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Original Research Article

Clinico-Cytomorphological Evaluation of Cervical Lymphadenopathy Supplemented by Cell Block Study

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Abstract

Background: Accurate diagnosis of the cause of lymphadenopathy can sometimes be challenging and can lead to delay in diagnosis causing delayed treatment and health issues.

Aim: This study evaluate various pathological entities involved in cervical lymphadenopathy and supplemented by cell block preparation.

Method: A prospective observational study was carried out on 136 cervical lymphadenopathy patients with age group of 3-83 years who presented to outpatient department of Ear, Nose & Throat (ENT), General surgery, and at admitted wards. Clinical history, fine needle aspiration cytology (FNAC) and other investigations were done.

Results: Female to male ratio was 1.4:1. A total 32 cell blocks were prepared in clinically suspected cases of malignancy and compared with FNAC and biopsy findings. Younger age group mostly presents as TB lymphadenopathy and non-specific lymphadenopathy. In elderly people, cervical lymphadenopathy presented mostly as metastatic deposits in cervical lymph nodes. The right side was more involved 54.42% cases, followed by left side in 34.56% cases and bilaterally in 11.03% cases. Majority lymph nodes (64.7%) were less than 3cms in size. Most of the lymph nodes were firm rubbery consistency (84.5%) seen mostly in TB, reactive and non-specific lymphadenitis, followed by hard consistency nodes (11.76%) seen in malignant cases, soft consistency nodes (3.67%) were seen in suppurative. Maximum number of lymph nodes (75.7%) were mobile and fixed lymph nodes were seen in 12.5% cases followed by matted nodes seen in 11.7%. On clinical diagnosis 76.47% cases were benign, out of which 42 cases (30.8%) were TB lymphadenopathy and 62 cases (45.58%) were chronic non-specific lymphadenopathy. Malignant cases accounted for 32 cases (23.52%) out of which Metastatic deposits accounted for 30 cases (22.05%) and Hodgkin's lymphoma accounted for 2 cases (1.47%). Fixity of underlying structure and skin is primarily seen in malignant cases with metastatic deposits. The commonest cause was due to Reactive lymphadenitis (38 cases), followed by TB lymphadenitis (33 cases), Chronic nonspecific lymphadenitis (19 cases), Granulomatous lymphadenitis (18 cases), Metastatic deposits (16 cases), suppurative lymphadenitis (3 cases), Acute lymphadenitis (2 cases), Lymphoma (2

cases), dermatopathic Lymphadenopathy (1 case) and inconclusive (4 cases). 16 cases were metastatic deposits in the neck followed by 2 cases of Hodgkin's lymphoma. The Ziehl Neelsen stain for acid fast bacteria (AFB) was positive in 10 out of the total of 33 cases of TB lymphadenitis. Out of 32 cell blocks made in clinically suspected malignant cases, 19 cases were showing malignancy, 13 cases were benign.

Conclusion: Reactive lymphadenitis was predominant cause for cervical lymphadenopathy in the present study followed by Tuberculosis. FNAC can strongly suggest a preliminary diagnosis, which can be followed up by biopsy for histopathology and immunohistochemistry for confirmation and final classification. The inconclusive diagnosis given in FNAC was diagnosed as Metastatic Squamous cell carcinoma on biopsy as well as in cell block. Use of supplemental cell blocks provide minimally invasive way of obtaining additional architectural information of pathological lesions and it augments the diagnosis of FNAC.

Keywords: Cervical lymphadenopathy, fine needle aspiration cytology, Carcinoma.

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Introduction

Lymphadenopathy is an abnormal increase in size or altered consistency of lymph nodes. It is a clinical manifestation of regional or systemic diseases and it serves as an excellent clue to the underlying disorder [1]. Cervical lymphadenopathy is one of the commonest clinical presentation. It can occur in any age group or sex and can be due to reactive, infective or neoplastic causes [2]. Malignancies are predominantly metastatic in nature with an incidence varying from 65.7% to 80.4% and lymphomas range from 2% to 15.3% among lymph nodes aspirated from all sites [3,4]. Knowledge about the pattern of lymphadenopathy in a population facilitates pathological reporting and helps clinicians in making focused investigation and planning treatment course [5].

