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Evaluation of pathologic lesions in superficial lymph node biopsies

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Abstract

Introduction: Lymphadenopathy can be due to any disease process involving lymph nodes. Enlargement of lymph node is a very common clinical symptom seen in outpatient department of any hospital. Lymphadenopathy can occur at any age group and at any site of the body. Detail clinical history for signs and symptoms, size of lymph nodes, presence of generalized lymphadenopathy, and hepatosplenomegaly help to arrive at provisional diagnosis. Histopathological examination of the lymph node biopsies is a gold standard test in the distinction between reactive and malignant lymphoid proliferations as well as for detailed subtyping of lymphomas.

Aim: The aim of present study is to analyze pathological spectrum of various neoplastic and non-neoplastic lesions affecting superficial lymph nodes in the neck, axilla, inguinal region and correlation with clinical findings.

Materials and Methods: The present study was a retrospective study conducted in the department of Pathology, at Chalmeda Anand Rao Institute of Medical Sciences, Bommakal Karimnagar,during the period from february 2014 to march 2015. Lymph node biopsies of all patients of both sexes and all age groups were included. Total 47 lymph node biopsies were selected for histopathological evaluation which constituted the study material. Among these 25 were from males and 22 were from females with male to female ratio being 1.2:1. The age of the patients ranged from 3 to 71 years with a mean age of 40-49 years.

Results: Out of total 47 cases, 15(31.9%) cases were tuberculous lymphadenitis ,13 cases (27.6%) were malignant lymphoma while metastasis was found in 10(21.2%) cases, reactive hyperplasia in 5(10.6%) cases, suppurative lymphadenitis in 2(4.2%) cases, castleman disease and kikuchi disease, the least common condition was seen in only one case(2.1%) each. Cervical lymph nodes were most commonly biopsied group of lymph nodes in our study.

Conclusion: Tuberculosis was the most common cause of lymphadenopathy, followed by malignant lymphoma and the cervical group of lymph nodes was most frequently affected.

Keywords: Lymph node biopsy, Tuberculous Lymphadenitis, Lymphadenopathy.

1. Introduction

The lymph node is one of the major anatomic components of the immune system.[1] The three major regions of a lymph node are the cortex, paracortex, and medulla.[2] Because the normal immune response leads to proliferation and expansion of one or more of the cellular components of lymph nodes, it leads to significant lymph node enlargement.[3] Lymphadenopathy refers to nodes that are abnormal in size, consistency or number, caused by the invasion or propagation of either inflammatory cells or neoplastic cells into the nodes. Enlargement of lymph node is a very common clinical symptom seen in outpatient department of any hospital. Lymphadenopathy can occur at any age group and at any site of the body. 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 are often characterized by non-specific reactive or chronic inflammatory and fibrotic changes.[4,5] Supraclavicular nodes are always worrisome for malignancy. Detail clinical history for symptoms and signs, size of lymph nodes, presence of generalized lymphadenopathy, and hepatosplenomegaly help to provisional diagnosis. Diagnostic lymph node biopsy is one of the frequent procedures in surgical practice. When node biopsy is indicated, selection of the most abnormal node will best enable the pathologist to determine a diagnosis.[6]

2. Materials and Methods

This is a retrospective study conducted in the Department of Pathology from February 2014 to March 2015 at Chalmeda Anand Rao Institute of Medical Sciences, Bommakal, Karimnagar which constituted the study material. Our study included 47 cases of superficial lymph node biopsy specimens received in the department of pathology for histopathological examination. Clinicodemographic data regarding age, sex, anatomical site of nodal biopsy and clinical information were obtained from histopathology request forms and register.

The specimens were fixed in 10% formalin for 24 hours after recording the gross morphological features – The size of nodes, shape, colour, consistency, presence of necrosis and matting, appearance on cut section and appearance of capsule were noted. 5mm thick bits (at least 2) were submitted for processing, 4-5 micron thick sections were cut with a microtome and stained with Haematoxylin and Eosin stain. The diagnosis of lymph node lesions was made on the basis of clinical presentation, gross morphology and light microscopic features of H & E. Special stains, such as ziehl neelsen, (ZN), reticulin, periodic acid-Schiff and van gieson was done whenever indicated by the pathologist. Immunophenotyping, immunohistochemistry and cytogenetic studies were not performed. Lymph node biopsies (e.g., cervical, axillary, inguinal) of all patients of both sexes and all age groups were included. Badly handled and poorly preserved lymph nodes specimens were not included in this study.

