

Research Article

Histopathological analysis of lymph nodes in patient with clinical lymphadenopathy - 266 cases

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ABSTRACT

Background: Lymphadenopathy is one of the most common clinical presentations among patients of all ages. This study has undertaken to study the histological patterns in various non-neoplastic condition, lymphoma and metastatic carcinoma in patient with lymphadenopathy and to do the clinico-pathological correlation with respect to age, sex and site of lymph node involved.

Methods: Total 266 cases of lymph node biopsy were studied, for a period of 28 months at Pathology department, Government Medical College, Surat, Gujarat, India. Tissues were adequately fixed in formalin and blocks prepared, sections cut and slides were prepared, stained by routine H&E stain. A complete and thorough histopathological examination of all the slides was undertaken.

Results: A total of 266 cases were studied, age range was 1-75 years, 136 were males and 130 were females. Out of 266 cases, 96 cases (36%) were non-specific lymph node hyperplasia, 81 cases (31%) were of metastatic deposits in lymph node, 70 cases (26%) were of specific non neoplastic conditions and 19 cases (7%) were of lymphoma.

Conclusions: Lymph node biopsy plays an important role in establishing the cause of lymphadenopathy. Among the biopsied nodes, non-specific lymph node hyperplasia was the most common followed by metastatic deposits, specific non neoplastic conditions especially tuberculous lymphadenitis and lymphoma. Non neoplastic conditions were more common in early age while neoplastic conditions were more common in late age. TB lymphadenitis was more common in HIV positive patients as compared to general population.

Keywords: Lymph node, Lymph node hyperplasia, Lymphoma, Lymphadenopathy

INTRODUCTION

Lymphadenopathy is one of the commonest clinical problems in patients being examined for various reasons or it may be a presenting sign or symptoms of the illness.^{1,2} It is the most common cause of swelling in the neck and is one of the commonest presentations in inflammatory and neoplastic disorders.³

Lymphadenopathy are either generalized or localized and signify.^{4,5}

- Benign condition such as reactive hyperplasia, acute or chronic inflammation.
- A primary malignancy of the lymphoid system like Hodgkin or Non-Hodgkin lymphoma.
- A Metastatic lesion of a solid tumor.

Generalized lymphadenopathy is seen in a large number of systemic illnesses while localized lymphadenopathy is more often seen with local infection or malignancy.⁶ First step in developing better therapies is the recognition of distinct specific disease entities by pathologists. Since there is no specific treatment for most forms of reactive lymphadenopathy, even a non-specific diagnosis is

helpful, because the main aim is to exclude a malignant process and treatable causes.⁷

Most cases of lymphadenopathy are primarily assessed by FNAC procedure and also it is a simple, quick, inexpensive and equally reliable procedure which can be used as a routine OPD procedure but the frequency of indeterminate or incorrect diagnosis is higher in comparison to excisional biopsy.⁸ Aspiration cytology of lymphoma is difficult to interpret and it does not distinguish reliably between Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL) as well as subtype of either. So excisional biopsy is the procedure of choice in suspected lymphoma. Histologic diagnosis depends on changes in the overall architectural pattern of the lymph node as well as identification of individual cell. Excisional biopsy yields more tissue for diagnostic studies facilitating preparation of multiple histological sections for routine and special stains as well as providing adequate material for culture. Although the advent of new immuno-histochemical analytic technique has improved the diagnostic accuracy of fine needle aspiration but histological examination of lymphoid tissue remains the gold standard for diagnosis.⁹⁻¹¹

In patients with HIV-related lymphadenopathy, exact nature of lymphadenopathy (infectious mononucleosis like syndrome, persistent generalized lymphadenopathy, opportunistic infection, lymphoma or kaposi sarcoma) can be determined only after lymph node biopsy.¹²

METHODS

The present study is based on a review of 266 cases of lymph node biopsy excised from various regions of the body, for a period of 28 months, at Pathology department, Government Medical College, Surat, India. Surgical resection specimens with lymph node dissection were excluded from the study. Tissue were adequately fixed in formalin fixative and blocks prepared, the section cut at 3-4 micron thickness and slides were prepared using routine H & E stain and supplemented as necessary by special stain like PAS, reticulin and AFB stain. In each case clinical notes were reviewed and records were made of the age and sex of the patient, the site of lymphadenopathy, associated systemic symptoms, the results of laboratory investigation and imaging study. These data were analyzed in relation to tissue diagnosis.