The general approach to cervical lymphadenopathy includes detailed clinical evaluation, fine needle aspiration cytology (FNAC) and open biopsy [6].

FNAC is an easy, quick and inexpensive technique for diagnosing enlarged lymph node with high degree of accuracy, but there are some limitations of FNAC which include high rate of nondiagnostic sampling, high rate of false-negative diagnoses in Hodgkin disease and incomplete classification of non-Hodgkin lymphoma [7,8].

Sometimes, FNAC does not give sufficient information for precise diagnosis, in such conditions cell block technique has been resorted to make the best use of the available material. Cell block preparation mimics histopathological sections, which helps in sub classification of various neoplastic lesions [9,10].

Objectives

- 1. To identify incidence and etiopathological entities involved in cervical lymphadenopathy.
- 2. To identify the distribution of lesions with respect to age and gender.
- 3. To study the different cytomorphological patterns associated with various lymphadenopathies.
- 4. To augment diagnosis of FNAC in cases suspicious of malignancy by making cell blocks out of additionally obtained material.

Methods

The present study is based on all the cases of cervical lymph node lesions received in the Department of Pathology, Mamata Super Speciality & General Hospital for FNAC during the period of November 2015 to October 2017. Ethical clearance has been obtained from Ethical Committee of Mamata General Hospital, Khammam.

Type of study: Two years prospective study.

Sample size: Total 136 cases with enlarged cervical lymph nodes FNAs supplemented with cell blocks.

Inclusion criteria: Patients with palpable cervical lymph nodes sent for FNAC in pathology OPD.

Exclusion criteria: Patients not willing for the procedure and lymph nodes with Secondary metastasis of known primary malignancy are excluded from present study.

Detailed clinical history taken from all the patients who referred to department of pathology for FNAC procedure. General physical examination and systemic examination performed as per prepared proforma, clinical diagnosis was made, informed consent taken, and procedure was explained to patient.

The skin over the area to be aspirated was cleaned thoroughly with iodine and spirit. Using 25-gauge disposable needle, attached to 10ml disposal syringe, the needle was deeply inserted in to lesion at the right angle to the skin surface. Once the lesion was entered, a negative pressure was created by retracting the plunger of the syringe. When the adequate quality of cellular material was withdrawn into the syringe, the suction was gently released to equalize the pressure. This prevents sucking of the aspirated material into the barrel of the syringe and loss of material for cytological examination. Then needle was withdrawn, and pressure was applied over the mass and tincture benzoin was applied to the side, where the needle was inserted so as to seal the puncture area. 3-4 excursion were made into the mass before withdrawal.

Slides were prepared from aspirate thus drawn and immediately wet fixed in 95% ethyl alcohol for Hematoxylin & Eosin and few were air dried for May- Grunwald Giemsa stain. Ziehl-Neelsen stain for Acid Fast Bacteria was done (suspected TB cases). Ultrasound guided FNAC performed whenever indicated. Stained smears were studied under light microscope and cytological diagnosis was made.

Cell block preparation:

For cell block analysis, the method followed in the present study was -tissue coagulum clot (TCC) method. In this method the remaining material in the aspirated syringe was allowed to clot, later pushed in the container containing mixture of 10% Formalin, 95% Alcohol and Allowed to fix for overnight. Then the cell button was processed as routine biopsv specimen and stained with Hematoxylin and Eosin (H&E) staining and slides were prepared. Stained smears were studied under light microscope and cytological diagnosis was made. Categorical data was expressed as frequency percentage.

Results

Out of 136 cases, cell blocks were made for 32 cases in clinically suspicious of malignancy and follow-up was done in suspected malignant cases.