3. Results and analysis

Amongst 47 cases of lymph node biopsies analysed in the present study, non neoplastic cases were 51% and neoplastic cases were 49%. Of the 47 lymph node biopsies analysed in the present study 15 cases were (31.9%) of tuberculous lymphadenitis, 13 cases (27.6%) were malignant lymphoma while metastasis was found in 10 cases (21.2%), non specific reactive hyperplasia in 5 cases (10.6%), suppurative lymphadenitis in 2 cases (4.2%), castleman disease and kikuchi disease, the least common condition was seen in only one case each (2.1%).

Maximum numbers of cases 31.9% were tuberculous lymphadenitis and least common cases were castleman disease and kikuchi disease, was seen in one case 2.1% each. In present study the patients observed were of wide range in ages from 3 years to 71 years. Maximum numbers of cases were seen in age group of 40-49 years (21.27%). Minimum numbers of cases were seen in age group of 0-9 years and 70-79 years (2.1%). Maximum numbers of nonneoplastic lesions (51%) were in age group of 30-39 years and maximum numbers of neoplastic lesion (49%) were in age group of 50-59 years. It is observed that there is a slight male preponderance for lymph node biopsy (53%) as compared to females (46%). M: F ratio was 1.2:1. The youngest patient was found to be 3 year female and oldest patient was 71 year old male. Majority of lymph nodes biopsied were from cervical lymph nodes (51%) followed by axillary lymph nodes (27.6%) and inguinal lymph nodes (21.27%) in the order of frequency. In our study, granulomatous lymphadenitis was the most common cause of generalised lymphadenopathy. This is probably attributable to the high prevalence of tuberculosis in this part of India.[7] Tuberculous lymphadenitis was diagnosed by the presence of caseating epithelioid granulomas.

There were seven cases of Non-Hodgkin's lymphoma (NHL) which accounted for 14.8 % of all lymph node biopsies affecting >49 years old age group with a male to female ratio of 2.5:1. Out of seven cases, three cases were anaplastic large cell lymphomas, three cases were follicular lymphoma, and a single case was small lymphocytic lymphoma.

There were six cases of Hodgkin's lymphoma (HL), which accounted for 12.7% of all lymph node biopsies. Hodgkin lymphoma was affecting 3 to 49 years old age group with a male to female ratio of 1:1.Mixed cellularity type was the most common subtype, seen in 5 cases followed by lymphocyte predominance in one case. Hodgkin's lymphomas were diagnosed on the basis of presence of typical Reed-Sternberg cell/variants against appropriate background.

There were 10 cases of metastatic lymph nodes, which accounted for 21.2% of cases. The majority of cases were found in the age group 50-70 years with a slight female predominance with female: male ratio of 3:2. Out of 10 cases, 6 had metastatic squamous cell carcinoma, remaining 3 cases were adenocarcinoma and 1 case was infiltrating ductal carcinoma of breast.

There were 5 cases of reactive lymphadenitis. Out of 5 cases, 3 were follicular hyperplasia, 1 case was sinus histiocytosis and the other was chronic non-specific lymphadenitis. The maximum number of cases was found in the age group 40-49 years. Three cases were found in men, and 2 cases were found in women, with a male: female ratio of 1.5:1. Reactive lymphoid hyperplasia was diagnosed with presence of active germinal centers containing heterogeneous population of lymphocytes, centrocytes, centroblasts and tingible body macrophages.

Other patterns of lymphadenopathies were identified in 4 cases comprising of 2 cases of suppurative lymphadenitis, 1 case of castleman disease and 1 case of kikuchi's necrotizing lymphadenitis. Suppurative lymphadenitis was diagnosed by the presence of collection of neutrophils, necrosis in the lymph node tissue. Castleman disease was diagnosed by presence of shrunken germinal centers with concentric expansion of the mantle zones with eosinophils and hyalinization around the vessels (hyaline type). Kikuchi's necrotizing lymphadenitis was diagnosed by necrosis without neutrophils, macrophages with crescent shaped nuclei and plasmacytoid dendritic cells.

