IJPRP

Original Research Article

Cytomorphological Study of Cervical Lymph Node Lesions: A Study of 173 Cases

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How to cite this article:

Amita S Patel, Gunvanti B Rathod, Kamlesh J Shah. Cytomorphological Study of Cervical Lymph Node Lesions: A Study of 173 Cases. Indian J Pathol Res Pract. 2019;8(3):255-262.

Abstract

Introduction: Cervical lymph node enlargement is frequent presentation in all age groups with a wide spectrum of diseases, ranging from infections to malignancy. Therefore, management of cases depends on lymph node pathology, which can be studied by collecting material through fine needle aspiration method that can be used as an outpatient procedure. Objectives: The study was undertaken to assess the cytomorphological features and incidence of cervical lymph node lesions on fine-needle aspiration cytology (FNAC) and to analyze the utility and diagnostic importance of FNAC in lymph node diseases. Materials and Methods: In this retrospective study, total of 173 patients were selected who had presented with cervical lymph node enlargement at Department of Pathology in our Tertiary Care Centre. Results: In this series of FNAC, 173 cases of cervical lymph nodes were analyzed. The age of patients ranged from 2 years to 85 years with slight male preponderance. Tubercular lymphadenitis comprised the majority (49.1%) followed by reactive lymphoid lesions (24.2%), metastatic malignancies (9.2%), granulomatous lymphadenitis (8%), acute suppurative lymphadenitis (6.9%), chronic nonspecific lymphadenitis (1.1%), necrotizing lymphadenitis (0.5%) and lymphoma (0.5%). Conclusion: FNAC is a simple, safe, reliable, inexpensive and the most diagnostic tool in early detection of lymph node lesions.

Keyword: Fine-needle aspiration cytology, Cervical Lymphadenopathy, Tuberculosis

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E-mail: amita1883@gmail.com Received on 19.03.2019, Accepted on 16.04.2019

Introduction

Lymph nodes are most widely distributed, easily accessible and an integral component

diagnostic purpose in the clinical practice [1].

The lymphoid system grows rapidly in

of the immune system. Their involvement is a common presentation and frequently examined for



childhood and reached its stable adult size till 20-25 years. Lymph nodes are pink gray bean shaped encapsulated organs which cluster along the lymphatic vessels of the body. There are hundreds of these small organs, but because they are usually embedded in connective tissue, they are not ordinarily seen. Infection and inflammatory stimuli elicit immune reaction within lymph nodes produce enlarged lymph nodes which are clinically palpable. The common sites of distribution are cervical, axillary, mediastinal, retroperitoneal, iliac, and inguinal regions. The cause of lymphadenopathy can range from an innocuous reactive lesion to tuberculosis to malignancy.

The fine-needle aspiration cytology (FNAC) in lymph node was first used by Greig and Gray in 1904 to diagnosed trypanosomiasis and Guthrie in 1921 systemically performed FNA on lymph nodes for diagnostic purpose [2]. Since then FNAC has been a simple, safe, rapid, reliable, and cost effective method of establishing the diagnosis of lesions and masses in various sites and organs and is the most convenient for outdoor as well as bedside indoor patients [3-7]. Also as a minimally invasive technique, it helps in early direction of appropriate investigations in conjunction with sophisticated CT, MRI and USG guided procedures.

The aim of this study is to highlight wonderful and diagnostic role of FNAC in different age group patients presenting with lymph node enlargement and to assess the cytomorphological features and incidence of various lymph node diseases on FNAC.

Materials and Methodss

This retrospective study was conducted over a period of 1 year from January 2017 to December 2017 in Department of pathology, GMERS medical college, Valsad which is a tertiary care centre to study the various cytomorphological features of neoplastic and non-neoplastic lesions of lymph nodes by FNAC in patients presenting with cervical lymphadenopathy and to determine the incidence of various lymph node diseases among them. Patients with significant cervical lymphadenopathy irrespective of age and gender were included in this study. A total of 173 cases of cervical lymphadenopathy of varied etiologies were considered. Study participants were subjected to standard FNA procedure after taking written informed consent from the patient or guardian (in case of paediatric patients).

After taking a brief clinical history, meticulous physical examination was done and the findings were noted. FNAC was performed using 22-24 Gauge needles attached to 10 ml syringes. Few passes were given with sufficient negative pressure then the needle was removed and the pressure was applied to the area of aspiration to avoid bleeding or hematoma formation. The aspirated material was smeared onto glass slides. Smears were fixed in methanol and stained with Haematoxylin & eosin stain and Papanicolaou stain. May Grunwald Giemsa (MGG) stain was done on air dried smears and Microscopic analysis was carried out. Ziehl-Neelsen (ZN) staining was done for Acid Fast Bacilli (AFB) whenever a cytological diagnosis of granulomatous disease was made and also in cases with abundant necrosis and suppuration. In cases where fluid was aspirated on FNAC, the fluid was centrifuged and smears were made from the sediment followed by the above staining methods.

