

A Study Of FNAC Findings Of Malignancy In Lymph Nodes With Special Emphasis On Metastatic Malignancy

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ABSTRACT:

Background & Objectives: Fine needle aspiration cytology (FNAC) is a reliable as well as an inexpensive diagnostic method. It is suitable for the developing countries like India for the diagnosis of lymphadenopathy at any approachable site. FNAC not only confirms the presence of metastatic disease, but also in most cases gives the clue regarding the origin of the primary tumor. The aim of the study was to find out the cytological diagnosis of metastatic lymph node lesions. **Methods:** A study was done on all metastatic lymph node lesions reported in Department of Pathology, Government Medical College, and Surat from January 2014 to December 2014. **Results:** In this study 555 cases of lymphadenopathy were analyzed of which 183 (32.9%) cases show evidence of malignant disease. Of these 183 cases 94.5% were metastatic malignancy and 5.5% were lymphomas. Male:Female ratio of 4:1 and age range of 10 yrs to 90 yrs. Cervical group of lymph node 158 (90.8% cases) was most commonly involved. The most common malignancy was metastatic squamous cell carcinoma seen in 128 cases (73.9%). **Conclusion:** FNAC of a lymph node is a very useful, simple and easy tool for diagnosis of metastatic malignancies and in cases of lymphoma it is helpful to guide for further work up.

Key-words: Fine Needle Aspiration Cytology, Lymph node, Metastatic Malignancy.

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INTRODUCTION

Lymph nodes were the first organs to be sampled by fine needle aspiration. FNAC is a primary method of diagnosis in reactive, infective and metastatic lymphadenopathy.¹ Malignancies in lymph nodes in our country are predominantly metastatic in nature with an incidence varying from 65.7% to 80.4% and lymphomas range from 2%.² FNAC not only confirms the presence of metastatic disease, but also gives the clue regarding the nature and origin of primary malignancy. FNAC is useful for the detection of recurrence and new metastasis. Cystic metastasis or aspirate of low grade malignancies compose most of false negative cases.³ Neck lymph node metastasis from occult primary constitutes

about 5-10% of all patients with carcinoma of unknown primary site. Metastasis in the upper and middle neck are generally attributed to head and neck cancers, whereas the lower neck involvement is often associated with primaries below the clavicle.⁴

Metastasis from Upper cervical nodes associated with upper aerodigestive tract, midcervical nodes associated with thyroid carcinoma, salivary gland, upper aerodigestive tract; also thymus or ovary, supraclavicular nodes associated breast or lung, also stomach, pancreas, prostate, testis, metastasis from axillary nodes associated breast (women), melanoma, lung, Metastasis from inguinal nodes associated with external genitalia,

melanoma and Undetectable primaries with nodal metastases associated with nasopharynx, retrotonsillar pillars.⁵ This study was undertaken with the aim of highlighting the role of FNAC's of lymph node in the diagnosis of suspected and unsuspected lymph node malignancy.

MATERIALS AND METHODS

Patients referred to the Department of pathology in Government Medical College, New Civil Hospital, and Surat for evaluation of lymph node enlargement and FNAC from January 2014 to December 2014 were included in the study. Thorough examination of the patients was done and also detailed clinical history was taken. The standard FNAC procedure was performed by using 10 ml disposable syringe and 22-23G needle and smears were prepared. Prepared Slides were stained with May Grunwald Giemsa (dry fixation), Hematoxylin & Eosin (wet fixation) and Papanicolaou (PAP-wet fixation). Slides were immediately fixed in 95% methanol for wet fixation and after air dried for dry fixation. All lymph node aspirates were evaluated and those showing malignant diseases were included in our study. When needed immune-cytochemistry was also used. At 42 cases of FNAC was inconclusive because of low cellularity due to deep seated/ small /fibrous swelling/ prominent cystic component, smear shows blood only and repeat FNAC not possible as patients lost to follow up or give negative consent for repeat FNAC. These cases were excluded from the study.

RESULTS

During the period of study, a total of 183 cases showed evidence of malignant disease on FNAC. Out of the 183 cases studied, 173 (94.5%) were metastatic tumors and 10 cases were suggestive of lymphomas (5.5%). The ratio of males to females was 4:1. The age of the patients ranged from 10 yrs to 90 yrs. The incidence was seen to peak at the age above 50 years showing 100 cases (57.8%), followed by 42

cases (24.3%) in the age group 41 to 50 years. There were 31 cases (17.9%) below 40 years of age. Table-1 shows the cytological diagnosis made on the lymph node aspirates. Squamous cell carcinoma 128 (73.9%) was the most common metastatic tumor in our study (Fig. 1). The cases where cytological features were not classical of squamous cell carcinoma or adenocarcinoma were put in the category of poorly differentiated malignancy 18 (10.4%). In our study adenocarcinoma was seen in 5 (2.8%) cases. (Fig.2)