Age of the patients range from 3 years to 83 years with mean age was 43 years. Maximum (44.11%) incidence of cervical lymphadenopathy was observed in the 21 to 40 years of age group. Among 136 cases, maximum number of lesions were noted in the females accounting for 80 cases (58.82%) compared to males 56 cases (41.17%) resulting in a female to male ratio of 1.4:1. The right side was more involved (74 cases) than left side (47 cases). Only few cases were seen to involve lymph nodes bilaterally (15 cases). We categorized the size of lymph nodes into two groups; the first group includes lymph nodes less than 3cms in size, second group was 3 to 6 cm in size. 88 cases of cervical lymphadenopathy were seen < 3cm, and 48 cases of lymphadenopathy were in 3-6cm in size. The most common site involved was in upper deep cervical (46 cases) followed by middle deep cervical (38 cases) and the lowest was seen in submental (4 cases). Most of the lymph nodes in the present study were firm rubbery consistency(84.5% cases) seen mostly in TB, Reactive and nonspecific lymphadenitis cases followed by Hard consistency nodes (11.76% cases) seen in malignant cases, soft consistency nodes(3.67% cases) were seen in suppurative and few TB cases.

In the present study, fixity was observed with respect to underlying structures and the skin. Present study shows maximum number of lymph nodes (75.7%) were mobile and fixed lymph nodes were seen in 12.5% cases followed by matted nodes seen in 11.7% of cases. Fixed nodes were mostly malignant cases with metastatic deposits in the neck. On clinical diagnosis 76.47% cases were benign out of which 42 cases (30.8%) were TB lymphadenopathy and 62 cases (45.58%) were chronic non-specific lymphadenopathy. Malignant cases accounted for 32 cases (23.52%) out of which Metastatic deposits accounted for 30 cases (22.05%) and Hodgkin's lymphoma accounted for 2 cases (1.47%).

FNAC lesions distribution: Cytological diagnosis by FNAC showed Reactive lymphadenitis entity found to be the most common accounted for 38 cases (27.9%) followed by TB lymphadenitis comprised of

33 cases (24.26%). Other entities included are chronic non-specific lymphadenitis, Granulomatous lymphadenitis, suppurative lymphadenitis, acute lymphadenitis and dermatopathic lymphadenitis were 19 cases (13.90%), 18 cases (13.2%), 3 cases(2.2%), 2 cases(1.47%) and 1 case(0.73%)cases(11.47%) respectively. 16 were metastatic deposits in the neck followed by 2 cases (1.47%) of Hodgkin's lymphoma. Out of 136 cases, 4 cases (2.94%) were inconclusive due to inadequate material obtained. The Ziehl Neelsen stain for AFB was positive in 10 out of the total of 33 cases of TB lymphadenitis. In two patients, numerous were AFB seen on the smear.

Cytological diagnosis by FNA showed 118 cases (86.76%) were benign, 18 cases (13.23%) were malignant in nature.

Metastatic deposits: Out of 16 cases of Metastatic deposits 14 cases were Squamous cell carcinoma deposits followed by 2 cases of Adenocarcinoma deposits.

Comparison of Cell block and FNAC: Total 32 cell blocks were made in clinically suspected cases of malignancy and FNAC findings were compared with cell block findings. Out of 32 clinically suspicious cases of malignancy FNAC showed 18 cases were malignant, 14 cases were benign and Cell block showed 19 cases were malignant and 13 cases were benign. One case was inconclusive on FNAC but it was diagnosed as Metastatic deposits on Cell block (Table 1). All cases which were malignant on FNAC and cell block were followed up in biopsy and compared (Table 2).

