

Histopathological and cytological spectrum of lymphadenopathy: a window to preliminary diagnosis

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Abstract

Introduction: Lymphadenopathy is a common clinical presentation of patients attending outdoor patient departments. The etiology varies with a wide spectrum ranging from inflammatory causes on one end to malignant on the other. In the present study, cytological and relevant histopathological diagnoses were done in 200 cases received in Department of Pathology. **Aims and objectives:** The present study aimed to find out the percentage of various lesions of lymph node and their prevalence according to age group and sex of patients. It also correlated the histo-cytodiagnosis in cases where both histology and cytology were available and compared the results of present study with similar other studies. **Materials and Methods:** This study was carried out in the department of pathology, Govt. medical college, Patiala. It included 200 cases of lymphadenopathies, either from Rajindra hospital or from health centers nearby. The cases were selected randomly. Lymph nodes included were of neck region, axilla, groin, from the extremities and the internal (mediastinal, abdominal and retroperitoneal). Apart from haematoxylin and eosin (H & E) stain, special stains like Ziehl-Neelsen stain and giemsa stain were done wherever needed. **Results:** Out of 200 cases, 93 (46.5%) cases were of reactive hyperplasia. Females were affected more commonly than males. Tuberculosis occurred more in younger patients whereas metastases were more common in older age group. Axillary lymph node was the most common lymph node involved. **Conclusion:** Histopathology gave accurate and confirmatory results than cytology. Lymph node evaluation is an integral part of patient management.

Keywords: Lymph node, Histopathology, Reactive hyperplasia

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Introduction

Lymph node is a major anatomic component of the immune system [1,2]. Lymph nodes are clustered in small groups or chains at strategic locations, where they drain the lymphatic vessels of various anatomic regions. The drainage involves not only the mechanical filtration of the foreign bodies in the lymph but also the recognition and processing of antigens. Peripheral nodes are more numerous in younger than in older persons while they are absent in the newborns [3]. Surrounded by a connective tissue capsule, lymph node is composed of outer part known as cortex and inner medulla. Both cortex and medulla represent B zones and therefore associated with humoral types of immune

responses [4]. Paracortex contains most of the T-cells [5]. Appearance of the follicles in the cortex varies according to their state of activity. Primary follicles appear as round aggregates of lymphocytes; secondary follicles appear following antigenic stimulation and are characterized by the presence of germinal centers [6].

The major functions of lymph nodes are filtration of lymph and processing of antigens. The immune response takes place in an integrated lymphoid system that includes the lymph nodes, spleen, and mucosa-associated lymphoid tissues (MALT) [7]. The size of a node to which some pathological significance can be attached depends on the site. For instance, in the cervical and axillary regions a lymph node >1cm is considered significant, while

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in the epitrochlear region a node as small as 0.5cm becomes important. On the other hand, a node should be >1.5 cm in the inguinal region to be considered as abnormal [8].

Superficial lymphadenopathy is a common finding and can be due to inflammation, metastatic malignancy or lymphoma [9]. Lymph nodes less than 1 cm in size are rarely malignant [10].

Lymph nodes are the most common site of metastatic malignancy and sometime constitute the first clinical manifestation of a disease [11,12,13]. Axillary and cervical lymph nodes are more likely to be informative in cases of generalized lymphadenopathy. Inguinal lymph nodes are to be avoided whenever possible because of the high frequency of chronic inflammatory and fibrotic changes present in them. Small superficial nodes may show only non-specific hyperplasia, whereas a deeper node of the same group may show diagnostic features [6].

Most enlarged lymph nodes are non-neoplastic and represent reaction to an infinite variety of antigens. In general, medical practice, neoplasia of lymph nodes is infrequent, about 1.1% of biopsies, whereas in referral centres their incidence may be as high as 60% [14,15,16].

In patients attending OPDs, reactive lymphoid hyperplasia is probably the most common diagnosis made [17]. The age of patients is one of the most important factors in determining the nature of enlarged lymph nodes. In children, most lymphadenopathies are benign, whereas in adults, the probability of malignancy increases with age [18].

Causes [19] of Lymphadenopathy can be non-neoplastic which include reactive lymphadenopathy due to rheumatoid arthritis, toxoplasmosis, early stages of infection with HIV, paracortical hyperplasia due to acute viral infections like infectious mononucleosis (IM), sinus histiocytosis/ reticular hyperplasia due to chronic gastritis caused by *Helicobacter pylori*, rheumatoid arthritis and granulomatous lymphadenitis like tuberculosis, sarcoidosis.

The neoplastic causes include primary as Non-Hodgkin and Hodgkin disease while secondary as metastatic deposits. Other rare entities like silicone

lymphadenopathy and dermatopathic lymphadenopathy have been described.

