

Cytomorphological Analysis of Neoplastic Lesions of Neck Nodes with Special Reference to Lymphomas

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ABSTRACT

Background: Neoplastic lesions of lymph node in cervical region pose a diagnostic delima and very often cytological diagnosis proves invaluable. An early diagnosis of the lesions is essential for proper management. To assess the frequency distribution and cytological analysis of various neoplastic lesions of lymph nodes with special reference to the lymphoma.

Materials and Methods: this is a cross-sectional study which provides analysis of 164 neoplastic lesions of lymph node out of 758 lymph node aspirate. Cytomorphological pattern and cellular detail are reviewed carefully and diagnosis were made. Histopathological and immunohistochemical correlation done wherever needed.

Results: Out of 164 neoplasms 86.59% secondary neoplasms (61.27% SCC, 19.72% Adenocarcinoma, 15.49% poorly differentiated carcinoma, 0.70% undifferentiated carcinoma, 0.70% mucoepidermoid carcinoma, 0.70% papillary thyroid carcinoma, 1.41% leukemic deposit), 12.2% lymphoid neoplasms. M:F = 1.2:1. Diagnostic accuracy was calculated as 98.67%, and false positive rate 1.3%. **CONCLUSION:** fine needle aspiration cytology is invaluable in rapid diagnosis of lymph node neoplasms of cervical region however histological confirmation and immunohistochemical analysis is mandatory in certain tumors specially lymphomas, poorly and undifferentiated carcinoma for accurate diagnosis and proper management.

Keywords: Lymph Node, Neoplasms, FNAC, Histopathology, Immunohistochemistry

Introduction

Lymph nodes are an important part of the immune system. Enlarged lymph nodes are quite common findings in day-to-day practice because lymph nodes become enlarged in a wide spectrum of diseases including infection, inflammatory conditions and malignancy. Management of such cases depends on lymph node pathology which can be studied by collecting material from the lymph node through fine-needle aspiration or excision biopsy. In 1921 Guthrie systematically performed lymph node aspiration for diagnostic purposes.^[1]

Role of FNA cytology in diagnosis of lymph node lesions in patient with persistent lymphadenopathy are to differentiate benign and malignant lesions, differentiate metastatic malignancies and malignant lymphoma, staging of known malignancy and confirmation of a suspected clinical condition like metastatic carcinoma. Aspirated material from lymph node can also be used for immunological marker analysis or studies. The availability of monoclonal antibodies against an increasing number of antigens specific to different cell lines is proving to be of great value in lymph node cytology. It particularly assists the pathologist in identification of source of tumour metastasizing lymph node and in the distinction between undifferentiated carcinoma and malignant lymphoma.

However, FNAC is the first line investigation in a patient with lymphadenopathy.^[2]

Aim of this study is to evaluate the diagnostic efficacy of FNAC in diagnosing neoplastic lesions of neck nodes and find out the most common neoplastic lesions in adult and in paediatric age groups.

Materials and Methods

This is a cross sectional prospective study that provides cytomorphological analysis of cervical lymph node neoplasms at a tertiary centre in North East India, from September 2014 to August 2017. Ethical clearance was obtained from hospital ethics committee. All total 164 neoplastic lesions out of 758 lymph node aspirates (both neoplastic and non neoplastic) were analysed. All cases within age group 0 to >60 years and both sexes are included in the study. All non tumorous benign lesions were excluded from the study. FNAC was performed using a 22 gauge needle. An average two passes were performed and minimum 4 slides were prepared. Two air dried and stained by Giemsa stain, while the remaining two slides were fixed in equal parts of ether and alcohol mixture and then stained with PAP (Papanicolau) stain. Smears showing enough cellular material to provide a diagnosis were considered satisfactory. Fine needle aspiration cytology (FNAC) results were correlated with histological findings whenever

available and immunological marker analysis were done in problematic cases.

All data collected were thoroughly cleaned and entered in to MS- Excel spread sheet and analysis were carried out. Statistical analysis was done to find out the diagnostic accuracy of the FNAC.

Results

164 neoplastic lesions of lymph node were analysed. Most commonly involved age group is 41 to 60 years. Males are more commonly affected than females (M:F = 1.2:1). Frequency distribution of neoplastic lesions in male and female shows highest relative frequency 0.511 and 0.500 can be seen in the age group of 41 to 60 years with simple frequency of 47 and 36 with percentage of frequency 51.000 and 50.000 respectively (Fig. 1).