Based on the cellularity, the smears were categorized as of high, moderate, and low cellularity. All the neoplastic and non-neoplastic lesions of lymph nodes by FNAC in patients presenting with cervical lymphadenopathy were included in this study. The smears which were hemorrhagic, with scanty cellularity to the extent that diagnosis could not be offered were labeled as inadequate for opinion and they were excluded from study.

The cytological diagnosis for each case was based on cytomorphology and available clinical information. The diagnoses were categorized broadly as tuberculous lymphadenitis, reactive lymphadenitis, metastatic lymphadenopathy, acute suppurative lymphadenitis, chronic nonspecific lymphadenitis, necrotizing lymphadenitis and lymphoma. If epithelioid granulomas were detected, but no caseation necrosis or AFB was seen, a diagnosis of granulomatous lymphadenitis was offered. The tuberculous lymphadenitis cases were further divided into three groups on the basis of cytomorphological analysis: group 1 - epithelioid granulomas without necrosis, group 2 - caseating epithelioid granulomas and group 3 - necrosis without epithelioid granulomas.

Results

This study analyzed 173 aspirates from the patients with cervical lymphadenopathy, out of which 96 were males and 77 females. The age of the patients varied from 2 years to 85 years with a mean age of 28.8 years. The youngest patient had acute suppurative lymphadenitis whereas the oldest patient had metastasis from squamous cell

carcinoma. The maximum incidences of cases were seen in the age range of 20-29 years. A slight male preponderance was noted with a male to female ratio of 1.2:1. The female's preponderance was particularly very high in 2nd decade of life whereas it was male preponderance in the 4rd decade of life. In younger age group and in elderly population, there was no significant difference in the incidence of disease amongst males and females [Table 1].

Lymph nodes of varying sizes were noticed on palpation for FNAC. The smallest lymph node measured 0.5 cm and the largest measured 10 cm in maximum dimensions. Most of the lymph nodes (130 cases, 75.1%) ranged in size between 1 and 2 cm, 6 cases (3.5%) were <1 cm and 37 cases (21.4%) were >2 cm in size [Fig. 1]. In 98 cases single lymph node was involved, two lymph nodes were involved in 1 case and more than 2 lymph nodes were found in 74 cases. The lymph nodes in tuberculosis were multiple, soft to firm, tender and matted; while

they were discrete in reactive lymphadenitis and firm to hard, non tender and fixed in majority of metastatic lesions. Cervical lymph node showed bilateral involvement in 20 cases. Cervical group of lymph node includes anterior, lateral and posterior cervical lymph nodes.

The most common cytological diagnosis made was tuberculous lymphadenitis in 85 cases (49.1%) followed by reactive lymphadenitis 42 cases (24.2%), 16 cases (9.2%) of metastatic malignancy, granulomatous lymphadenitis 14 cases (8%), acute suppurative lymphadenitis (6.9%), 2 cases of chronic non specific lymphadenitis (1.1%), single case of necrotizing lymphadenitis and a single case of non Hodgkin's lymphoma (0.5%) of each [Table 2].

The majority of cases recorded were those of tuberculous lymphadenitis 85 (49.1%) cases [Fig. 2] were further divided into three groups on the basis of cytomorphological analysis; group 1: epithelioid

90 80 70 60 No. of cases 50 40 30 20 10 0 Ch NS TB LN Rec Ac S NHL Met Gra Nec ■ >2 cm 15 14 1 0 3 3 0 1 ■ 1-2 cm 38 2 11 9 2 0 0 <1 cm 4 0 0 2 0

Size of lymphadenopathy

Fig. 1: Size of lymph node in different lesions

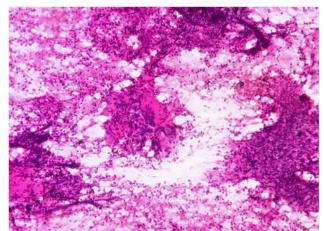


Fig. 2: Aspirates from tuberculous lymphadenitis show well-formed granulomas, giant cell with epithelioid cells in the background of necrosis and inflammatory cells (H&E, 40X).

granulomas without necrosis – 15/85 (17.6%), group 2: caseating epithelioid granulomas – 49/85 (57.7%) and group 3: necrosis without epithelioid granulomas – 21/85 (24.7%). Acid fast bacilli positivity on ZN staining [Fig. 3] was seen in 35 out of 85 cases (41.1%) of tuberculous lymphadenitis [Table 3].

