Original Article

Histomorphological patterns of lesions in lymph node biopsies

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Abstract

Introduction: Lymph node biopsies are routinely performed for the evaluation of lymphadenopathies. Tuberculosis and other infections are the major causes of lymphadenopathy in developing countries. The pattern of lymph node enlargement is different for different age groups. Malignancies are common in adults as compared to children.

Objective: To find out the frequency of diseases causing lymphadenopathy along with the demographics of the population under study, and to correlate site and size of lymphadenopathy with the histopathological diagnosis.

Materials and Methods: A total of 163 patients whose lymph nodes biopsies were performed from January 2015 to June 2018 were included in the study. All demographic and laboratory data were recorded on a proforma and analyzed using SPSS version 22.

Results: A total of 163 biopsies were studied with ages ranging from 03 to 96 years. Female patients were 57.05% and male patients 42.94%. In the studied cases, 74.84% were found to be non-neoplastic, 13.5% neoplastic while 11.65% of cases biopsies were either unremarkable or non-lymphoid tissue was biopsied. Reactive hyperplasia was the commonest lesion accounting for 50.3% of cases, followed by tuberculosis (23.3%), metastatic carcinoma (6.2%), lymphoproliferative disorders (1.84%), Hodgkin's lymphoma (3%), non-Hodgkin's lymphoma (2.45%) and non-caseating granulomatous lymphadenitis (1.22%) respectively. Lymph node size was found to be greater than 2cm in only 25.7% of cases.

Conclusion: Reactive hyperplasia and tuberculosis are the most common diagnosis in lymph node biopsies. Lymph node biopsy is a diagnostic and reliable histologic investigation to differentiate non-neoplastic lesions from neoplastic lesions, and further classify the disease based on microscopic findings in both cases.

Keywords: Lymphadenopathy, Reactive Hyperplasia, Tuberculous Lymphadenitis, Neoplasia.

Introduction

Lymph nodes are discrete ovoid lymphoid structures present throughout the body. They drain lymph from different parts of the body and become involved in many pathological conditions. Lymphadenopathy refers to an abnormal change in size, shape, or consistency of lymph nodes. The causes may be broadly divided into neoplastic and non-neoplastic. Non-neoplastic causes include infections, drug reactions, lipid storage disorders, and non-specific inflammatory conditions.[1]

Clinically, lymphadenopathy may be peripheral or visceral. Peripheral lymphadenopathies are easily detected by general physical examination and are often biopsied as they are easily accessible for lymphadenectomy. However, visceral lymphadenopathy requires laparotomy or imaging assistance.[2] Among the peripheral nodes, those in the upper part of the body (cervical, supraclavicular, axillary) are preferentially biopsied than lower limb nodes (popliteal, inguinal, or femoral), as the former are more likely to yield definitive diagnosis whereas the latter is often characterized by non-specific reactive or chronic inflammatory and fibrotic changes.[1,2]

Lymph node biopsies are routinely performed for the evaluation of lymphadenopathies. Tuberculosis and other infections are a major cause of lymphadenopathy in developing countries especially in regions where HIV is common, whereas in developed countries; non-specific reactive hyperplasia predominates.[3]

The pattern of lymph node enlargement is also different for different age groups. Malignancies are more common in adults as compared to children. Reactive hyperplasia to minor stimuli is a significant cause of lymphadenopathy in children.[1,4] Generally in primary health care, patients older than 40 years with lymphadenopathy, without any obvious cause, have chances of malignancy about 4% and in patients under 40 years of age, this chance is about 0.4%.[5]

Considering numerous causes of lymphadenopathy, it has become essential to define diseases presenting with lymph node enlargement. The intent of this study is the etiological evaluation of lymphadenopathy, in relation to age and gender of patients and pattern of lymph node distribution in biopsy samples.

Materials and Methods

This descriptive, cross-sectional study was conducted to study different causes of lymphadenopathy in our setup, and to correlate site and size of lymphadenopathy with the histopathological diagnosis. A total of 163 patients who underwent lymph node biopsies were included in this hospital-based, non-interventional study. The specimens obtained were processed for histopathological examination. All the lymph node biopsy specimens received from January 2015 till June 2018 were included. Specimens with incomplete records were excluded from the study.

A pre-designed proforma was used to record all the demographic and laboratory data including age, gender, site of biopsy, size of largest lymph node biopsied, and a clinical diagnosis made based on morphology and cut section appearance.

Results

A total of 163 biopsies were studied with an age range of 03 to 96 years. Majority of cases were age group of 10-19 years. Age-wise distribution of lymphadenopathy is given in Table-I.