Most commonly involved group of lymphnodes is deep upper cervical group of lymph nodes.

Out of 164 neoplasms 140 (85.36%) were secondary neoplasms, 20(12.2%) lymphoid neoplasms, 2(1.22%) Langerhan cell histiocytosis, 2 leukemic deposits (1.22%).

Among secondary neoplasms, most commonly occurring neoplasms was squamous cell carcinoma (62.14%). In case of Haematolymphoid neoplasms, most common neoplasm was Non Hodgkins lymphoma (NHL) (50%). (Table 1 Fig 2),(Representative microscopic pictures: Fig 3,4 and 5)

HPE was available in 75 cases, 74 were consistent with cytological diagnosis one was inconsistent, which was diagnosed as reactive hyperplasia of lymph node (False positive). Diagnostic accuracy for malignant tumors of lymphnode was calculated as 98.66% .

We encountered 20 cases (12.2%) of lymphoma. Histopathology was available in 13 tumors (8 NHL,5HL). Out of 8 NHL 7 were consistent with cytological diagnosis, one was inconsistent, which was diagnosed as reactive hyperplasia of lymph node on histopathology(False positive). Immunohistochemistry was possible in 6 cases, 3 were diagnosed as small lymphocytic lymphoma (SLL; CD5, CD20 positive) and 3 were diagnosed as Diffuse large B cell Lymphoma (DLBCL; CD20, BCL2, BCL6 positive). All 5 cases of Hodgkins lymphoma were consistent with cytological diagnosis and were positive for CD 30, CD15.

Table 1: Number of cervical lymph node neoplasms for different age groups in male and female.

Cervical lymph node Neoplasms		
Age in years	Number of cases	
	Male	Female
0 to 20	6	5
21 to 40	17	13
41 to 60	47	36
More than 60	22	18
Sum	92	72
Mean	23	18
SD	±17.340	±13.140
SEM	±8.670	±6.570
N	4	4

Table 2: Cytological diagnosis of the 164 cases of cervical lymph node Neoplasms according to sex.

Different type of cervical lymph node malignancy in male and female		
Type of cervical lymph node neoplasm	No. of cases	
	Male	Female
Metastatic squamous cell carcinoma	47	40
Metastatic adenocarcinoma	10	18
Metastatic poorly differentiated carcinoma	16	6
Metastatic undifferentiated carcinoma	1	0
Metastatic Papillary carcinoma thyroid	0	1
Metastatic mucoepidermoid carcinoma	1	0
Leukemic deposit	2	0

Different type of cervical lymph node malignancy in male and female		
Type of cervical lymph node neoplasm	No. of cases	
	Male	Female
Langerhan cell histiocytosis	1	1
Non hodgkins lymphoma	8	4
Hodgkins lymphoma	6	2
SUM	92	72
Mean	9.200	7.200
SD	±14.242	±12.752
SEM	±4.503	±4.032