Next frequent diagnosis was reactive lymphadenitis with 42 (24.2%) cases. In all cases, the size of lymph node was \leq 2 cm in diameter.

A total of 16 (9.2%) cases were diagnosed as metastatic deposits in the study mainly from oral cavity with marked male preponderance. Lymph node size was ≥ 2 cm in 14/16 (87.5%) cases. Maximum cases of metastatic deposits in the study were those of squamous cell carcinoma (14 cases, 87.5%) [Fig. 4] followed by poorly differentiated carcinoma and papillary carcinoma of kidney (1 case, 6.2%) each. Out of 16 cases, 4 cases (25%) had history of tobacco chewing since 5 to 45 years.

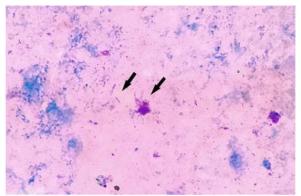


Fig. 3: Smear showing acid fast bacilli (arrows) in a background of necrosis (ZN staining, 100x)

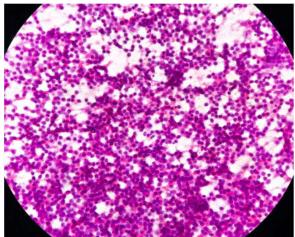


Fig. 4: Aspirates from reactive lymphadenitis, showing polymorphous population of lymphoid cells and tingible body macrophages (H & E, 40x).

Granulomatous Lymphadenitis was observed with 14 cases (8%) in our study. A total of 12 cases (6.9%) of acute suppurative lymphadenitis have been recorded in this study. The present study also comprised 2 (1.1%) cases diagnosed as chronic non Specific Lymphadenitis and 1 (0.5%) cases of necrotizing lymphadenitis. There was a 1 (0.5%) case of Non Hodgkin's lymphoma.

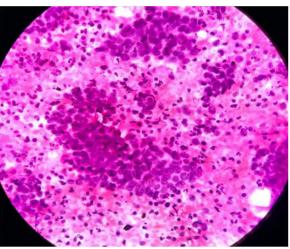


Fig. 5: Aspirates from metastatic squamous cell carcinoma – clusters and scattered neoplastic squamous cells with highly pleomorphic cells having ample basophilic cytoplasm (H & E, 40x).

Table 1: Age and gender distribution of 173 cases of cervical lymphadenopathy

Age	No. of male cases	No. of female cases	Total	Percentage (%)		
0-9	11	8	19	10.9		
10-19	15	16	31	17.8		
20-29	22	26	48	27.7		
30-39	16	15	31	17.8		
40-49	21	7	28	16.1		
50-59	4	1	5	2.8		
60-69	4	3	7	4		
≥70	3	1	4	2.3		
	96	77	173	100		

Table 2: Cytomorphological diagnosis of cervical lymph node lesions

Sr. No.	Cytomorphological Diagnosis	No. of cases	Percentage (%)	
1	Tuberculous lymphadenitis	85	49.1	
2	Reactive Lymphadenitis	42	24.2	
3	Metastatic lymphadenitis	16	9.2	
4	Granulomatous lymphadenitis	14	8.0	
5	Acute suppurative lymphadenitis	12	6.9	
6	Chronic non specific lymphadenitis	2	1.1	
7	Necrotizing lymphadenitis	1	0.5	
8	Non-Hodgkin lymphoma	1	0.5	
		173	100	

Table 3: Cytomorphological findings of tuberculous lymphadenitis. * AFB: Acid fast bacilli

Cytomorphological findings	No. of cases (%)	AFB* positivity		
Epithelioid granulomas without necrosis	15 (17.6)	1		
Caseating epithelioid granulomas	49 (57.7)	10		
Necrosis without epithelioid granulomas	21 (24.7)	15		
Total	85 (49.1)	35 (41.1%)		

Table 4: Comparison of the present study with the other studies.