 Table 1: Comparison of diagnosis by cell block, FNAC in clinically suspected cases of malignancy (n=32)

Diagnosis	FNAC diagnosis	Cell block diagnosis			
Metastatic deposits	16	17			
Hodgkin's lymphoma	02	02			
TB lymphadenitis	03	03			

Reactive lymphadenitis	10	10
Inconclusive	01	-
Total cases	32	32

Comparative diagnosis of FNAC, Cell block and Biopsy: In the present study, 19 cases which were malignant on cell block were confirmed in biopsy. The inconclusive diagnosis given in FNAC was diagnosed as Metastatic Squamous cell carcinoma on biopsy as well as in cell block (Table 2).

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Diagnosis	FNAC	Cell block	Biopsy	
Metastatic SCC	14	15	15	
Metastatic Adenocarcinoma	02	02	02	
Hodgkin's lymphoma	02	02	02	
Total	18	19	19	

Table 2: Comparative diagnosis of FNAC, Cell block and Biopsy



Figure 1: Hematoxylin and Eosin staining. a. Smears show Polymorphous population of lymphoid cells along with tingible body macrophages (40x). b. Smears show extensive caseous necrosis in TB lymphadenitis (40x). c. Smears show Epitheloid granulomas in TB lymphadenitis (40x). d. Smears show polymorphous population of lymphocytes in various stages of maturation along with pigment-laden macrophages, immunoblasts, dendritic cells, and monocytoid blast cells in the background of eosinophils and plasma cells in case of DLN

(40x). e. Smears show Squamous cell carcinoma deposits in the background of lymphoid population (40x). f. Smears show Adenocarcinoma deposits in cervical lymph node (40x).



Figure 2: Hematoxylin and Eosin stain. a. Smears show Reed Sternberg cell (RS) seen in case of Hodgkin's lymphoma (40x). b. Cell block section shows SCC deposits in cervical lymph node (40x). c. Cell block section shows keratin pearl formation in SCC deposits of cervical lymph node(40x). d. Cell block section shows Adenocarcinoma deposits in cervical lymph node (40x). e. Cell block section shows Monotonous population of lymphoid cells in the background of inflammatory cells in case of Hodgkin's lymphoma (40x).

Discussion

In the present study Age of the patients varied from 3 years to 83 years with mean age was 43 years. Youngest patient was 3 years old with cytological diagnosis of 'Tubercular lymphadenopathy'. Oldest patient was 83 years old with cytological diagnosis of 'Metastatic deposits in lymph node'.

Shakya G *et al* [11] also stated most the patients with cervical lymphadenopathy were

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seen in 21-30 years of age group. Most of the young cases attributed to TB lymphadenitis and chronic non-specific lymphadenitis. Most of the cases with secondaries in cervical lymph nodes were seen in the age group of 41-60 and 61-83.

In the present study 80 females (59%), and 56 males (41%) presented with lymph node swellings. Below table shows Female to Male ratio of lymph node lesions in various studies and the present study.

Female: Male ratio in the present study was 1.4:1 which slight female predominance is. It was closest to studies of Wahid *et al* [12] and Mustafa *et al* [13] in which Female: Male ratio was 1.6:1 and 1.1:1 respectively. But most of the other studies showed Male predominance which is not comparable to present study.

Distribution of lesions according to Laterality

The right side (54.5%) was more involved than left side (34.5%) and very few cases were seen to involve bilaterally (11%). These findings were comparable with study done by Shrivastava *et al* [14] who found 46.8% with right side presentation, 35.9% left side presentation and 17.15% of bilateral presentation.

Distribution of lesions according to its size

The size of the cervical lymph nodes in the present study was less than 3 cms in 88 cases (64.7%), between 3 to 6 cm was in 48 cases (35.3%). The size of the neck nodes is important because staging of lymph node usually depends on size according to AJCC classification. Most of the nodes which are more than 3cm were usually TB and secondaries in the neck. The smaller nodes were either malignant or chronic non-specific lymphadenopathy. P.C.Chamyal *et al* [15] found 69.1% of nodes were less than 3cm, 20.9% were in between 3 to 6cm rest of 10% were more than 6cm.