Table-I Age-wise distribution of lymphadenopathy

Age group (years)	Number (n)	Percentage (%)
<10	18	11.04
10-19	44	27.00
20-29	35	21.47
30-39	25	15.33
40-49	11	6.74
50-59	11	6.74
≥60	19	11.65
Total	163	100

Out of 163 cases, female patients were 93 (57.05%) and male patients were 70 (42.94%). The male to female ratio was 1:1.32. (Table-II)

Table-II Gender wise distribution of lymphadeno-pathy

Gender	Number (n)	Percentage (%)	Ratio (male: female)
Male	70	42.94	
Female	93	57.05	1:1.32
Total	163	100	

To check the relationship between gender and lymph node lesions we applied Chi-square test. We tested the hypothesis "There is no association among female gender and lymph node lesion" against the alternative "There is association among female gender and thyroid lesion" at 0.05 level of significance. The results were $X2=163$, $df=1$, p-value=0.000. As the p-value <0.05, we rejected our null hypothesis of no association between female gender and lymph node lesion.

In this study, all lesions were divided into two groups: neoplastic or non-neoplastic. Neoplastic lesions were 22 accounting for 13.50% of all the lesions. The majority of these lesions were in the age group ≥ 60years. Most common among neoplastic lesions were metastatic lesions followed by Hodgkin lymphoma, non-Hodgkin lymphoma, and unclassified lymphoproliferative disorders respectively. Age-wise distribution of neoplastic disorders is given in Table-III.

Table- III Age-wise distribution of neoplastic disorders (n=22)

Age group (years)	Hodgkin's lymphoma (n)	Non-Hodgkin's lymphoma (n)	Metastatic Lesions (n)	Unclassified lymphoproliferative disorders (n)
<10	-	-	-	-
10-19	1	-	-	1
20-29	-	-	-	-
30-39	-	-	-	-
40-49	-	2	3	-
50-59	3	1	1	-
≥60	1	1	6	2

Non-neoplastic lesions were 122 accounting for 74.84% of all the lesions. The peak age group was 10-19 years. The most common non-neoplastic lesion was reactive hyperplastic lymphadenopathies followed by tuberculous granulomatous lesions and other granulomatous lesions respectively.

Table-IV Age-wise distribution of non-neoplastic lesions(n=122)

Age group (years)	Reactive hyperplasia (n)	Tuberculous granulomatous lesions (n)	Other Granulomatous lesions (n)
<10	14	2	-
10-19	23	12	-
20-29	15	14	2
30-39	13	9	-
40-49	4	1	-
50-59	4	-	-
≥60	7	2	-

In 19 cases (11.65%), biopsies were either unremarkable or non-lymphoid tissue was biopsied. The most frequently biopsied lymph node group was abdominal lymph nodes followed by cervical, inguinal, and axillary lymph nodes respectively. In 30 cases, sites other than these were biopsied. Diagnostic yield for each lymph node group was calculated by the given formula:
Diagnostic yield = (number of biopsies with specific histopathological findings ÷ total number of biopsies) × 100
The abdominal lymph node group gave the highest diagnostic yield while the group giving the lowest diagnostic yield was the axillary lymph node group.

Table-V Diagnostic yield of different lymph node groups(n=163)

Site of biopsy	Total biopsies(n)	Unremarkable biopsies(n)	Diagnostic yield (%)
Cervical	50	6	88
Axillary	8	2	75
Inguinal	15	2	86.6
Abdominal	60	6	90
Other sites	30	3	90

Table-VI Site of lymphadenopathy in relation to neoplastic and non-neoplastic lesions

Site of biopsy	Non-neoplastic lesions(n)			Neoplastic lesions(n)			
	Reactive	Tuberculosis	Non-caseous granuloma	HL	NHL	Metastatic lesions	Unclassified lympho-Proliferative disorders
Cervical	19	13	-	4	3	4	1
Axillary	4	1	-	-	-	1	-
Inguinal	8	2	-	1	-	1	1
Abdominal	35	14	1	-	-	4	-
Other sites	16	8	1	-	1	-	1

HL: Hodgkin's lymphoma; NHL: Non-Hodgkin's lymphoma

The size of lymphadenopathy was greater than 2cm in 42 cases (25.77%). Out of 22 neoplastic lesions, 12 lesions were greater than 2cm accounting for 54.5% of cases. While in non-neoplastic lesions only 30 lesions were greater than 2cm out of 122 accounting for 24.5% of cases.

Table-VII Size of lymphadenopathy in relation to neoplastic and non-neoplastic lesions

Size of Lymphaden opathy (cm)	Non-neoplastic lesions (n)	Neoplastic lesions (n)	P-value
≥2	30	12	
<2	92	10	0.004
Total	122	22	

Statistical comparison was made between size of lymphadenopathy among neoplastic and non-neoplastic lesions using Chi-square test which revealed significant relationship between size of lymphadenopathy and type of lesion.