In our study, metastatic ductal carcinoma was seen in 8 (4.6%) cases where all the female patients presented with breast lumps. One case had axillary, supraclavicular lymphadenopathy. Among the thyroid carcinoma metastases, we noted 1 (0.6%) case of papillary carcinoma of thyroid. This case was presented with the thyroid swelling and lymph node enlargement, and hence the metastasis from papillary carcinoma could be diagnosed. (Fig 3A & 3B) In our study, we noted 1 (0.6%) case of metastasis from mixed germ cell tumors. This case was a previously diagnosed as a case of seminoma of the testis, who later presented with multiple cervical and supraclavicular lymph node enlargement, and hence the diagnosis of metastasis from mixed germ cell tumors was offered. The smears showed two cell populations, macro nucleoli at places & scant /vacuolated/eosinophilic cytoplasm. The background was tigroid with scattered lymphocyte. (Fig 4)

In the present study, 1 (0.6%) case showed metastatic melanoma in inguinal lymph nodes. Metastatic small cell carcinoma was seen in 2 (1.2%) cases where the patient had a suspicious mass lesion in the lung. In our study, we noted 2 (1.2%) cases showed cytological features of malignant small round cell tumor and 3 (1.7%) case of nasopharyngeal carcinoma. 1 (0.6%) case of metastatic neuroendocrine carcinoma presented with cervical swelling. In our study, we noted 1 (0.6%) case of Pleomorphic carcinoma/sarcoma. This case

was presented with multiple cervical lymph node and swelling over the chest wall. The smears are extremely cellular with little tendency for the malignant cells to aggregate. An admixture of small round cells with high nucleo-cytoplasmic ratios, large spindled or polygonal cells with scant to moderate volumes of cytoplasm, and numerous bizarre tumor giant cells may be observed. The most common entities in the differential diagnosis are pleomorphic carcinomas of diverse sites and sarcomas. (Fig 5)

In the present study diagnosis of lymphoma/leukemia was suggested in 10 cases. Out of which 6 cases were of suspicious/suggestive of Hodgkin's lymphoma, 2 cases were of suspicious/suggestive Non Hodgkin's lymphoma and 2 cases were known cases of leukemia so a diagnosis of leukemic infiltration was offered. Further work-up for confirmation of the diagnosis was advised in all cases. Table-2 showed that the most common group involved by metastasis was cervical group 157 (90.8%) cases. The most common type of metastasis in cervical group was squamous cell carcinoma, whereas in the supraclavicular node, adenocarcinoma was the most common type. In the axillary nodes, carcinoma breast was the most common.

DISCUSSION

FNAC is of considerable value in the documentation of metastasis in known primary, occult tumors and disease staging. FNAC is a reliable diagnostic tool as it has less complication is a simple procedure and can be repeated easily. More than 90% of lymph node metastasis are diagnosed by initial aspiration.³ We have studied 173 cytologically diagnosed cases of lymph node metastasis. The commonest group of lymph node metastasis was cervical group, 157 cases (90.8%). These findings correlated with a study by Dowerah et al (67.5%),¹ Wilkinson et al (62%),² Mohanty et al (58.2%)⁶ and Mohan et al (57.6%).⁷ Maximum numbers of cases were in the age

group of 51-70 years, which are 91 cases (52.3%) followed by age group of below 50 years (42.5%). This was comparable to Mamatha et al.⁴

Out of 173 cases, 138 (79.8%) were males and 35 (20.2%) were female patients. Male to female ratio was 4:1. These findings were similar to studies done by Dowerah et al (2.6:1),¹ Wilkinson et al (1.5:1)² and Babu et al (6.8:1)⁸ but Ghartimagar et al³ noted the incidence of metastasis were more in female (54 cases, 58%) as compared to male (39 cases, 42%) with male to female ratio 1:1.25. This variation may be due to different study population or geographic variation, genetic factors, environmental factors like association between stomach cancer person who work in coal mining and those who work processing, timber, nickel, rubber and habitual factor like a high intake of salt preserved food smoking, reduced fruit or vegetable intake, drinking habits, barbecued or grilled cooking in Nepal.

In our study, the percentage of metastasis (94.6%) was much higher than that of lymphomas (5.4%). In a study by Wilkinson et al² the percentage of metastatic disease was 90% and lymphomas comprised 5%, which was similar to our study, however, Bosch et al⁹ found higher cases of lymphomas 67.5% and 32.5% metastatic tumors. This variation may be due to different study population, geographic variation or in our set up the most of the patients were from lower socioeconomic status presented late in the metastatic disease. Squamous cell carcinoma 128 (73.9%) was most common microscopic varied in our study. These findings correlated to study done by Mamatha et al (56%),⁴ Mohan et al (52.8%),⁷ Babu et al (70.6%),⁸ Adhikari et al 41.8%¹⁰ however Ghartimagar et al³ noted most common malignancy was adenocarcinoma seen in 67%. This correlates with higher rates of cancers of upper aerodigestive tract in India, possibly due to the habit of smoking, tobacco chewing, Areca nut chewing and alcohol consumption in the Indian population.