Table 1: Pathology

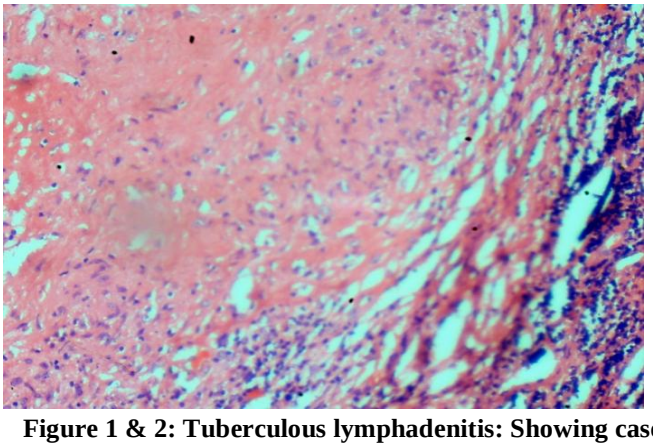
Pathology	No. of Cases	Percentage
Tuberculous lymph node	15	31.9%
Malignant lymphoma	HL -6 NHL – 7	12.7% 14.8%
Metastasis	10	21.2%
Reactive lymph node	5	10.6%
Suppurative	2	4.2%
Kikuchi disease	1	2.1%
Castlemen disease	1	2.1%
Total	47	100%

Table 2: Lymph nodes biopsy

Age Group	Cervical LN		Axillary LN		Inguinal LN	
	Male	Female	Male	Female	Male	Female
0-9	-	1	-	-	-	-
10-19	-	2	1	-	-	-
20-29	1	3	2	1	-	-
30-39	1	2	1	1	-	-
40-49	2	4	1	2	3	-
50-59	2	3	-	3	2	-
60-69	2	0	1	-	1	-
70-79	1	-	-	-	4	-
Total	24		13		10	-

Table 3: Lymphadenopathy

Age group	Tuberculous		HL		NHL		Metastasis		Reactive hyperplasia		Suppurative		Castleman disease		Kikuchi Disease
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	F
0-9	-	-	-	1	-	-			-	-	-	-		-	
10-19	1	1	1	-	-	-	-	-	-	1	-	-	-	-	-
20-29	2	1	-	1	-	-	1	-	-	1	-	-	-	-	1
30-39	2	2	1	-	-	-	-	1	1	-	-	-	-	1	-
40-49	-	2	1	1	1	-	-	2	2	-	1	-	-	-	
50-59	1	1	-	-	2		-	3	-	-	-	-	-	-	-
60-69	2	-	-	-	1	1	3	-	-	-	1	-	-	-	-
70-79	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-
Total	8	7	3	3	5	2	4	6	3	2	2	-	-	1	1
	15		6		7		10		5		2		1		1



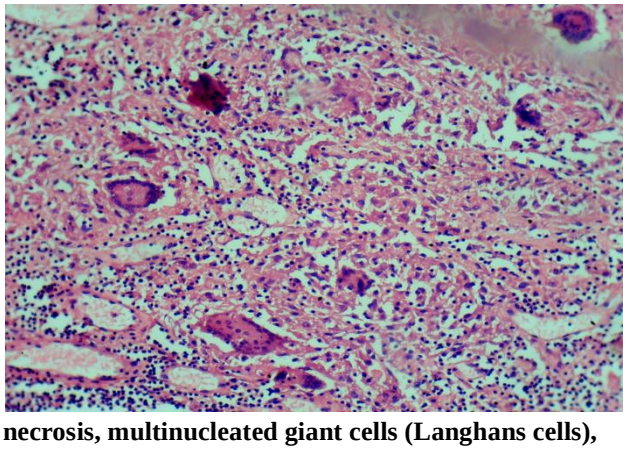


Figure 1 & 2: Tuberculous lymphadenitis: Showing caseous necrosis, multinucleated giant cells (Langhans cells), epithelioid cells and lymphocytes (H & E, 40x)

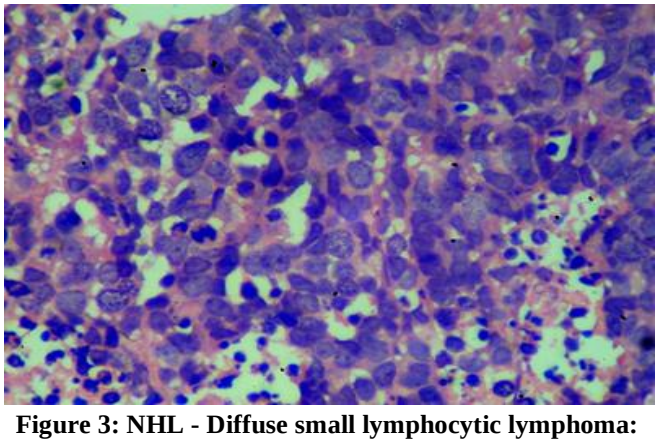


Figure 3: NHL - Diffuse small lymphocytic lymphoma: Monotonous proliferation of small lymphocytes effacing the architecture of the lymph node. (H & E, 40x)

