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Analysis of causes of cervical lymphadenopathy using fine needle aspiration cytology and excision biopsy at tertiary hospital in India

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Abstract
Introduction: The presentation of cervical lymphadenopathy is common, but its diagnosis is sometimes difficult. Fine Needle Aspiration Cytology (FNAC) is a simple, inexpensive, rapid investigative procedure to confirm clinical diagnosis with minimal trauma and low complication rate.
Aim: To determine the diagnostic accuracy of FNAC and to correlate diagnosis with FNAC and subsequent histopathological examination of excised biopsy specimens.
Materials and Methods: The study was done from data collected from 2013 to 2015. Total 100 Patients with cervical lymphadenopathy were clinically evaluated and FNAC, excision biopsy were done and analysed.
Results: FNAC is most sensitive in diagnosing secondary deposits in neck nodes with sensitivity of 88.9%. FNAC is least sensitive in diagnosing lymphomas with sensitivity of 78.6%.FNAC is 100% specific in diagnosing Tubercular lymphadenitis, Lymphomas and secondary deposits in neck nodes. FNAC is 96% specific in diagnosing chronic nonspecific lymphadenitis and 94% specific in diagnosing Reactive changes in cervical lymph node. Overall average sensitivity and specificity of FNAC of cervical lymphadenitis is 65% and 98% respectively.
Conclusion: FNAC is a very useful diagnostic tool in patients having significant lymphadenopathy. The metastatic carcinomas, especially squamous cell carcinoma and tuberculous lymphadenopathy can be diagnosed by FNAC with a high degree of accuracy. There is significant limitation in the diagnosis of low grade Non-Hodgkin's lymphoma from reactive hyperplasia.

Keywords: Cervical lymphadenopathy, tuberculosis, lymphoma, chronic lymphadenitis, Fine Needle Aspiration Cytology (FNAC), excision biopsy

Introduction
During the 5th week of gestation, two paired (jugular, iliac) and two unpaired (root of me sentry, cisterna chyli) endothelial sacs arise as outgrowths from the venous channels. These sacs form the primordia of the lymphatic system. Thoracic duct forms at 6-8 weeks1.

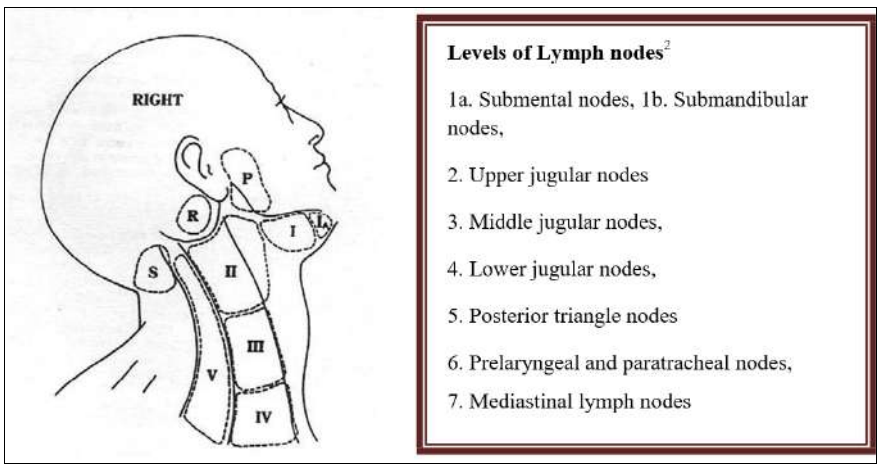

Fig 1: Levels of lymph nodes in neck.

Lymphadenopathy is common manifestation of many diseases. Lymphadenopathy is defined as an abnormality in the size or character of lymph nodes, caused by the invasion or propagation of either inflammatory cells or neoplastic cells into the node. There are about 800 lymph nodes in the body of which 300 are in the neck. There are many causes for cervical lymphadenitis; tuberculosis is still a common cause for lymphadenitis.

