.001
NightSweat	5 (3.8)	5 (15.2)	18 (40)	28 (13.5)	<0.001
WeightLoss	29 (22.3)	16 (48.5)	35 (77.8)	80 (38.5)	<0.001
Lymph nodePain	19 (14.6)	12 (36.4)	0 (0)	31 (14.9)	<0.001
Generalized Lymphadenopathy	7 (5.4)	1 (3)	9 (20)	17 (8.2)	<0.001
Size > 2cm	57 (43.8)	20 (60.6)	36 (80)	113 (54.3)	<0.001
Immobility of lymph node	2 (1.5)	0 (0)	8 (17.8)	10 (4.8)	<0.001
Lymph nodeTenderness	42 (32.3)	18 (54.5)	0 (0)	60 (28.8)	<0.001
Splenomegaly	2 (1.5)	1 (3)	6 (13.3)	9 (4.3)	=0.001

was Hodgkin's lymphoma (44.4%) and the least was metastasis (22.2%).

Frequency distribution of clinical signs and symptoms had significant relationship with pathologic findings. For example, fever, night sweat and weight loss were seen mostly in malignancy and some infections and none of malignant nodes had pain or tenderness. Size larger than 2cm and generalized lymphadenopathy and splenomegaly was more common in malignancy. (Table-III) The most common location of lymphadenopathy was neck area and in this location we had the most malignant cases. Axillary area was in second place after neck and in third place was inguinal area (Table-IV).

There was no significant relationship between pathologic findings and consistency of lymphadenopathy. (p.value = 0.08) most of

lymphadenopathies were firm and most of malignant nodes were also firm.

DISCUSSION

In this study we determined frequency distribution of histopathologic findings of lymph node biopsies and relationship between these findings and clinical signs and symptoms. There were 130 (62.5%) cases of reactive lymphadenopathy, 33 (15.9%) cases of infectious lymphadenopathy and 45 (21.6%) of malignant lymphadenopathy, including 20 cases (9.6%) of Hodgkin's lymphoma, 15 cases(7.2%) of non Hodgkin's lymphoma and 10 cases (4.8%) of metastasis.

According to these results, frequency distribution of pathologic findings had no significant relationship with patients age, may be because

Table-IV: Frequency distribution of of lymphadenopathy locations by pathologic findings

Locations	Pathologic Finding			Total No.(%)
	ReactiveNo.(%)	InfectiousNo.(%)	MalignantNo.(%)	
Cervical	68 (52.3)	20 (60.6)	25 (55.6)	113 (54.3)
Axillary	33 (25.4)	10 (30.3)	10 (22.3)	53 (25.5)
Inguinal	13 (10)	1 (3)	6 (13.3)	20 (9.6)
Abdominal	13 (10)	0 (0)	3 (6.7)	16 (7.7)
Other	3 (2.3)	2 (6.1)	1 (2.2)	6 (2.9)
Total	130 (100)	33 (100)	45 (100)	208 (100)

of few malignant cases in our study, although we used two different ways for dividing age groups. Similarly in the study by Memon W et al. there was no relationship between pathologic findings and age.¹⁰

In other studies ages older than 40 was one risk factor for malignancy.¹⁻³ We also found no relationship between pathologic findings and gender as reported, by Yaris N et al. In some studies this factor was not included in criterions.¹

We found significant relationship between cough and pathologic findings. Cough was seen mostly in infections and malignancies. In similar studies we couldn't find any result about this factor effect.

About "B" symptoms including fever, night sweat and weight loss, most of patients with malignancy had "B" symptoms that is significantly higher than benign groups (P.value < 0.001). Thus our findings here are like all other studies that introduce "B" symptoms as useful and important factor in approach to lymphadenopathy.^{2,3,6}

In our study there was significant relationship between pathologic findings and pain or tenderness of lymph node; none of the malignant cases had pain or tenderness and we can say that presence of pain or tenderness can predict infectious or less common reactive causes. However sometimes because of fast enlargement of malignant lymph node or hemorrhage in it's necrotic center we may see pain or tenderness.^{2,3}

There was significant relationship between pathologic findings and generalized lymphadenopathy. From total 17 cases of generalized lymphadenopathy 9 cases (53%) had malignancy and this is similar to other studies.^{1,2,8} In many studies and text books we can see that generalized lymphadenopathy is almost always due to important systemic diseases.^{3,6}

We couldn't find any significant relationship between location of lymphadenopathy and pathologic findings because statistically the results did not show it. Fifty five percent of all cases were cervical lymphadenopathy. Also in Nilgun et al. study there was no significant

relationship between location of lymphadenopathy and pathologic findings.¹ On the other hand, many sources have revealed that lymphadenopathy in some places like supraclavicular and abdominal has more risk of malignancy.^{2,3,6}

In our study as well as according to some after studies there is no clinically distinct difference between firm, elastic and hard consistency and many young physicians can not distinguish between them. We collect all of these three types of consistency as 'firm'. There was no significant relationship between consistency of lymph node and pathologic findings. Many studies confirm that we can not approach to patient only by consistency of lymphadenopathy.^{2,6} and consistency of lymph node can not predict whether lymphadenopathy is benign or malignant. There was significant relationship between pathologic findings and size of lymphadenopathy. Most of malignant (80%) and infectious (60%) nodes had diameter larger than 2cm and most of reactive nodes were smaller than 2cm. In some studies, researchers used two diameters of lymph node (area) and they said that significant size of lymph node is 2.25cm² or more.^{2,3} It seems that using two diameters of lymph node is more reliable.

There was significant relationship between pathologic findings and mobility of lymph nodes. Most of those lymph nodes that were not mobile, were malignant. But many studies have showed that we can not trust on mobility of lymphadenopathy to determine whether it is benign or malignant. On the other hand, fixed lymph nodes that have adhesion to surrounding tissues may be due to metastatic cancers and lymph nodes involving in lymphomas are usually mobile.^{3,8}

In our study there was significant relationship between splenomegaly and pathologic findings; among nine cases of splenomegaly, six cases had malignancy. We can say splenomegaly with lymphadenopathy almost always show systemic and important diseases (mostly malignancies and some infections like infectious mononucleosis) and these results are confirmed by many other studies.^{2,6,8}

CONCLUSIONS

According to our study, for evaluation of lymphadenopathy we should consider important signs and symptoms like "B" symptoms, size >2cm, generalized lymphadenopathy, fixed lymph node and splenomegaly. In our study, from 208 cases, 52cases had no signs like fever, night sweat, weight loss, splenomegaly and generalized lymphadenopathy and size of their lymphadenopathy was equal or smaller than 2cm. Thus we can say that 75% of our cases really needed surgical biopsy.

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