A complete and thorough histopathological examination of all the slides was undertaken and reviewed in detail for various neoplastic and non-neoplastic conditions.

RESULTS

A total of 266 cases were included in the study out of which 136 were males and 130 females. The age range was 1-75 year. Out of 266 cases, 96 cases (36%) cases were of non-specific lymph node hyperplasia, 81 cases (31%) were of metastatic deposits in lymph node, 70

cases (26%) were of specific non neoplastic conditions, 19 cases (7%) were of lymphoma.

The age-wise incidence of lymphadenopathy was more in middle age-group patients (21-40 years) in whom tuberculosis was more common.

Table 1: Age wise distribution of cases.

Age group (years)	No. of cases (%)
0-10	31 (11)
11-20	30 (11)
21-30	55 (21)
31-40	55 (21)
41-50	42 (16)
51-60	37 (14)
> 60	16 (6)
Total	266 (100)

Table 2: Age wise distribution of cases according to underlying pathology.

Age	Non neoplastic conditions	Neoplastic conditions
<40 years	134 (78 %)	37 (22 %)
>40 years	32 (34 %)	63 (66 %)
Total	166	100

Cervical region was the commonest sites found followed by mesenteric, axillary, inguinal and other regions.

Non-neoplastic conditions were more common in early age while neoplastic conditions were more common in late age. Non-neoplastic conditions accounted for 166 cases (62%), out of which non-specific lymph node hyperplasia was found in 96 (36%) cases and specific non-neoplastic conditions was found in 70 (26%) cases, and most of them are of tuberculous lymphadenitis.

Neoplastic conditions accounted for 100 cases (38%), of which 19 cases (7%) were of lymphoma; and among lymphoma cases 13 cases were of non-Hodgkin lymphoma, 5 cases were of Hodgkin lymphoma and 1 case was reported with two differential diagnosis: Hodgkin lymphoma/peripheral T cell lymphoma and immunohistochemistry was advised for further confirmation. Hodgkin lymphoma was more common in pediatric age-group, while non - Hodgkin lymphoma was more common in late age-group. 81 cases (31%) of metastatic lesion accounted for rest of the neoplastic conditions. The commonest primary site for metastatic carcinoma was breast followed by gastro – intestinal tract, oropharynx, thyroid, genitourinary tract and skin in decreasing order of frequency. In 7% of cases, the primary sites were not known.

There were 8 cases presented with generalized lymphadenopathy. Out of these, 3 cases were of non specific hyperplasia, 3 cases were of non-Hodgkin

lymphoma and 2 cases were of tuberculous lymphadenitis.

Table 3: Distribution of non-neoplastic & neoplastic conditions in pediatric age group (upto 16 years of age) in various studies.

Type of lesion	Karadeniz et al	Present study
	No. of cases (%)	No. of cases (%)
Non-neoplastic	159 (81)	45 (87)
Neoplastic	37 (19)	07 (13)
Total	196 (100)	52 (100)

Table 4: Distribution of cases according to region of lymph node involved.

Site	No. of cases (%)
Cervical	105 (39.6)
Mesenteric	73 (27.4)
Axillary	52 (19.6)
Inguinal	17 (6.4)
Retroperitoneal	08 (3.0)
Mediastinal	02 (0.7)
Femoral	01 (0.4)
Generalized	08 (2.9)
Total	266 (100)

Table 5: Distribution of non specific lymph node hyperplasia.