Distribution of lesions according to site

In present study most common cases were found in upper deep cervical area which accounted for 33.8% followed by middle deep cervical accounted for 27.9%, least common was submental contributing 2.94%. The present study is comparable with N.H. Hafez *et al* [16] study who stated commonest site of involved cervical lymphadenopathy was upper deep cervical lymph nodes constituting 37.6%. In contrast, Chamyal *et al* observed that anterior cervical lymph nodes were most commonly involved which accounted for 65.5% followed by posterior cervical accounted for 20.9%.

Distribution of lesions according to consistency

In present study, firm rubbery consistency lymph nodes were 84.5% mainly associated with TB and nonspecific lymphadenopathy, there are 11.76% of nodes are hard consistency and these were metastatic in origin which presented as secondaries in the neck. Cystic and soft consistency lymph nodes were felt in suppurative lymphadenopathy and few cases of TB lymphadenitis also. Present study is comparable to Swapnil Arun et al [17] and P.C. Chamyal et al studies.

Distribution of lesions according to fixity

The mobile nodes were seen in 75.7% cases, matted nodes were seen in 11.7% cases. In present study all the matted nodes were diagnosed as TB lymph nodes. Fixed nodes were 12.5% cases. All cases of fixed nodes were secondaries neck except one case which was inconclusive on FNA. Study done by Chamyal *et al* depicts mobile, fixed and matted were of 60.0%, 23.6% and 16.4% respectively.

Distribution of lesions according to clinical diagnosis

In the present study on clinical diagnosis 76.47% cases were benign out of which 42 cases (30.8%) were TB lymphadenopathy and 62 cases (45.58%) were chronic non-specific lymphadenopathy. Malignant cases accounted for 32 cases (23.52%) out of which Metastatic deposits accounted for 30 cases (22.05%) and Hodgkin's lymphoma accounted for 2 cases (1.47%). Chamyal *et al* found that benign lesions accounted for 57.2% and malignant cases constitute of 40.9% in their clinical diagnosis.

Cytomorphological diagnosis of various lymph node lesions

In the present study most common entity was Reactive lymphadenitis (27.9%) followed by TB lymphadenitis (24.26%). The present study is comparable with Shakya G *et al* [11] study in which most common entity is Reactive lymphadenitis followed by TB lymphadenitis. In contrast other studies like Shrivastava *et al* [14] and Kumar *et al* [18] found TB lymphadenitis is most common entity followed by Reactive lymphadenitis.

In the present study incidence of other entities like Chronic non-specific lymphadenitis, Granulomatous lymphadenitis, Suppurative lymphadenitis, Acute lymphadenitis and Dermatopathic lymphadenitis is 13.9%, 13.2%, 2.2%, 1.47% and 0.73% respectively. In the present study 4 cases (2.94%) were inconclusive on FNAC because of inadequate material obtained. Shrivastava et al and N.Ahmed et al [19] also stated 0.16% and 4% of cases respectively were inconclusive on FNAC because of insufficient material. In such cases biopsy was advised.

Incidence of TB lymphadenitis

In the present study incidence of TB lymphadenitis is close to most of the other studies except Kumar *et al* study (47.67%). Shakya G *et al* study stated that cytomorphological features of epithelioid

and giant cells with caseous necrosis was associated with higher percentage of AFB positivity, one disadvantage is the inherent delay in culture result but PCR and other amplification techniques become more common which will reduce the detection time for the organism will improving the value of FNAC. Kafi AH et al (20) stated that a suspicious clinical history of TB coupled with positive aspirate, blood, sputum or urine tests for AFB and good response to anti-TB therapy supports the diagnosis of TB. In the present study TB is most frequently seen in below the age of 40 years where as malignancy was seen mostly above 40 years of age. This is comparable to study done by Kamini R Patel et al [21].

In our current study, the Ziehl Neelsen stain for AFB was positive in 10 out of the total of 33 cases of TB lymphadenitis. In two patients, numerous were AFB seen on the smear.