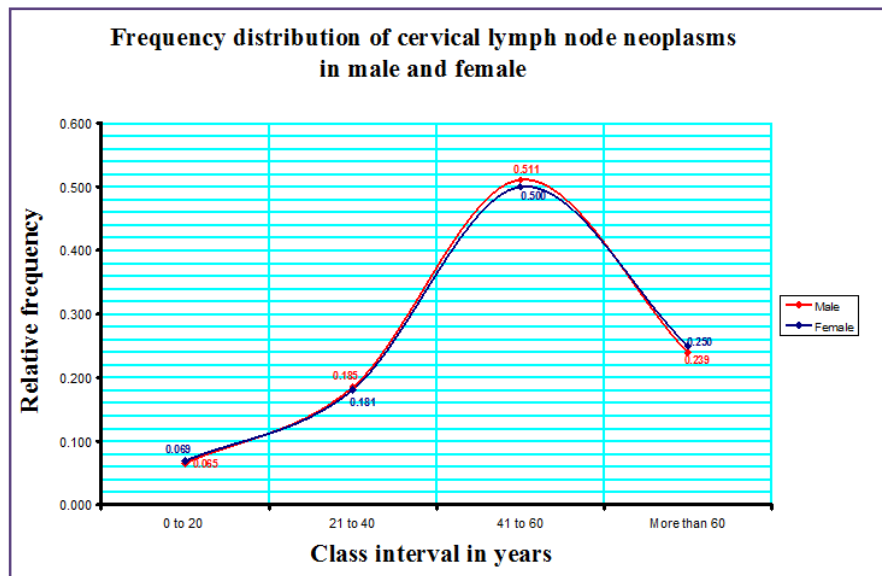


Fig. 1: Relative frequency of cervical lymph node neoplasms in male and female in different age group.

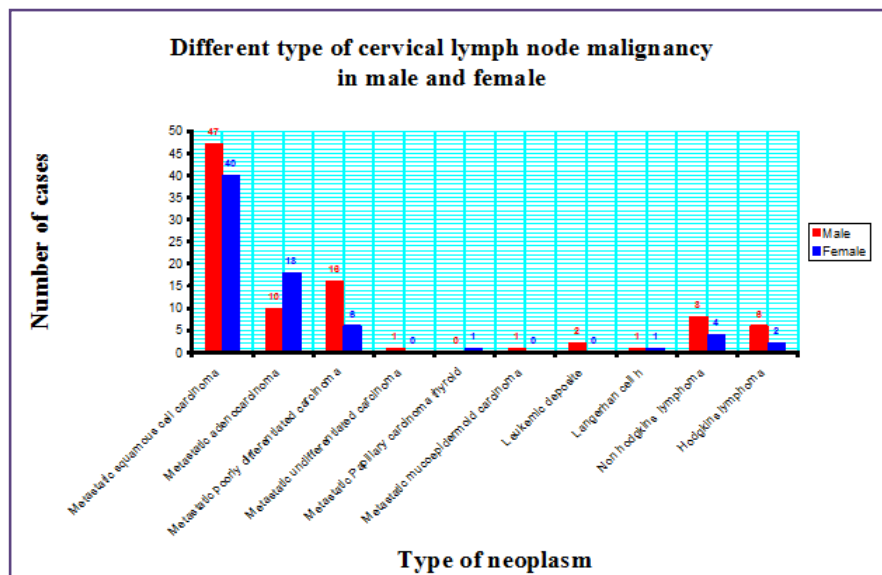


Fig. 2 : Numbers of cases of different types of cervical lymph node neoplasms in males and female.

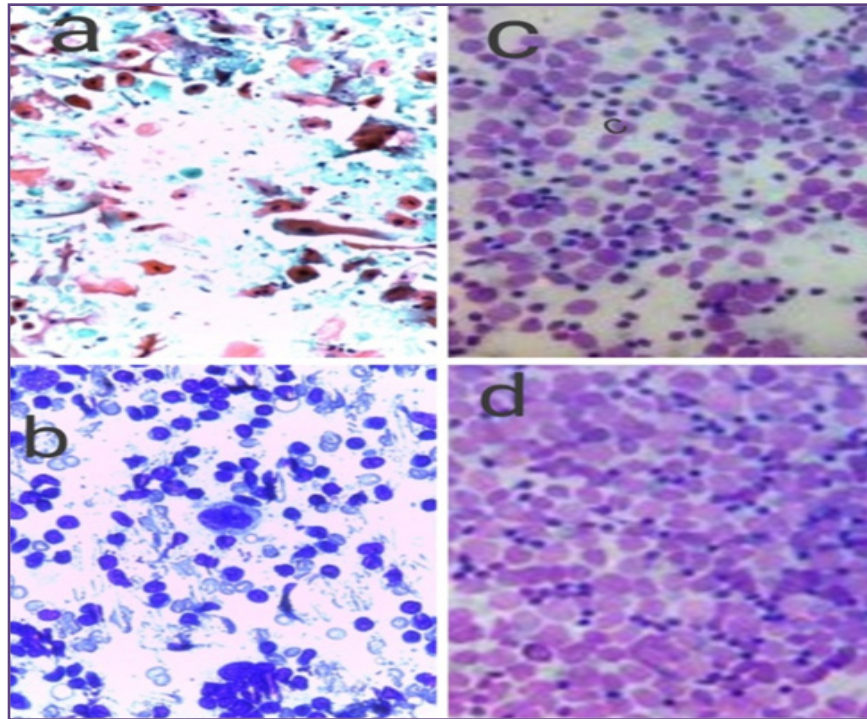


Fig. 3: a.Cytological smear of squamous cell carcinoma.(Pap stain,40X10). b. Cytological smear of Hodgkin's lymphoma (Giemsa stain,40X10) c. Cytological smearof small lymphocytic lymphoma(SLL)(MGG stain,40X10) d. Cytological smear of large cell lymphoma(MGG stain,40X10).