Non specific lymph node hyperplasia	No. of cases (%)
Reactive follicular hyperplasia	47 (49)
Sinus histiocytosis	33 (34)
Non specific Lymphadenitis	14 (15)
Acute lymphadenitis	02 (2)
Total	96 (100)

Table 6: Distribution of specific non-neoplastic conditions.

Specific non-neoplastic conditions	No. of cases (%)
Tuberculous lymphadenitis	61 (87)
Granulomatous lymphadenitis	03 (4)
Angiofollicular hyperplasia	02 (3)
Parasitic granuloma	02 (3)
Toxoplasma lymphadenitis	01 (1.5)
Sinus histiocytosis with massive lymphadenitis	01 (1.5)
Total	70 (100)

In present study 4 cases were HIV positive, among these, 2 cases presented with generalized lymphadenopathy. Furthermore among 4 HIV positive cases, 2 cases were diagnosed as tuberculous lymphadenitis, 1 cases was NHL and 1 was non specific hyperplasia.

Table 7: Distribution of neoplastic conditions (lymphoma).

Neoplastic conditions (lymphoma)	No. of cases (%)
Hodgkin lymphoma	05 (26)
Non-hodgkin lymphoma	13 (69)
Other: Hodgkin lymphoma/ peripheral T cell lymphoma	01 (5)
Total	19 (100)

Table 8: Distribution of neoplastic conditions (metastatic deposits from primaries mentioned below).

Neoplastic conditions (metastatic deposits from primaries mentioned below)	No. of cases (%)
Breast	33 (41)
GIT	17 (21)
Oropharyngeal	15 (19)
Thyroid	05 (6)
Genitourinary tract	04 (5)
Skin	01 (1)
Unknown	06 (7)
Total	81 (100)

Table 9: Metastatic deposits with their primary site as breast.

Breast	No. of cases
Invasive ductal carcinoma	31
Invasive ductal carcinoma with neuroendocrine features	01
Invasive ductal carcinoma with mucinous carcinoma	01
Total	33

Table 10: Metastatic deposits with their primary site as GIT.

GIT	Oesophagus	Stomach	Colon	Rectum	Total
Adenocarcinoma	0	4	2	3	9
Adenosquamous carcinoma	0	0	1	0	1
Signet ring carcinoma	0	0	1	0	1
Squamous cell carcinoma	1	2	0	0	3
Undifferentiated carcinoma	1	2	0	0	3
Total	2	8	4	3	17

Table 11: Metastatic deposits with their primary site as oropharynx, tongue, larynx and nasopharynx.

Oropharyngeal	Tongue	Larynx	Naso-pharynx	Total
Squamous cell carcinoma	6	7	0	13
Undifferentiated carcinoma	0	0	2	2
Total	6	7	2	15

Table 12: Metastatic deposits with their primary site as thyroid.

Thyroid	No. of cases
Medullary carcinoma	02
Papillary carcinoma	01
Follicular carcinoma	01
Oncocytic carcinoma	01
Total	05

Table 13: Metastatic deposits with their primary site as GUT, Kidney, Bladder and Cervix.

Genitourinary tract	Kidney	Bladder	Cervix	Total
Wilms tumor	01	00	00	01
Papillary urothelial carcinoma	00	01	00	01
Squamous Cell Carcinom (SCC)	00	00	01	01
Adenocarcinoma	00	00	01	01
Total	01	01	02	04

Table 14: Metastatic deposits with their primary site as skin.

Skin	No. of cases
SCC	01

Table 15: Metastatic deposits with their unknown primary site.

Unknown primary	No. of cases
Adenocarcinoma	02
SCC	01
Undifferentiated carcinoma	03
Total	06

Table 16: Cases with generalized lymphadenopathy.

1	Tuberculous lymphadenitis
2	NHL
3	CRH
4	HL-MC/PTCL
5	CRH
6	HL
7	Chronic non-specific lymphadenitis
8	Tuberculous lymphadenitis

DISCUSSION

Results were compared with various studies on lymph node biopsy. In present study percentage (%) of diagnostic lymph node biopsy successful in establishing the diagnosis and helping in deciding the line of management is 64% (in rest 36 % cases, biopsy show lymphoid hyperplasia/inflammation).