The present study was done to study neoplastic and non-neoplastic conditions of lymph nodes and their prevalence according to age group and sex, to correlate the histo cytodiagnosis in cases where both histology and cytology were available.

The importance of this study lies in the fact that FNAC findings are primary diagnostic tools in evaluation of enlarged lymph nodes and hence aid in the early diagnosis of the disease. This can be of utmost importance at the primary health care level. Lymph node biopsy plays an important role in typing of lymphoma and helps in cases, which cannot be diagnosed by FNAC [20].

Material and methods

This prospective study was carried out on 200 cases of lymphadenopathy in the Department of Pathology, Government Medical College, Patiala. The patients came to this department for FNAC from attached Rajindra hospital and TB & chest diseases hospital.

Patients also came from Mata Kaushalya civil hospital and other health centres around Patiala. Excision biopsy samples of lymph nodes were received in 10% formalin.

The cases were selected randomly. It was taken into account that maximum cases with both cytological and histopathological examination were included. Age, sex, site of lymph node, duration of lymph node enlargement, history of fever and weight loss was noted.

The cases in which more than one group of lymph nodes were enlarged, were put under the site from which excision biopsy was taken. Patients who returned with recurrence of enlarged lymph nodes (defaulters in tuberculosis) were excluded from the study and were counted as a single case.

All relevant history, except the cytological diagnosis was provided during the examination of excision biopsy specimens, to remove any observer bias. Gross findings included size, colour, consistency and cut section (in excision biopsy). Special stains like Zeihl Neelsen and Giemsa stain were applied wherever needed.

Results

Out of 200 cases of lymph nodes, 93 cases were of reactive etiology (46.5%) and 23 cases of tuberculous lymphadenitis (11.5%). Malignancy, both primary (7.0%) and secondary (32.5%) constituted 39.5%. Rest of the 2.5% amounted to inconclusive sections. There were 14 cases (7%) of primary malignancy and 65 (32.5%) of metastatic deposits. In 5 cases (2.5%), the diagnosis was inconclusive, only description was given (Table1).

Maximum number of females, 41(20.5%) were in the 4th decade followed by 36(18%) in 5th decade. Maximum number of males, 15(7.5%) were in the 2nd decade and over 60 years of age followed by 10(5%) patients in 3rd decade (Table 2).

Table-1: Histopathological diagnosis in 200 lymph node cases.

Lesion		No. Of cases	% age	
Non- neoplastic (n=116)	Reactive	93	46.5%	58%
	Tuberculosis	23	11.5%	
Primary malignancy		14	07.0%	
Metastatic		65	32.5%	
Inconclusive		05	02.5%	
Total		200	100%	

Table-2: Age and Sex wise distribution of 200 cases.

Age (in yrs.)	Male (%)	Female (%)
0-10	09(04.5)	02(01)
11-20	15(07.5)	10(05)
21-30	10(05)	11(05.5)
31-40	04(02)	41(20.5)
41-50	05(02.5)	36(18)
51-60	10(05)	20(10)
> 60 yrs	15(7.5)	12(06)
Total	68 (34)	132 (66)

Table-3: Cytological and histopathological correlation.

Histopathological diagnosis with no of cases	Cytological diagnosis				
	Reactive	Tubercular	Lymphoma	Mets(SCC)	Mets(ADENO)
Reactive,32	32				
TB,17		17			
Lymphoma,07	01	01	05		
Met(ADENO),04	01				03
Met(SCC),06				06	
Total, 66	34	18	05	06	03

Table-4: Site wise distribution of lymph node.

Site	No. of cases	Percentage (%)
Axillary	77	38.5
Cervical	39	19.5
Mesenteric	28	14
Inguinal	13	06.5
Gall bladder	07	03.5
Posterior auricular	05	02.5
Submandibular	05	02.5
Supraclavicular	04	02
Submental	04	02
Iliac	03	01.5
Appendicular	02	01
Gastric	02	01
Pre tracheal	02	01
Omental	02	01
Infra clavicular	01	0.5
Jugulo diagastric	01	0.5
Generalized	01	0.5
Para aortic	01	0.5
Sapheno femoral	01	0.5
Testicular	01	0.5
Posterior triangle neck	01	0.5

Out of 34 cases diagnosed as reactive on histopathological examination, all the cases were found reactive on cytological examination and similar in tuberculous lesions also but in case of lymphoma, 2 cases were benign on cytological examination. In case of metastatic malignancy, 1 case was benign on cytological examination (Table 3). Out of 200 cases, 77 (38.5%) cases presented with axillary lymph node enlargement, 39 (19.5%) with cervical node, 28 (14%) with mesenteric node, 13 (6.5%) with inguinal lymph node, rest of the cases with other nodal enlargement (Table 4).