The most common histopathological diagnosis in this study was reactive hyperplasia (50.3%) followed by tuberculous granulomatous lesions (23.3%), metastatic lesions (6.1%), Hodgkin's lymphoma (3%), non-Hodgkin's lymphoma (2.4%), unclassified lymphoproliferative disorders (1.8%) and other granulomatous lesions (1.2%) respectively. 19 biopsies (11.6%) were unremarkable.

Table-VIII Incidence of diseases causing lymphadeno-pathy

Histopathological diagnosis	N (%)
Reactive hyperplasia	82 (50.3%)
Tuberculous granulomatous lymphadenopathy	38 (23.3%)
Other granulomatous lesions	2 (1.22%)
Hodgkin's lymphoma	5 (3%)
Non-Hodgkin's lymphoma	4 (2.45%)
Metastatic lesions	10 (6.13%)
Unclassified lymphoproliferative disorders	3 (1.84%)
Unremarkable	19 (11.65%)

Discussion

In this study, we determined the incidence of different diseases causing lymphadenopathy. There were 82 cases (50.3%) of reactive hyperplasia, 40 cases (24.5%) of granulomatous lymphadenopathy, and 22 cases (13.42%) of malignant lymphadenopathy while 19 cases (11.65%) yielded unremarkable results.

In our study, cases of malignant lymphadenopathy were clustered in age groups >40 years. Only 2 cases out of 22 occurred before 40 years of age. However, in a study conducted by Zahir ST et al[6], there was no significant relationship between pathologic findings and age, which may be attributed to fewer malignant cases included in this study.

In our study, there were 93 females and 70 males. Male to female ratio was found to be 1:1.32. In other studies, by Roy et al[7] and Maula et al[8], the male-dominant ratio of 1.7:1 and 1.2:1 was seen respectively. In our study, lymphadenopathy due to non-neoplastic lesions was seen in 122 (74.84%) cases whereas; due to malignant involvement was seen in 22 (13.50%) cases. Similarly, in studies conducted by Kasturi et al[9] and Abdul Ghafoor et al[10], benign lesions were found to be more common than malignant lesions.

Neoplastic lesions were found to be more common in the study by Roy et al[7] conducted in India, may be because the study was conducted in a setting that works as a referral center where specialized diagnostic techniques are used for malignancy detection.

In our study, the most common benign lesion causing lymphadenopathy was reactive hyperplasia (50.3%) followed by granulomatous lymphadenopathy (24.5%). Similarly, in a study by Zahir ST et al[6],

lymphadenopathy due to reactive hyperplasia (62.5%) was found to be more common than due to infectious etiology (15.9%). Reactive hyperplasia was also more common in studies conducted by Moore et al[5] and Vachhani AB et al.[14]

However, in studies by Maula et al[8], Abdul Ghafoor et al[10], Saraswat A et al[13], tuberculosis was the commonest cause of lymphadenopathy accounting for 44.4%, 63.3% and 39% of cases respectively. The variations in percentage by which tuberculosis contributes to lymphadenopathy might be explained by geographic variations, age distribution, the immunological status of the patients, and the setting in which a particular study was conducted.

In our study, metastatic lesions were 10 (6.13%) followed by Hodgkin's lymphoma (3%), non-Hodgkin's lymphoma (2.45%), and unclassified lymphoproliferative disorders (1.84%) respectively. In the study by Mbata GC et al[11], there was a predominance of metastatic neoplasms among the malignancies.

However, lymphomas were found to be more common in other studies by Atiqur Rahman et al[12], Kasturi et al[9] and Abdul Ghafoor et al.[10]

Table-IX Incidence of various diseases causing lymphadenopathy in different studies

Study	Place	Non-neoplastic lesions (%)			Neoplastic lesions (%)	
		Reactive	Tuberculosis	Other lesions	Lymphoma	Metastatic lesions
Abdul Ghafoor et al[10]	Pak	36.11	44.4	-	15.2	4.16
Kasturi et al [9]	India	32	26	1	33	8
Mbata GC et al [11]	Nigeria	32.6	28.3	2.8	17	19.7
Moore et al [5]	USA	47.8	36	-	8.5	2.6
Apoorva et al[13]	India	6.4	63.3	13.7	5.7	3.2
Present study	Pak	50.3	23.3	1.22	5.45	6.13

In our study, there was a significant relationship between histopathological diagnosis and the size of lymphadenopathy. Out of all the malignant causes of lymphadenopathy, 54.5% of malignancies had lymphadenopathy ≥2 cm while in the case of lymphadenopathy due to non-neoplastic lesions, only 24.5% of cases had lymphadenopathy ≥2 cm. Similarly, in a study by Zahir ST et al[6], there was a significant relationship between histopathological diagnosis and the size of lymphadenopathy.