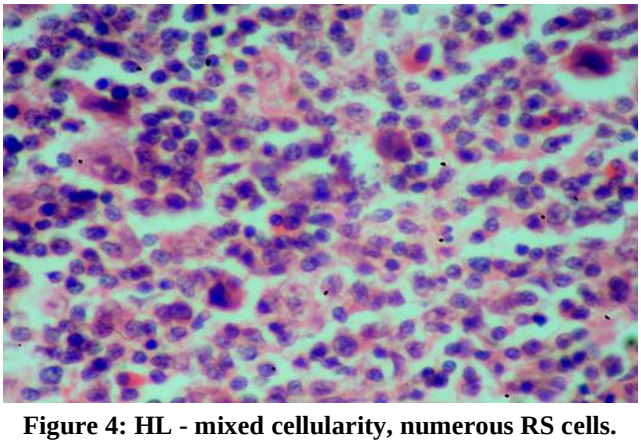


Figure 4: HL - mixed cellularity, numerous RS cells. (H & E, 40x)

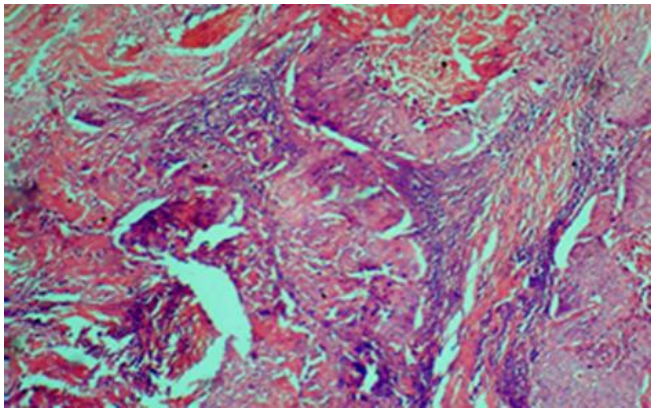


Figure 5: Metastatic Squamous cell carcinoma: Showing malignant cells in nesting pattern. (H & E, 20x)

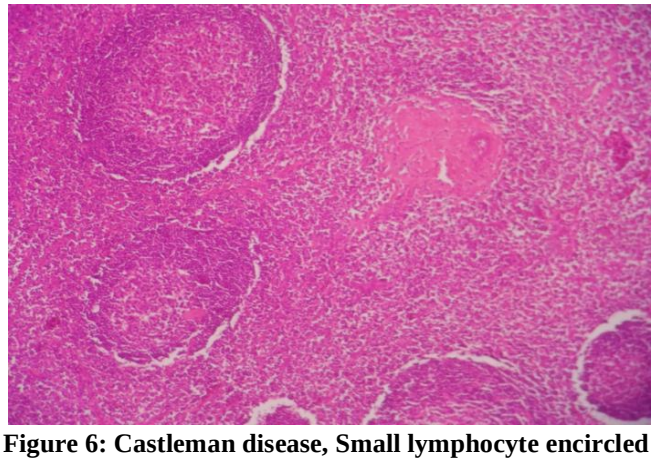


Figure 6: Castleman disease, Small lymphocyte encircled follicles with concentric "onion skin" layers and marked inter-follicular vascular proliferation (H & E, 20x)

4. Discussion

Palpable lymph nodes offer an important diagnostic clue to the etiology of the underlying condition. Though fine needle aspiration cytology is commonly used to establish the etiological diagnosis, excision biopsy and histopathology of the lymph node remains the "gold standard" for diagnosis of lymphadenopathy.[8-10] In the present study, cervical lymph nodes were the most frequently biopsied constituting 57% of nodal biopsies. This is consistent with virtually all other lymph node studies.[11,12] Next common group includes axillary and inguinal lymph node biopsies which comprised 27.6% and 21.27% respectively. Studies done by Khan *et al*[13] and Rahman *et al*[14] also support this, as they found cervical group of lymph node as the most commonly involved nodes.

This study included 47 lymph node biopsies among these 25 were from males and 22 were from females with male to female ratio being 1.2:1. Similar observation of male dominance was found in another study.[13] In present study nonneoplastic lesions constituted (51%) and neoplastic lesions (49%) of all biopsies. Of the non-neoplastic lesions, tuberculosis was the commonest lesion accounting for 31.9%. It has been reported by several authors that tuberculosis is one of the predominant cause of lymph node enlargement in adults in tropics like India.[15,16] Study by Khan *et al*[13] and Umer *et al* [17] found tuberculosis in 33.3% and 55.4% respectively. Our study also supports this as it showed maximum percentage of tuberculous lymphadenitis. The variation of tuberculosis in percentage might be due to geographic variation,age, number of patients included in study and immunological status of the patients.