Rate of positive diagnosis was 41% in study of Salzstein et al, 63% in Sinclair et al and 7% in Anthony et al.^{10,12,13} The data of present study was almost comparable showing high yield of specific tissue diagnosis. Yield of specific tissue diagnosis in the present study was highest for axillary lymph node biopsy (82.7%) followed by cervical (75.2%) and lowest yield was found in inguinal node (52.9%). In the Sinclair et al and Anthony et al, high yield was found in cervical node.

In the present study 62% cases were of non-neoplastic lesions which was comparable to the study of Sinclair et al (53%) and Yeutsu (60%) et al.⁴

In present study, among 174 peripheral L.N. biopsy, large no. of cases with benign lesions were found in patient <30 years of age while malignant lesion especially metastatic were more common in patient older >30 years of age which was comparable to the study of Yeutsu et al and Anthony et al.

In the present study most cases (31.3%) belong to the middle age group (21-40 years) in which both specific and non-specific non-neoplastic lesions were common and among the specific lesions tuberculous lymphadenitis was most common.

Tuberculosis (TB) is a widely prevalent disease in India, compare to other regions of the world. Bailey et al and Al Nousairy showed in their studies that TB is the most common disease in developing countries affecting the cervical lymph nodes.^{15,16}

In present study large no. of cases (87%) of TB lymphadenitis was found among the various specific non-neoplastic conditions, while in the study of Anthony et al,

6% cases were of TB lymphadenitis (among the various specific non-neoplastic conditions). Present study suggests that in developing studies like India TB lymphadenitis is more prevalent especially in middle age group as compared to developed countries. Ord and Matz et al also found higher prevalence of TB lymphadenitis in age group of 21-40 years.

In present study among 4 cases of HIV patients, 2 cases are of TB lymphadenitis. Shafer et al found that TB lymphadenitis was more common in HIV positive patients as compared to general population.¹⁸

In present study only 7% cases of lymphoma found which was less as compared to other studies, Yeutsu et al (12%), Anthony et al (19%) and Sinclair et al (37%).

In present study 31% of metastatic deposits as compared to study of Yeutsu et al (28%), Anthony et al (41%) & Sinclair et al (10%).

Above findings suggests that in present study non-neoplastic lesions are more frequent than neoplastic condition and also that incidence of lymphoma is less compared to other study carried out in developed countries.

Karadeniz et al studied 196 cases of lymphadenopathy in pediatric age group (upto 16 years of age) and he found 81% non-neoplastic and 19% neoplastic lesions in lymph nodes.¹⁹ The present study also shows large number of cases (87%) of non-neoplastic and 13% cases of neoplastic lesions in lymph node biopsies of pediatric patients (upto 16 years of age). So both the studies show comparable results suggesting low rate of neoplastic conditions in pediatric patients.

CONCLUSION

Lymph node biopsy plays an important role in establishing the cause of lymphadenopathy. Among the biopsied nodes, non-specific lymph node hyperplasia was the most common followed by metastatic deposits, specific non neoplastic conditions specially tuberculous lymphadenitis and lymphoma.

So lymph node biopsy should be routinely done to find out the common cause of lymphadenopathy like non specific lymph node hyperplasia and specific non neoplastic conditions like tuberculosis.

Non neoplastic conditions were more common in early age while neoplastic conditions were more common in late age. The commonest site of lymphadenopathy was cervical, followed by mesenteric, axillary, inguinal, and others. Among lymphoma cases, Hodgkin lymphoma was more common in pediatric age group while NHL was more common in late age group. The commonest primary site for metastatic carcinoma was breast followed by gastro-intestinal, oropharynx, thyroid, genitourinary and

skin in decreasing order of frequency. TB lymphadenitis was more common in HIV positive patients as compared to general population.

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