Causes for cervical lymphadenopathy [3, 4, 5, 6]
Inflammatory

Acute lymphadenitis

a. Non specific
b. Specific–e.g. Streptococcus, staphylococcus, cat scratch disease, measles, plague, infectious mononucleosis, toxoplasmosis, CMV infection

Chronic lymphadenitis

a. Non specific
b. Specific – e.g. Tuberculosis, syphilis, tularaemia, brucellosis, filariasis, sporotrichosis, actinomycosis, HIV

Eoplastic

1. Benign
2. Malignant

a. Primary-lymphomas or leukemias
b. Secondary

- Squamous cell carcinoma from larynx, pharynx, upper1/3rd of esophagus, cheek, scalp, tongue
- Adenocarcinoma from gastrointestinal cancers, thyroid, breast, testis, kidney
- Malignant melanoma
- From unknown origin

Miscellaneous

1. Allergic lymphadenopathy as in serum sickness, silicon lymphadenopathy.
2. Secondary to ingestion of anticonvulsant drugs: eg. Phenytoin, carbamazepine and from other drugs such as primidone, gold, sulfasalazine, captopril, atenolol, allopurinol.
3. Amyloidosis
4. Glycogen and Lipid storage diseases
5. Sarcoidosis
6. HIV related lymphadenopathy

Though the presentation of lymphadenopathy is common its diagnosis is sometimes difficult. Fine needle aspiration cytology (FNAC) is the study of cells obtained through a small gauge needle, under negative pressure provided by an airtight syringe7. FNAC is a simple, inexpensive, rapid investigative procedure to confirm clinical diagnosis with minimal trauma and low complication rate8. The material obtained from FNA can be used for diverse group of special techniques like cytochemistry, bacteriological culture, immunocytochemistry, ultrastructural studies and molecular hybridization9.For determining the diagnostic accuracy of FNAC; it is a usual practice to correlate clinical diagnosis with FNAC and subsequent histopathological examination of excised biopsy specimens.

Aim

To determine the diagnostic accuracy of FNAC and to correlate diagnosis with FNAC and subsequent histopathological examination of excised biopsy specimens.

Materials and Methods

The study group comprises of patients with complaints of lymph nodal swellings in neck attended surgical outpatient department from 2013 to 2015. This study consists of 100 cases.

Inclusion Criteria: Patients more than 12 years of age with cervical lymphadenopathy

Exclusion Criteria

1. Patients where FNAC and/or biopsy of node could not be carried out were excluded. (cold abscess / ulcer / sinus)
2. Patients presenting with other swellings of neck

After a detailed history and thorough examination, clinical diagnosis was made; the patients are explained about the procedure. FNAC was done with 22 or 23 gauge needle FNAC diagnosis were compared with histopathology after surgical excision of lymph nodes and its sensitivity and specificity were determined by –

$$\text{Sensitivity} = \frac{\text{True positive}}{\text{True positive + False negative}} \times 100$$

$$\text{Specificity} = \frac{\text{True negative}}{\text{True negative + False positive}} \times 100$$

Results

Detailed results are represented in table. Out of 100 patients, 77% are nonneoplastic and 23 % are neoplastic etiology. Most common being tubercular lymphadenitis seen in 51%, contact history of TB in Tubercular lymphadenitis present in 13.7%, size of lymphnode < 3 cm in 70.6%, 17.6% had bilateral involvement, caseation was seen in 45 %, chest xray findings are positive in 25.5 % of TB lymphadenitis cases.

Table 1: Characteristics of patients

n=100	Variables	No. of cases	%
Age in yrs	12 to 20	28	28%
	21-30	32	32%
	31-40	9	9%
	41-50	13	13%
	51-60	8	8%
	> 60	10	10%
Sex	Male	54	54%
	female	46	46%
C/F	swelling	100	100%
	fever	29	29%
	malaise	21	21%
	Loss of appetite	17	17%
	loss of weight	14	14%
	Cough	14	14%
	Dysphagia	3	3%
	Change of voice	2	2%
other LN	Cervical + axillary	6	6%
	Cervical + inguinal	14	14%
	Generalized (all 3)	5	5%
HPE diagnosis	TB	51	51%
	Chronic nonspecific	16	16%
	Reactive	10	10%
	HL	5	5%
	NHL	9	9%
	secondaries	9	9%

Table 2: Distribution of Tubercular lymphadenitis

Site	TB lymphadenitis
level I	7.80%
level II	19.60%
level III	9.80%
level IV	5.80%
level V	29.40%
level VI	
More than 1 level	27.60%

Of the 9 cases of malignant secondaries, 4 from the Nasopharynx, 2 from the thyroid papillary carcinoma and 1 from Lung. The remaining 2 cases had occult primary.