Discussion

The present study comprised of 200 cases of lymphadenopathy referred to the department of pathology, Government Medical College, Patiala. The results of histopathology and cytological findings were compiled, scrutinized and compared with other studies. Out of total 200 cases, 68 were males and 132 were females, revealing a female preponderance with female to male ratio of 1.9:1. The age of patients ranged from 4 years to 100 years. The study conducted by Dandapat et al (1990) had a ratio of 1.2:1 [21] while Shrestha et al (2007) reported a female to male sex ratio of 1.04:1, also showing female preponderance [22]. The study conducted by Lee B et al (1999) reported a ratio of 1.5:1 [23]. In the present study, age ranged from 4 to 100 years with mean of 40.9 years. In the study of Dandapat et al, the age ranged from 1-65 years with the mean of 33 years.

In our study, out of 200 cases of lymph nodes, 116 (58%) cases were classified as benign, 79 (39.5%) cases as malignant and 5 (2.5%) cases were inadequate. Out of 116 cases of benign, 93 (46.5%) cases were reactive and 23 (11.5%) cases were of tubercular etiology. Out of 79 cases, 14 cases i.e., 7% were of primary malignancy and 65 i.e., 32.5% were of metastatic deposits. The most common cause of lymph node enlargement in all studies was reactive hyperplasia. In a study conducted by Zahir et al (2009) the most common cause of lymph node enlargement was reactive hyperplasia followed by malignancy than infectious disease [24]. In a study by

Thomas et al (1995), most common cause was reactive hyperplasia followed by granulomatous pathology than malignancy [25]. Out of 200 cases, the most common lymph node involved was axillary in 77 cases (38.5%) followed by 39 cases of cervical lymph node (19.5%) and 28 cases of mesenteric lymph node (14%) along with 13 cases inguinal lymph node. The most common lymph node involved was axillary which was in concordance with previous studies conducted by Ojo et al (2005) [26] and Lee B et al (1999) [7]. In present study metastatic deposits were most common cause for axillary lymph node enlargement. Also Lee B et al and Ojo et al showed the same results.

In the present study, age ranged from 4 to 100 years, in the study of Hirachand et al (2009) [27], age ranged from 3-85 years, in the study of Shaikh et al (2010) [28], age ranged from 10-70 years, in the study of Dandapat age ranged from 1-65 years.

In the present study 39.5% cases were found as neoplastic lesions, which constitute both primary malignancy as well as metastatic malignancy. In study conducted by Shaikh et al (2010), 20% cases were of neoplastic etiology. In study conducted by Olu-Eddo et al (2006) [29], 20% cases were of neoplastic etiology. The result of present study was analyzed and compared with other studies. Hodgkin's and Non-Hodgkin's lymphoma are the primary malignancy of lymph nodes. Hodgkin's lymphoma was originally described by Thomas Hodgkin in 1832 [30] and characteristic Reed-Sternberg cell are present in this type. Classical Hodgkin lymphoma, because of its variable cellularity, can resemble various reactive lymphadenopathies and other lymphomas [31,32].

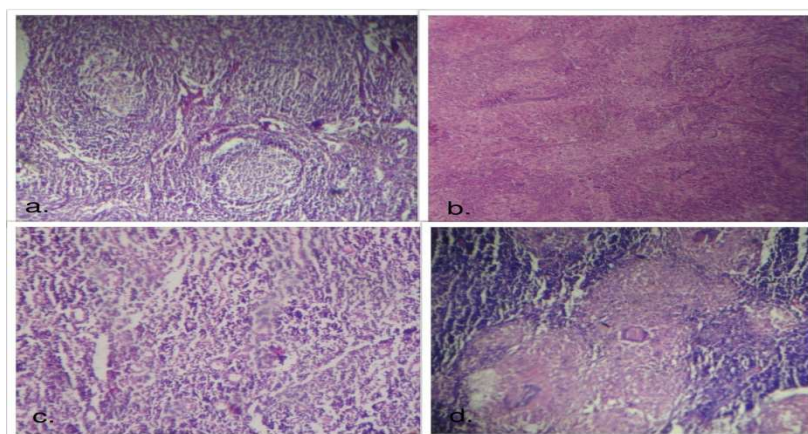


Figure-1: a) Follicular hyperplasia (H & E, 400X), b) Sinus hyperplasia (H & E, 400X), c) Paracortical hyperplasia (H & E, 400X), d) Granulomas in lymph node (H&E, 400X)