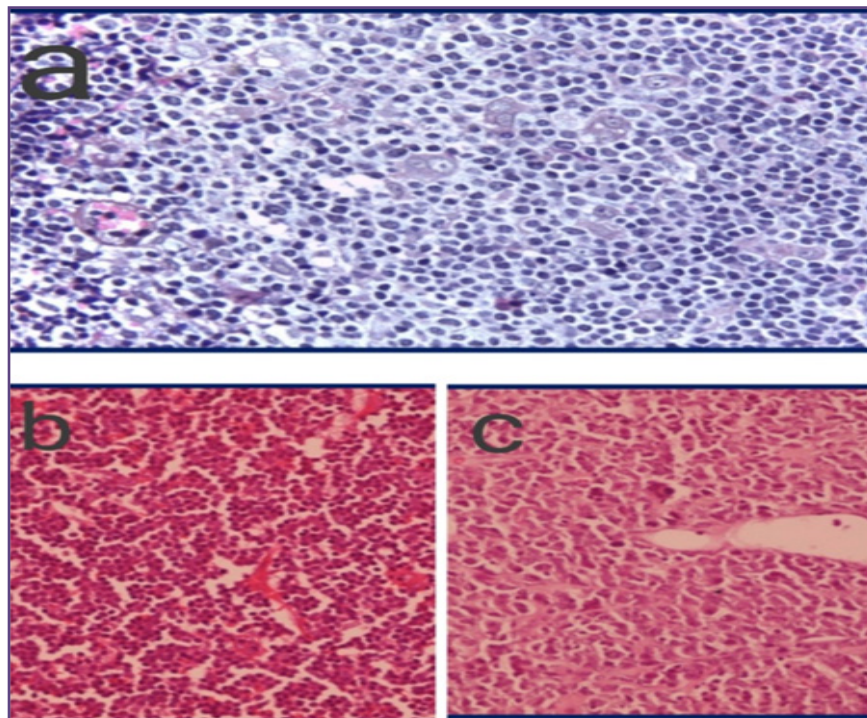


Fig. 4: a. Tissue section of Hodgkins lymphoma(H&E, 40X10), b. Tissue section of NHL(SLL, H&E, 40X10) c. Tissue section of NHL, Large cell lymphoma(H&E,40X10).