In squamous cell carcinoma tumor cells are seen mostly in sheets and singly scattered. The cells had dense cytoplasm with hyperchromatic nuclei in Giemsa stain and the cells show cytophilic or orangeophilic cytoplasm with pyknotic nuclei in PAP stain. In well differentiated squamous cell carcinoma, the tumor cells show individual cell keratinization. The tumor cells often show necrotic material in the background. So in case of scanty cellularity with abundant necrotic material, a careful search for the tumor cells is required.^{11,12} In our study, adenocarcinoma was seen only in 5 (2.8%) cases (Fig.2). These findings are well correlated with Wilkinson et al study,² however Ghartimagar et al³ noted, most common malignancy was adenocarcinoma seen in 67%. Often it becomes difficult to distinguish between adenocarcinoma and poorly differentiated squamous cell carcinoma when the cell clusters show thick nuclear membrane and prominent nucleoli. Cells with abundant clear cytoplasm also raise a suspicion of metastasis from the renal tumors.³

In our study 1 cases of papillary thyroid carcinoma showed a metastatic deposit in lymph nodes (Fig.3A and B). Although certain typical nuclear alterations (nuclear overlapping along with the characteristic vesicular nuclei with nuclear grooving and intranuclear inclusion) help define PTC; none of them are diagnostic of PTC in isolation. Accurate diagnosis of papillary carcinoma, therefore, depends upon recognition of the combination of the most common features. A papillary architecture may be present but is not required for the diagnosis.^{13,14,15}

In the present study out of total 128 cases of squamous cell carcinoma are showing 52 (40.6%) cases shows cystic changes and 7 cases show granulomatous reaction. It has been observed that certain squamous cell carcinoma sub-sites more commonly produce metastasis that are cystic. Presence of keratinous debris and foreign body giant cell formation indicates

the possibility of keratinising squamous cell carcinoma. The aspiration of metastatic lymph-nodes with cystic changes often become hypocellular due to the presence of fluid. Any centrifuged deposits should be carefully examined for any malignant cells. A repeat aspiration from any palpable mass left after aspiration of fluid may yield cellular material. An image guide FNAC from the solid area of the swelling can also be helpful.¹² Smears with polymorphs and necrosis could be misdiagnosed as abscesses or suppurative lymphadenitis. The smear with granuloma and necrosis could be misdiagnosed as a granulomatous lymphadenitis. These cases should be carefully examined for any malignant cells in proper clinical context.¹¹

CONCLUSION

FNAC of lymph nodes is a very useful, simple and effective diagnostic tool in the evaluation of lymph-node malignancies. Fine needle aspiration cytology not only confirms the presence of metastatic disease but also help to detect occult primary malignancy. It has been observed that certain squamous cell carcinoma sub-sites more commonly produce metastasis that are cystic. Smears with polymorphs and necrosis could be misdiagnosed as abscesses or suppurative lymphadenitis. The smear with granuloma and necrosis could be misdiagnosed as a granulomatous lymphadenitis. In these cases repeat FNAC should be performed to rule out metastasis from squamous cell carcinoma. For the diagnosis of lymphomas, it can suggest a preliminary diagnosis, which can be followed by histopathology for confirmation. Hence the cytopathologist plays an important role in the diagnosis of lymph node malignancies.

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Table 1: Cytological diagnosis of aspirated lymphnodes and their frequency			
Sr.	Pathological subtypes	No. of cases	Percentage
1	Carcinoma	2	1.2%
2	Squamous cell carcinoma	128	73.9%
3	Ductal Carcinoma of breast	8	4.6%
4	Poorly differentiated malignancy	18	10.4%
5	Adenocarcinoma	5	2.8%
6	Small cell carcinoma	2	1.2%
7	Neuroendocrine Carcinoma	1	0.6%
8	Malignant Round cell tumor	2	1.2%
9	Papillary carcinoma of thyroid	1	0.6%
10	Pleomorphic carcinoma/sarcoma	1	0.6%
11	Mixed germ cell tumor	1	0.6%
12	Malignant Melanoma	1	0.6%
13	Nasopharyngeal carcinoma	3	1.7%
	TOTAL	173	100%