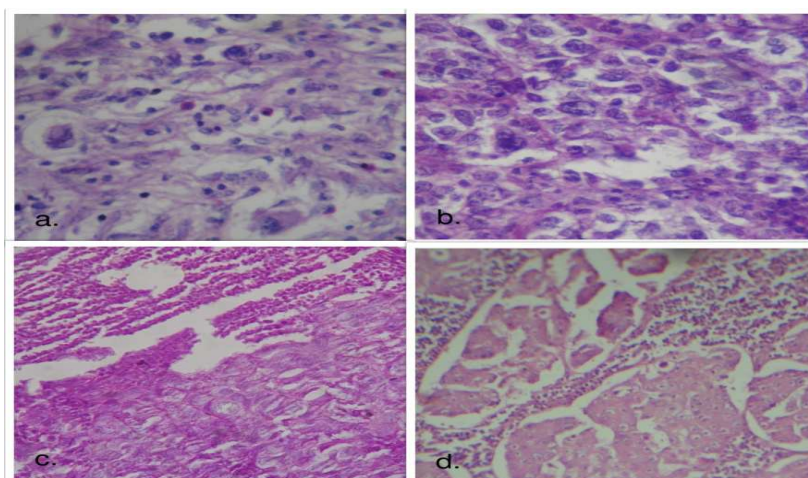


Figure-2: a) Hodgkin's Lymphoma (H & E, 400X), b) Non-Hodgkin's Lymphoma, Large cell type (H & E, 400X), c) Adenocarcinomatous secondaries (H & E, 400X), d) Squamous Cell Carcinoma secondaries (H & E, 400X).

Granulocyte-rich cases of classical Hodgkin lymphoma can resemble suppurative lymphadenitis or neutrophil-rich anaplastic large-cell lymphoma [33]. Histiocyte-rich cases can resemble granulomatous disorders. Reed-Sternberg like cells that occur in some reactive lymphadenopathies such as infectious mononucleosis, as well as in non-Hodgkin lymphomas, can be problematic for diagnosis [34]. Cases of classical Hodgkin lymphoma with many neoplastic cells, such as the syncytial variant of nodular sclerosis type, can resemble large B-cell lymphoma or anaplastic large-cell lymphoma.

Classical Hodgkin lymphoma can also resemble T-cell / histiocyte-rich large B-cell lymphoma or peripheral T-cell lymphoma [35]. For these reasons, fine needle aspiration cytology (FNAC) is considered less accurate for the diagnosis of Hodgkin lymphoma than it is for non-Hodgkin lymphoma [36].

Cytology was available in 66 cases for correlation. The comparison of present study with Dhingra [37] and Hirachand was done. In the present study 116 cases were placed in benign category with cytology available in 52 cases, out of which 3 cases were proved to be malignant on histopathology. Thereby making the accuracy in diagnosing benign lesions to be +6%. Dhingra described that out of 80 cases labeled as benign on cytology, 2 cases turned out as malignant on histopathology examination giving an accuracy of +2%. Hirachand described that out of 48 cases of benign on cytology examination, 45 cases were benign on histopathology giving an accuracy of +6%. In the present study 34 cases were of Non-specific lymphadenitis on cytological examination. Out of these 32 cases were confirmed as non-specific lymphadenitis on histopathology giving an accuracy of +6%. 18 cases were of Tuberculosis on cytology, out of these 17 cases were confirmed as Tuberculosis on histopathology giving an accuracy of +5%. In the present study 79 cases were placed in malignant category with cytology available in 14 cases. All cases were malignant on histopathology giving an accuracy of 100%. Dhingra described that out of 10 cases labeled as malignant on cytology, 9 turned out as malignant on histopathology giving an accuracy of +11%. Hirachand described that 24 cases were malignant on cytology when compared with histopathology 22 cases turned out as malignant giving an accuracy of +9%. In the present study, 5 cases were of Primary Malignancy on cytological examination. All of these 5 cases were confirmed as Primary Malignancy on histopathology giving an accuracy of 100%. 9 cases of metastatic malignancy were present on cytology. All of these 9 cases were confirmed as metastatic malignant on histopathology giving an accuracy of 100% (Table 3).

Conclusion

It was concluded from the present study that histopathology gave definitive diagnosis as compared to cytology. Lymphadenopathy is a common clinical presentation with >50% cases being benign. Females were affected more commonly than males. In the present study, female to male ratio was 1.9:1. Tuberculosis being more common in younger age group warrants the need for definite treatment and management process.

Metastases, particularly adenocarcinomatous deposits are more common in elderly age group. Simple examination of lymph node cytology/histopathology can help in clinical diagnosis of many cases.

Abbreviations

FNAC: Fine needle aspiration cytology, **HIV:** Human immunodeficiency virus, **TB:** Tuberculosis, **WHO:** World health organization, **IM:** Infectious mononucleosis, **H&E:** Haematoxylin & Eosin.

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