N.	Name of authors	Total no.	Non neoplastic lesions (%)					Neoplastic lesions (%)			Other (%)	
No.		of cases	TB LN	Rea LN	Ac S LN	Gra LN	Ch NS LN	Nec LN	Met LN	NHL	HL	
1	Gayathri et al. [3]	1774	14.65	26.22	3.94	14.7	18.5	-	21.2	0.56	0.17	-
2	Mohanty et al. [7]	355	7.88	34.36	11.26	20.28	2.81	-	18.30	3.66	0.28	1.12
3	Kumar et al. [8]	214	47.6	44.3	-	0.9	-	-	2.8	4.2		
4	Baji et al. [11]	1905	47.1	32.7					13.9	0.9	1.1	6.4
5	Awasthi et al. [12]	222	53	36					7	4		
6	Bhatta et al (13)	206	35.9	54.3	1.4	-	-	-	6.3	1.9		
7	Shilpa et al. [14]	943	48.5	27.4	6.9	-	-	-	23.9	1.7	0.2	0.2
8	Nikethan et al. [18]	322	45.34	18.01	3.12	13.97	3.72	-	13.35	0.6	1.2	-
9	Sharma et al. [20]	268	54.5	7.8	21	16.8	-	-	10.4	1.5	0.8	
10	Nirmal et al. [21]	278	44.6	35.4	9.3	-	-	-	11.3	0.7	0.3	0.7
11	Present study	173	49.1	24.2	6.9	8	1.1	0.5	9.2	0.5	0	

Discussion

Inflammatory processes whether it is symptomatic or asymptomatic are the most common causes of peripheral lymphadenopathy and it is of great clinical significance as underlying disease may range from treatable infectious etiology to malignant neoplasm and requires accurate diagnosis so that proper treatment guideline can be started as soon as possible. Although the surgical excision of a peripheral lymph node is relatively simple, but the drawback is that procedure does require anesthesia, hospitalization, time consuming and the patient may get a scar for lifetime.

While on the other hand, FNAC is a simple, safe, reliable, quick, inexpensive and important diagnostic tool of establishing the diagnosis of lesions and masses in various sites and organs [3-9] Enlarged lymph nodes were the first organs to be sampled by FNAC [10]. However, this procedure has limitations and pitfalls.

In the present study, we made an attempt to present our experience with 173 FNAC cases of palpable cervical lymph node swellings and diagnosis based on the cytomorphological spectrum of lymph node lesions.

In this study, maximum number of cases recorded in age group of 20-29 years and slight male preponderance with male: female ratio of 1.2:1. This is in accordance with various other studies with

similar finding [3,5,8,9,11-19]. While Some authors have reported slight female predominance [20-22]. The male predominance could be accounted for more susceptibility of males due to high outdoor activities compared to females.

Tuberculous lymphadenitis was most often (54.1%) seen in the third and fourth decades, while 59.5% of reactive lymphadenitis cases were seen in first two decades of life. Reactive lymphadenitis due to underlying acute bacterial or viral infection was the commonest cause of significant lymphadenopathy in children. All the neoplastic lesions were seen above 40 years of age (100%). Males showed preponderance of tuberculous lymphadenitis, lymphoma metastatic and lymphadenitis, while reactive hyperplasia showed a slight female preponderance. The study done by Shilpa et al. [14] and Kochhar et al. [19] showed the highest incidence of tuberculous lymphadenitis was seen in second and third decades with female preponderance and decreasing incidence with age.

The present study showed significant correlation with size of lymph node involved as all 42 cases (100%) of reactive lymphadenitis had \leq 2 cm sized lymph nodes and out of 16 cases of metastatic lymphadenitis, 14 cases (87.5%) had \geq 2 cm to 10 cm sized lymph nodes. The study conducted by Reddy et al. [23] found significant correlation with various site and diagnosis where as a study done by Vimal et al. [9] found no correlation based on

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size of lymph node.

In this study, we observed non-neoplastic lesions like tuberculous lymphadenitis, reactive lymphadenitis, acute suppurative lymphadenitis, granulomatous lymphadenitis, chronic non specific lymphadenitis and necrotizing lymphadenitis to neoplastic lesions like metastatic lymphadenitis and non Hodgkin's lymphoma which were in accordance with majority of studies [Table 4].

Tuberculous lymphadenitis was the most common lesion and was reported in 85/173 cases (49.1%) which was correlated with the other studies [11-14,17,21,23]. The high rate is due to low socioeconomic status, illiteracy, incomplete treatment and resistance to the treatment. However some studies showed reactive hyperplasia as a most common finding [3,5,7]. This difference may be due to different study population and socioeconomic condition of the patients. In our study TB lymphadenitis cases were associated with systemic symptoms i.e. fever, cough, fatigue, weight loss and anorexia. Our study had 14 cases that had completed their anti tubercular treatment but had persisting nodes or new emerging nodes which were in accordance with the study done by chand et al. [24]. As in present study, tuberculous lymphadenitis was found in all age groups, results in the continuous transmission of the disease in the population. Hence, the diagnosis of this helps in preventing and treating the disease.