Table 3: Sensitivity and specificity of FNAC overall and in various diseases

	Sensitivity	Specificity
Tubercular	88.23%	100%
Chronic nonspecific	87.50%	94%
Reactive	80%	96.70%
Lymphoma	78.60%	100%
Secondaries	88.90%	100%
Overall	87.65%	98%

Discussion

In this study, maximum number of cases 60 (60%) were between 12-30 years age group. 54 cases were males and 46 cases females.The male to female ratio was 1.17:1.Out of these 100 cases, 51 cases (51%) were confirmed as tubercular, 16 cases (16%) as chronic non-specific lymphadenitis, 14 cases (14%) as lymphomas, 10 cases (10%) as Reactive lymphadenitis and 9 cases (9%) as secondaries.

Table 4: Showing histopathological diagnosis in various studies

Diagnosis	M Karthikrajan *et al.* [10]	Bhavani C *et al.* [11]	Sreenidhi GM et al. [12]	Jha B C et al. [13]	Anastosio Serrano Egae *et al.* [14]	Present study
Tubercular %	51	42.26	72.2	63.8	63.3	51
Chronic nonspecific %	15	9.19	21.11	5.9		16
Reactive %	16	35.47		9.6		10
Hodgkins lymphoma %	10	1.14	4.44	20.7	36.87	5
Nonhodgkins lymphoma %						9
Secondaries %	8	11.32	2.22			9

In various studies conducted in India, benign pathologies consisting tuberculosis, chronic nonspecific lymphadenitis and reactive lymphadenopathy accounts for 77% to 93.3% but in western study by Anastosio Serrano Egae et al. was 63.13%. This reflects malignant cervical lymphadenopathy was more in western population than Indian population. The ratio of non-neoplastic and neoplastic lesions in present study was 3.83: 1. Benign cervical lymphadenopathy was common in India and majority being tubercular lymphadenitis inspite of DOTS and DOTS plus – may be due to Multi Drug Resistant tuberculosis (MDR TB), immunosuppression (HIV and AIDS) and poor patient compliance to antitubercular drugs.

FNAC is most sensitive in diagnosing secondary deposits in neck nodes with sensitivity of 88.9%. FNAC is least sensitive in diagnosing lymphomas with sensitivity of 78.6%.FNAC is 100% specific in diagnosing Tubercular lymphadenitis, Lymphomas and secondary deposits in neck nodes. FNAC is 96% specific in diagnosing chronic nonspecific lymphadenitis and 94% specific in diagnosing Reactive changes in cervical lymph node.

Overall average sensitivity and specificity of FNAC of cervical lymphadenitis is 87.65 % and 98% respectively which is comparable to other studies quoted in table.

Table 5: Sensitivity and specificity of FNAC in Various studies

	M Karthikrajan *et al.* [10]	Jha B C *et al.* [13]	Anastosio Serrano Egae *et al.* [14]	Present study
Sensitivity %	86	92.8	94.1	87.65
Specificity %	100	100	96.9	98

Conclusion

FNAC can be used as a frontline investigation with further investigations on the basis of FNAC result. FNAC was found to be reliable and cheapest method of diagnosis without any significant morbidity and with good patient compliance. The metastatic carcinomas, especially squamous cell carcinoma and tuberculous lymphadenopathy can be diagnosed by FNAC with a high degree of accuracy. Although FNAC is useful in clinical management, there is significant limitation in the diagnosis of low grade Non-Hodgkin's lymphoma from reactive hyperplasia, because of high false negative rate in cases of substantial nonmalignant component but FNAC can assess correctly high grade Non-Hodgkin's lymphoma. Lack of tissue architecture can be overcome on FNAC samples by subjecting them to dual parameter flow cytometry, T-cell, B-cell tumour markers and immunocytochemistry analysis. However, histopathological examination remains the most dependable diagnostic tool

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