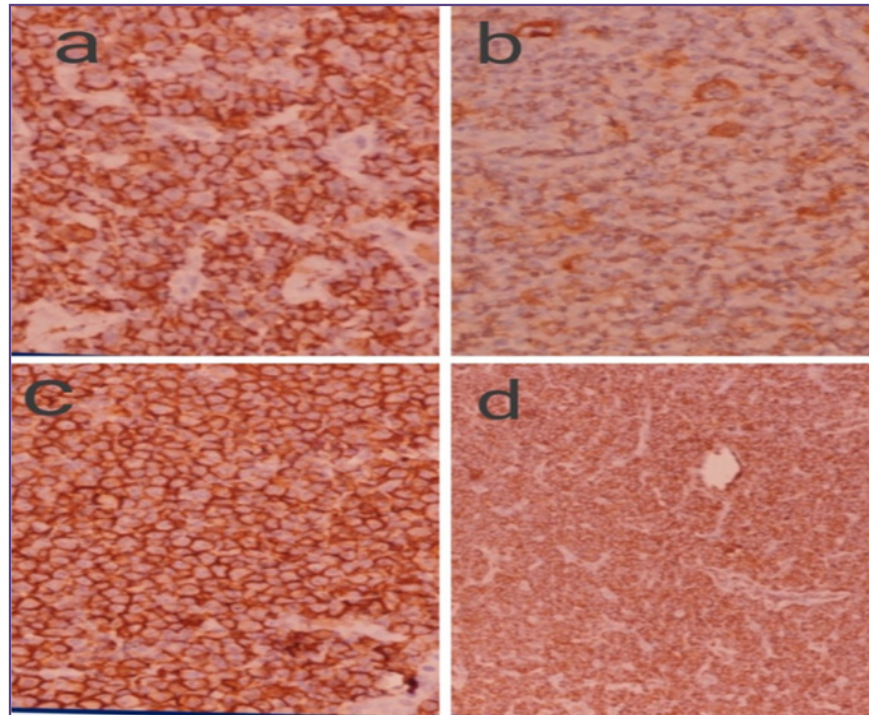


Fig. 5. a. Tissue section of NHL(DLBCL)Bcl2 positive(IHC stain,40X10) b.Tissue section of Hodgkins lymphoma,CD30 positive(IHC stain, 40X10) c. Tissue section of NHL,DLBCL,CD20 positive(IHC stain,40X10) d. Tissue section of NHL,SLL,CD20 positive (IHC stain,40X10).

Discussion

Lymph nodes which are clinically suspicious for metastasis along with lymphomas are one of the most common indications for FNAC. Metastatic lymph nodes are the most commonly encountered lesions in the head and neck. One very important aid in diagnosis of head and neck neoplasm is looking at the neck level involvement.

In cancer of oral cavity and submandibular glands commonly involved group is level 1 group of lymph nodes however upper deep cervical group of lymph nodes are involved in case of malignancy of nasopharynx, larynx, oesophagus, oral cavity and nasal cavity etc.^[3] In the present study upper cervical group (level-2) of lymph nodes (43.29%) are most commonly involved lymph node group.

Metastatic SCC is the most common histological type of carcinoma in the present study (62.14%), rate of which is slightly higher in comparison to some studies.^[4,5,6,7] It may be because of increasing malignancies of oral cavity, pharynx and esophagus in our region, probably due to use of multiple tobacco products.^[8] This needs proper, scientific population based research to evaluate the actual etiological cause. Our findings are similar with the studies done by Raju et al^[9], Melek et al,^[10] Maniyar U Amit et al,^[7]

however findings are somewhat different from I bagwan,^[4] U Jindal et al,^[5] Gunbanti Rathod.^[6]

Cytologically, in differentiated SCC tight clusters or loosely scattered single cells showing various degree of keratinization were seen. Most of the aspirated cells tend to be mature but a careful search for hyperchromatic irregular nuclei showing more malignant features is important for a confident diagnosis. Because in rare occasions, the branchial and epidermal cyst aspirate with its content of mature squamous cells may closely mimic a differentiated metastatic carcinoma.^[10] The less differentiated SCC are more difficult to diagnose, but cells with abundant dense opaque cytoplasm arranged in sheet with occasional keratin pearl formation and giant cell reaction to keratin are useful diagnostic clues. Many metastatic nodes have superadded infection which on FNAC reveals neutrophils, histiocytes, necrotic debris and individual scattered keratinized cell. Differential diagnosis includes acute suppurative pathology, infected branchial and epidermal cysts, necrotic SCC. In those cases re-aspiration from the edge of the mass rather than from the centre is more contributory.^[10,11,12]

In case of metastatic cervical lymph node primary is most often from nasopharynx, pharynx, larynx, esophagus and oral cavity.^[13,14] In the present study, most of the cases had known primary detected in larynx, esophagus, oral cavity

and nasopharynx. However in some case primary was unknown.

Main diagnostic pitfall of FNAC in metastatic SCC is that it can not diagnose subcapsular micro metastasis and extranodal spread cytologically, for which we must correlate with histopathological examination, and immunohistochemistry (IHC) if needed.