The cytomorphological pattern in tuberculosis is divided into three patterns [Table 3]. First was epithelioid granulomas without necrosis (17.6%) in present study followed by caseating epithelioid cell granulomas (57.7%) and AFB positivity was maximum with necrosis without epithelioid granulomas pattern (24.7%) which correlated with findings of other authors [9,14,17].

In the current study, second most common cases recorded were those of reactive hyperplasia 42/173 cases (24.2%). Since infections from oral cavity, ears, nose, and para nasal sinuses drain into these nodes; reactive lymphoid hyperplasia is a common finding [11]. Etiology is ranging from bacterial, viral, fungal or nonspecific and more often affects children rather than the elderly. These findings were in accordance with other studies [11-14,17,21,23].

Metastatic lymphadenitis was observed in 16/173 (9.2%) cases in our study which is comparable with the study done by Sharma et al. [20]. The primary was most often from the oral cavity, which was similar finding observed by Hirachand

et al. [6] and Singh et al. [16]. Males outnumbered females in these cases (M: F= 6.6: 1). Maximum cases were seen in age groups 40-85 years with squamous cell carcinoma being the most common histological type (87.5% of all metastatic lymph nodes) which was similar to the study by Singh et al. [16] and Kochhar et al. [19] observed 75% and 83.78% respectively. However some study showed high rate of metastatic lymphadenitis [3,7,14]. The reason for higher metastasis is the regional variation and different study population, genetic factors, environmental factors and habitual factors like smoking and tobacco consumption. Rates for oral cavity, pharynx, oesophagus and larynx are highest in India, probably due to the habit of using multiple tobacco products [18].

The other frequent diagnosis in this study was observed to be granulomatous inflammation with 14/173 cases (8%). The incidence of granulomatous inflammation was observed to vary from 0.9% to 20.28% in other studies [Table 4]. Granulomas have variety of differential diagnosis causing lymphadenopathy other than tuberculosis including sarcoidosis, carcinoma, lymphoma, fungal diseases, cat scratch disease, collagen vascular disease and disease of the reticuloendothelial system [25].

Acute suppurative lymphadenopathy was observed in 12/173 (6.9%) cases with majority of cases in 30 -39 age groups which is comparable with the study done by other workers ranged from 1.4% to 21% [Table 4].

The present study also comprised 2/173 (1.1%) cases diagnosed as chronic non specific lymphadenopathy on cytology. This correlated with the study of Mohanty et al. [7] and Nikethan et al. [17] who found the incidence to be 2.81% and 3.72% of all lymph nodes aspirated respectively. However Gayathri et al. [3] observed 18.5% cases chronic non specific lymphadenitis.

Other pathology in our series was necrotizing lymphadenitis which was found in 1/173 (0.5%) cases in accordance with 1.1% observed by Duraiswami et al. [22].

Other cytological diagnosis in the present study was Non Hodgkin's lymphoma which was found in 1 (0.5%) aspirates comparable with the study done by other workers ranged from 0.56% to 4.2%. [Table 4] With the help of specialized investigation like flow cytometry and immunohistochemistry in adjunct to FNAC the diagnosis of NHL can be made much easier.

Conclusion

In conjunction with clinical picture of the patients, the accessibility of the enlarged lymph nodes for palpation and puncture, the rich cellularity of the smear due to the high yield of the aspirated material with proper technique and the ease with which the all variety of diagnosis with the hallmark features can be differentiated from lymphocytes makes the technique of FNA very useful in investigation of lymphadenopathy. A cytological follow-up of the lesions is also easily possible by FNAC study.

FNAC has been yet again proved as an inexpensive, reliable and accurate diagnostic tool for the clinical set up in developing countries for the first line of investigation for lymphadenopathy. It helps in diagnosing metastatic diseases and gives the clue regarding the origin of the primary tumor which can be confirmed by advanced technique like immunohistochemistry on FNAC smear and early diagnosis can save the patient from high mortality and morbidity.

Abbreviations

TB LN - Tuberculous lymphadenitis

Rea LN - Reactive lymphadenitis

Ac S LN - Acute suppurative lymphadenitis

Gra LN - Granulomatous lymphadenitis

Ch NS LN - Chronic non specific lymphadenitis

Nec LN - Necrotizing lymphadenitis

Met LN - Metastatic lymphadenitis

NHL - Non Hodgkin's lymphoma

HL - Hodgkin's lymphoma

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