In the studies by Zahir ST et al[6], Abdul Ghafoor et al[10] and Atiqur Rahman et al[12], the most common site of the biopsy was cervical lymph nodes. This might be due to the easy accessibility of cervical lymph nodes for biopsy. In our study, the most common biopsies were of abdominal lymph nodes. This may be because many of these samples were obtained during surgeries performed on the abdomen.

Most cases of lymphomas were diagnosed on biopsies taken from the cervical region (77.7%). Cervical and abdominal lymph nodes were found to be the commonest sites for metastatic deposits (80% cases of metastatic lymphadenopathy). Many sources have revealed that lymphadenopathy in the supraclavicular region and some other places has increased risk of malignancy. However, in study by Zahir ST et al[6], no significant relationship between pathologic findings and site of the biopsy was seen.

In the present study, abdominal lymph nodes and cervical lymph nodes gave the highest diagnostic yield (90% and 88% respectively), while axillary lymph nodes gave the lowest diagnostic yield (75%). In a study by Atiqur Rahman et al[12], abdominal and axillary lymph nodes gave the highest diagnostic yield (67.9%), while submental and submandibular lymph nodes gave poor diagnostic yield. This might be because there were only fewer biopsies taken from the submental and submandibular regions in the given study.

Conclusion

Reactive hyperplasia and tuberculosis are the most common of histomorphological patterns of lymph node biopsies in developing countries accounting for 50.3% and 23.3% respectively. Malignancy and lymphomas are other common causes. Moreover, the abdominal lymph node group gave the highest diagnostic yield. Different methods are employed for the diagnosis of lymph node lesions such as FNAC, core needle biopsy but excision of lymph nodes and study after routine H&E staining is the gold standard in differentiating neoplastic from non-neoplastic

lesions. However, in reaching a definite diagnosis as well as in the further classification of lymphomas, immunohistochemical markers must be applied.

References

1. Rosai J. Lymph nodes. Rosai and ackerman's surgical pathology. 10th ed. ST.Louis: Elsevier Mosby; 2011.p1771-1899.
2. Sibanda EN, Stanczuk G. Lymph node pathology in Zimbabwe: A review of 2194 specimens. Q J Med. 1993;86:811-7.
3. Longo D, Fauci A, Kasper D et al. Harrisons Manual of Medicine. 18th ed. US: McGraw-Hill Professional; 2012.
4. Narang P, Narang R, Narang R et al. Prevalence of tuberculous lymphadenitis in children in Wardha district, Maharashtra State, India. Int J Tuberc Lung Dis. 2005;9(2):188-94.
5. Moore SW, Schneider JW, Schaaf HS. Diagnostic aspects of cervical lymphadenopathy in children in the developing world: a study of 1,877 surgical specimens. Pediatr Surg Int. 2003;19(4):240-4.
6. Zahir ST, Azimi A. Histopathologic findings of lymph node biopsy cases in comparison with clinical features. Pak J Med Sci. 2009;25(5):728-33.
7. Roy A, Kar R, Basu D et al. Spectrum of histopathologic diagnosis of lymph node biopsies: A descriptive study from a tertiary care center in South India over 5½ years. Indian J Pathol Microbiol. 2013;56(2):103-8.
8. Maula F, Iqbal Z, Anwar K et al. Histopathological pattern of lymph node biopsies taken in three teaching hospitals of Bannu (KPK). Pak J Chest Med. 2012;18(2):3-6.
9. Krishnatreya K, Borgohain M, Kr.Das J. Pattern of histopathological diagnosis of lymph node biopsies at a tertiary care hospital in Northeast India. Panacea J Med Sci. 2017;7(3):112-6.
10. Ghafoor A, Sajjad M, Mustafa A et al. Histopathological pattern of lymph node lesions in Agency Head Quarter Hospital Miranshah, North Waziristan Agency, KPK, Pakistan. KJMS. 2015;8(2):160-3.
11. Mbata GC, Nweke IG, Egejuru RO et al. South Eastern Histologic Pattern of Lymph Node Biopsies in a Tertiary Hospital in Nigeria. J AIDS Clin Res. 2015;6:475-8.
12. Rahman A, Biswas MA, Siddika ST et al. Histopathological Evaluation of Lymph Node Biopsies: A Hospital Based Study. J Enam Med Col. 2012;2(1):8-14.
13. Saraswat A, Rajender A, Purohit K et al. Lymph Node Biopsy: Spectrum and Clinical Significance as Diagnostic tool at Tertiary Care Center. JEMDS. 2015;4(6):1008-14.
14. Vachhani AB, Bhuva K, Jasani JH et al. Histopathological study of lymph node biopsy. Int J Biomed Adv Res. 2013;4:790-5.