Incidence of Reactive Lymphadenopathy in various studies

In present study Incidence of Reactive lymphadenopathy was 27.9% which was closest to Priya R *et al* [22] and Shrivastava *et al* study 34.64% and 20.92% respectively.

Incidence of Metastatic deposits

In the present study Incidence of Metastatic deposits was 11.7% which was closest to Kamini R Patel et al (10.71%) and N.Ahmed et al (12%). Present study found that out of 16 cases of Metastatic deposits most common Squamous cell carcinoma(SCC) was deposits(87.5%) by followed Adenocarcinoma deposits(12.5%). Swapnil Arun More et al study also stated that SCC is the commonest metastatic tumor in cervical lymph node.

Incidence of Lymphoma

Incidence of Lymphoma's in present study was closest to Kumar *et al* and Shrivastava *et*

al study. In the present study there were 2 cases of lymphomas, both of them were Hodgkin's lymphoma. Shakya G *et al* study also found 2 cases of lymphomas out of which both were Hodgkin's lymphoma.

Incidence of Chronic non-specific lymphadenitis

In the present study Incidence of Chronic non-specific lymphadenitis was 13.90 which is closest to Shrivastava *et al* (8.7%) and Kamini R Patel (25.0%). Priya R *et al* found incidence of 34.64%.

Incidence of Suppurative lymphadenitis:

In the present study incidence of suppurative lymphadenitis was 2.20% which is close to rest all studies. Incidence of David SK *et al* [23], Swapnil arun more *et al*, Priya R *et al*, Mamatha K *et al* [24] and Shakya G *et al* are 4.%, 6.66%, 8.4%, 10% and 12.4% respectively.

In the present study incidence of Granulomatous lymphadenitis was 13.2% which was closest to Mamatha K *et al* (17.7%) and N.H.Hafez *et al* (6.4%). Incidence of other studies were Kumar *et al* (0.94%), Priya R *et al* (30.4%).

Incidence of Acute lymphadenitis in present study was 1.47% which was close to other studies Shrivastava *et al* (2.9%) and Kamini R Patel (7.65%).

Dermatopathic lymphadnopathy

In the present study there is one case of Dermatopathic lymphadenopathy (DLN) in which patient had severe dermatitis all over body. Srinivasamurthy *et al* [25] has reported one case of DLN and stated that characteristic large histiocytic aggregates is the single most consistent feature that helps in the diagnosis of DLN and suggested that in patients presenting with generalized lymphadenopathy with enlarged cervical, axillary and inguinal group of lymph nodes the differential diagnosis of DLN should be kept in mind even in the absence of any obvious skin lesion.

Incidence of benign and malignant lesions

In the present study incidence of benign (88.26%), malignant (13.23%) was closest to Kamini R patel *et al* and N Ahmed S *et al* studies. Total 32 cell blocks were made in clinically suspected cases of malignancy and FNAC findings were compared with cell block findings.

Out of 32 clinically suspicious cases of malignancy, FNAC showed 18 cases were malignant, 14 cases were benign and Cell block showed 19 cases were malignant and 13 cases were benign. One case was inconclusive on FNAC but it was diagnosed as Metastatic deposits on Cell block.

In a Basnet S *et al* [26] study, out of 15 malignant cases diagnosed on FNAC which were all confirmed in biopsy but only 13 cases were diagnosed on cell block. In his study diagnostic accuracy was higher in FNAC due to the inconclusive diagnosis of lymphoma to diagnose lymphoma and sub classify in the cell block was impossible.

Conclusion

Reactive cervical lymphadenopathy is commonest clinical presentation with variable etiology ranging from inflammatory to malignancy, it is important for clinicians in Early diagnosis. FNAC can strongly suggest a preliminary diagnosis, which can be followed up by biopsy for histopathology and Immunohistochemistry for confirmation and final classification. Use of supplemental cell blocks provide minimally invasive way of obtaining additional architectural information of pathological lesions and it augments the diagnosis of FNAC.

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