Adenocarcinoma is common in females, in most of the cases primary were seen in breast, lung and ovary. Metastatic adenocarcinoma of the head and neck mostly originate from salivary glands and thyroid.. Tandon et al(2008),^[15] Shaha et al(1986)^[16] and Kusum et al(1995)^[11] reported 14.0% 15.21% and 13.87% cases of metastatic adenocarcinoma respectively. Cytologically, in adenocarcinoma the individual cells are usually large cuboidal to columnar with moderate to abundant cytoplasm, often with pale blue extra-cellular mucinous fluid background. Some cells may even exhibit vacuoles with definite signet ring cell morphology. The nuclei are round to oval with irregularly thickened nuclear membranes and prominent nucleoli. Sometimes, it gets increasingly difficult to rule out a poorly differentiated squamous cell carcinoma from adenocarcinoma.^[4]

Poorly differentiated carcinoma and undifferentiated carcinoma (15.4% ; 0.71%) are less common metastatic neoplasms which needs evaluation(IHC, molecular technique) to find out the primary for appropriate treatment. Tippu Ishar et al found 3.12% undifferentiated carcinoma which is higher than our study(0.71%).^[17] We encountered 1.14% of leukemic deposits which is little bit higher than findings of Tippu Isher et al (0.62%).^[17]

The availability of monoclonal antibodies against an increasing number of antigens specific to different cell line is proving to be of great value in lymph node cytology. It particularly assist the cytologist in identification of source of tumours metastasizing lymph nodes and in the distinction between undifferentiated carcinoma and malignant lymphoma.⁽²⁾ Immunohistochemistry (IHC) was advised in two cases of poorly differentiated carcinoma to confirm histopathological diagnosis. It gave 100% diagnostic accuracy.

We encountered 20 cases of lymphoma (12.2%). Percentage of lymphoma in other studies ranged from 4.0% to 19.3%.^[5,12,17] Lymphomas are common in males (M:F=2.3:1). It is more common in 0-20 years followed by 21-40 years. In our study we found 12 cases (60.00%) of non Hodgkins lymphoma (NHL) and 8 cases (40%) of Hodgkins lymphoma (HL). Patra et al (1983)^[18] reported 75% lymphomas as non Hodgkins lymphoma and 25% of

the cases as Hodgkins lymphoma. El Hag et al(2003)^[12] reported 66.66% cases of NHL and 33.33% cases of HL which is comparable to our findings.

In the present study all cases of NHL cytological smears comprised of sheets of singly dispersed monotonous population of lymphoid cells with fine nuclear chromatin & occasional nucleoli. Sometimes it is difficult to differentiate reactive hyperplasia and NHL cytologically, particularly when aspiration are from follicular centre.

There are divergences of opinion regarding role of FNAC on primary diagnosis and sub-classification of NHL on FNAC smears.^[19,20] This difficulty is particularly problematic when less than pure monomorphic lymphocyte population exist (polymorphous population giving picture of reactive hyperplasia of lymph node) in the smears. Again a major disadvantage in the FNA smears is the inability to identify follicular growth pattern which is a major prognostic factor.^[21]

After introduction of WHO classification, the major emphasis has been given on cell morphology and immunophenotype rather than the growth pattern.

We faced some diagnostic difficulties in case of lymphoma. It is difficult to diagnose B cell or T cell lymphomas cytologically. And sub-classification of different type of NHL was problematic because of overlapping of cytological features. Therefore, histopathological examination was advised in all cases. Even in histopathological ground sub-classification of lymphoma was difficult. For confirmatory diagnosis we did selected immunohistochemical (IHC) markers analysis on paraffin block sections to sub-classify NHL and HL. Immunohistochemistry (IHC) gave 100% positivity.

Therefore, FNAC combined with histopathology and IHC is helpful in accurate diagnosis of NHL. According to other authors also, IHC has undisputed value for tumor sub typing in case of lymphomas.

In all five histopathologically positive cases of Hodgkins Lymphoma, Immunohistochemistry was applied. Histopathologically they were classified as classical H.L. All cases were positive for CD15 and CD30.

The cornerstone of cytodagnosis of HL is the findings of Reed-Sternberg(RS)/Hodgkin's cells in an appropriate polymrphous cellular background.^[22] In the present study although Reed-Sternberg (RS) cells were found in all the cases categorized as HL, atypical mononuclear cells with prominent nucleoli apparently outnumbered them and proved to be a better indicator in cytological evaluation.

Conclusion

FNAC is the most valuable method in early detection of lymphnode neoplasms both primary and metastatic neoplasms. Histopathology gives confirmatory diagnosis. However, in case of lymphoma immuno-histochemical analysis is mandatory for its subclassification and accurate diagnosis and treatment.

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