TABLE 2 Distribution according to site and type of malignant lymph node lesions					
Cytological diagnosis	Cervical LN	Axillary LN	Inguinal LN	Supraclavicular LN	Total
Carcinoma	2	0	0	0	2
Squamous cell carcinoma	126	0	2	0	128
Ductal Carcinoma of breast	0	8	0	0	8
Poorly differentiated Malignancy(carcinoma)	18	0	0	0	18
Adenocarcinoma	1	0	1	3	5
Small cell carcinoma	2	0	0	0	2
Neuroendocrine Carcinoma	1	0	0		1
Malignant Round cell tumor	2	0	0	0	2
Papillary carcinoma of Thyroid	1	0	0	0	1
Pleomorphic carcinoma/sarcoma	1	0	0	0	1
Mixed germ cell tumor	0	0	0	1	1
Malignant Melanoma	0	0	1	0	1
Nasopharyngeal carcinoma	3	0	0	0	3
Total	157	8	4	4	173

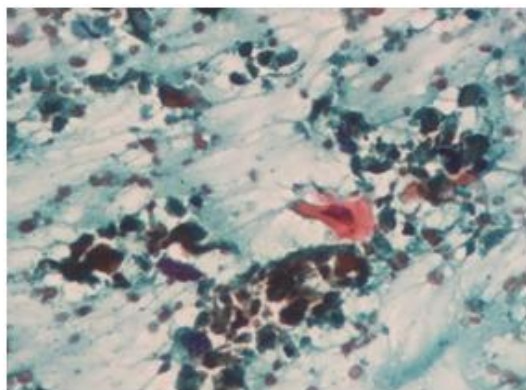


Figure 1: Cytology smear from squamous cell carcinoma showing scattered malignant squamous epithelial cells with dense cytoplasm along with necrotic debris (PAP, X40)

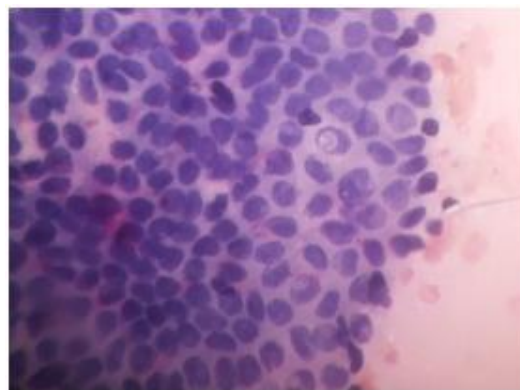


Figure 3B: Cytology smear from papillary carcinoma showing intra-nuclear inclusion. (H&E, X100).

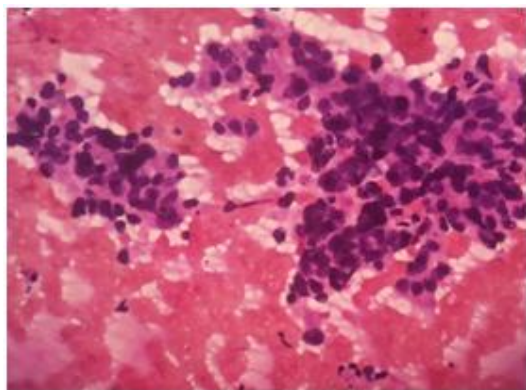


Figure 2: Cytology smear from a denocarcinoma showing malignant cells arranged in clusters and forming acini at places (H&E, X40).

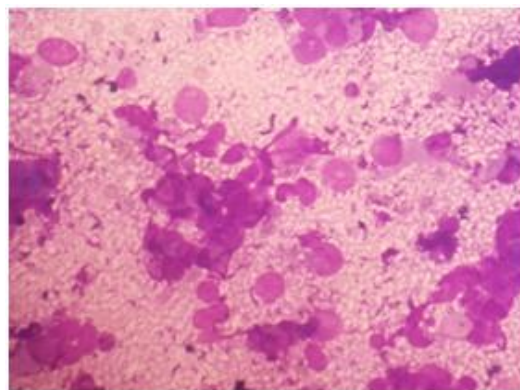


Figure 4: Cytology smear from mixed germ cell tumor showing malignant cells having high N: C ratio and tigroid background (MGG, X40)

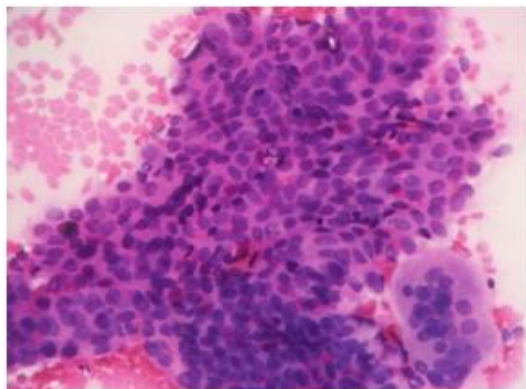


Figure 3A: Cytology smear from papillary carcinoma showing papillaroid fragments with anatomical borders and giant cell reaction. (H&E, X40).

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