In the present study, lymphoreticular malignancies accounted for 27.6% of all cases, while metastatic disease accounted for 21.2% of all cases. In a study by Moore *et al*[10], 8.5% of cases were lymphoma, while 2.62% of cases were metastatic disease. In a study by Amr *et al*, 35% of cases were lymphomas and 20.5% of cases were metastatic deposits which were comparable with our study.[18] Lymphomas were 2nd most common lesion seen in our study with 27.6% contrary to our study, a study conducted by Shaikh *et al* found that reactive hyperplasia as the second most common cause after tuberculosis.[19] Our study showed more cases of Non-Hodgkin's lymphoma than Hodgkin's lymphoma which is similar to study done by Roy *et al*.[20] Also in western world NHL is reported more common than HL.[21]

In present study there were 10 cases of metastatic lymph nodes, which accounted for 21.2% of cases. Out of which 6 cases were metastatic squamous cell carcinoma, 3 cases were metastatic adenocarcinomas and 1 case was metastatic infiltrating ductal carcinoma. In study conducted by Moore *et al*[10] frequency of metastatic deposit in lymph node which was comparable with present study results. In study conducted in Nigeria by Akinde *et al*[22] and by Anunobi C *et al* [23] frequency of metastatic deposit in lymph node in above studies is higher than our study, it may be due to small number of cases in present study and incidence of malignancy may be much higher in Nigeria. There is a wide variation in metastatic tumours affecting lymph nodes.

Of the non-neoplastic lesions, 10.6% were reactive lymphadenitis, and 31.9% were granulomatous lymphadenitis. In contrast, in a study by Sibanda *et al*, the prevalence of reactive hyperplasia was 33%, and that of granulomatous lymphadenitis was 26.7%.[8] Similarly, in a study by Oluwale *et al*, 29.3% of nodes were reactive, while 19.3% were granulomatous.[24] In a study by Moore *et al*, 47.8% of nodes were reactive, and 36.3% were granulomatous.[10] The higher incidence of granulomatous lymphadenitis in the present study is probably due to the high prevalence of tuberculosis in this part of India.[7]

Other patterns of lymphadenopathies were identified in 4 cases comprising of 2 cases of suppurative lymphadenitis (4.2%), 1 case of castleman disease (2.1%) and 1 case of kikuchi's necrotizing lymphadenitis (2.1%). Castleman disease and kikuchi was seen as the least common cause of superficial lymphadenopathy in our study as well as other studies published them as rare case reports.

Kikuchi-Fujimoto disease, characterized by histiocytic necrotizing lymphadenitis, closely mimics tuberculosis, and lymphoma are two most common etiologies

of cervical lymphadenitis. It is a rare, benign, and self-limited disease.[25] Etiology of this disease is unknown. Microscopically, it is characterized by lymphadenitis with paracortical coagulative necrosis, focal proliferation of histiocytes, and extensive karyorrhexis.

Castleman disease (CD) was first described in 1956 by Benjamin Castleman, who identified a group of patients with solitary hyperplasic mediastinal lymph nodes with small germinal center resembling Hassall's corpuscles of the thymus.[26]

Castleman's disease (CD) is an uncommon disorder characterized by a benign proliferation of the lymphoid tissue that may be localized or unicentric Castleman's disease (UCD) and disseminated or multicentric Castleman's disease (MCD). [27] Histologically, CD can be classified as hyaline-vascular (HV) type, plasma cell type, or a mixed type. Our case was hyaline vascular variant of CD characterised by small prominent hyalinized follicles associated with a marked inter-follicular vascular proliferation. This type of disease is now known as Unicentric CD.

5. Conclusion

From our study it can be concluded that superficial lymphadenopathy was a common clinical problem affecting all age groups and both sexes. Lymph node biopsy plays an important role in arriving at accurate diagnosis. It has also proven to be less expensive than multiple blood tests when investigating the cause of enlarged lymph nodes. Though lymph node involvement by non-neoplastic diseases is much more common than malignancies, malignancies are being reported more in biopsies as non-neoplastic diseases are treated on basis of fine needle aspiration cytology report. The commonest cause of superficial lymphadenopathy is tuberculosis, castleman disease and kikuchi-Fujimoto disease is the least common cause of superficial lymphadenopathy. It is important for physicians to be aware of these findings, and wherever necessary, to advise that a lymph node biopsy be undertaken.

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