



## Clinicocytological study in evaluating the primary site of tumor in patients presenting with metastatic tumors in lymph node

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### ABSTRACT

Enlarged lymph nodes are easily accessible for fine needle aspiration cytology (FNAC) and plays major role in diagnosis of primary and secondary malignancies. Correct diagnosis of metastatic tumors by FNAC saves patient from invasive and costly diagnostic procedures and helps the surgeons to formulate therapeutic strategy in treatable primary tumors.

Patients presented with palpable lymphadenopathy and suspicious of metastasis referred for cytological evaluation and cytologically diagnosed as metastatic lymphadenopathy from September 2011 to September 2013 were collected. Thorough examination of the patients and detailed clinical history was taken. Multiple smears were studied and clinicocytological correlation was done to find out the primary tumor.

Total number of cases studied was 64. The commonest group of lymph node was cervical followed by axillary and inguinal group. Maximum number of cases was in the age group of 50-70 years Male to female ratio was 1.4:1. Nasopharynx was the commonest primary site followed by breast. In 11% cases tongue was primary site and in 5% cases esophagus. Oropharynx and larynx was primary in 2 cases. Primary from lung, parotid and perennial skin was noted in 1 case each. Histopathological follow-up was available in 30 cases. Histopathological correlation of cytologically confirmed primaries showed concordance in 28 cases and 2 cases were discordant

FNAC is rapid and safe technique. Thorough clinicocytological evaluation is effective method to detect the primary tumor and act as cost effective diagnostic procedure. Hence this study was done to evaluate the utility of clinicocytological study in diagnosis of primary in metastatic lymphadenopathy.

### INTRODUCTION

Enlarged lymph nodes are easily accessible for fine needle aspiration cytology (FNAC) and are of importance especially for diagnosis of primary as well as secondary malignancies.<sup>[1]</sup> It plays significant role in developing countries like India, as it is a cheap and simple procedure and has almost no complications.<sup>[2]</sup> Sometimes diagnosis given on cytological material is accepted as the only diagnosis without histopathological correlation especially in advanced malignancies. It also provides clues for occult primaries and sometimes also surprises the clinician who does not suspect a malignancy.<sup>[1]</sup>

Localizing the primary malignant tumor in metastatic lesions helps in more specific and effective treatment.<sup>[3]</sup> However identification of primary site in patients presenting with

metastatic tumor requires extensive and exhaustive investigations. Such strategy costs patient a longer hospital stay with the experience of painful and distressing investigations and it also leads to an unacceptable cost effectiveness ratio to the health care system.<sup>[4]</sup> Diagnosis of primary site in patients presenting with metastatic tumors is a challenging task for the clinicians and cytopathologists. If careful evaluation of clinical presentation is done and correlated with the cytological features of the metastatic lesion, it provides better clue of the primary and helps in early detection and specific management of the lesion.<sup>[5]</sup> It also saves patient from invasive and costly diagnostic procedures.<sup>[1,4]</sup>

Neck lymph node metastases from occult primary constitute about 5%-10% of all patients with carcinoma of unknown primary site. Metastases 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.<sup>[6]</sup> Most frequent cytological finding in neck lymph node metastasis is squamous cell carcinoma, particularly when the upper neck is involved. Thoracic and abdominal primaries especially from lung, esophagus, stomach, ovary or pancreas should be sought in case of involvement of lower neck lymph node with cytological features of adenocarcinoma.<sup>[1,6]</sup>

Hence this study was done to emphasize the role of cytological study and correlation of clinical presentation in evaluating the primary site of tumor in patients presenting with metastatic tumors in lymph node.

## MATERIALS AND METHODS

Patients referred to the Department of pathology in BLDEU'S Shri B.M.Patil Medical College, Hospital and Research centre, Bijapur for evaluation of metastatic lymph node enlargement and cytologically diagnosed as metastatic malignancy from September 2011 to September 2013 were included in the study. Inclusion criteria were all patients clinically presented with metastatic lymphadenopathy and cytologically diagnosed as metastatic tumor. Exclusion criteria were patients clinically presented with metastatic lymph node but cytologically diagnosed as reactive lymph node.

Thorough examination of the patients was done and also detailed clinical history was taken. Standard FNAC procedure was performed by using Cameco syringe pistol with 10ml disposable syringe and 22-23G needle and multiple smears were prepared. Smears fixed in absolute alcohol were stained with Haematoxylin and Eosin (H&E) and Papanicolaou stains while air dried smears were stained with May-Grunewald Giemsa (MGG) stain. Histopathological follow-up and immunohisto-

chemistry markers study such as CK 7 and CK 20 was done on histopathology specimens wherever feasible. Chi square test was applied to evaluate the efficacy of cytological study and clinical correlation in diagnosis of primary tumors in patients presenting with metastatic tumors.

Ethical committee clearance was obtained from institutional ethical committee on 20.10.2011

## RESULTS

Total number of cases studied for clinicocytological diagnosis of metastatic lymph node tumors were 64. The commonest group of lymph node was cervical group seen in 49 cases constituted to 77% of cases followed by axillary group in 12 (18%) and inguinal group in 3(5%) cases. Maximum number of cases was in the age group of 50-70 years amounting to 54.6% followed by age group of 71-90 years constituting to 23.5%. Out of 64 cases, 38(60%) were males and 26 (40%) were female patients. Male to female ratio was 1.4:1.

In our study, hoarseness of voice, cough, difficulty in swallowing was the commonest clinical presentation in 37 cases (57.8%) followed by general deterioration and weight loss in 27(42.2%) cases.

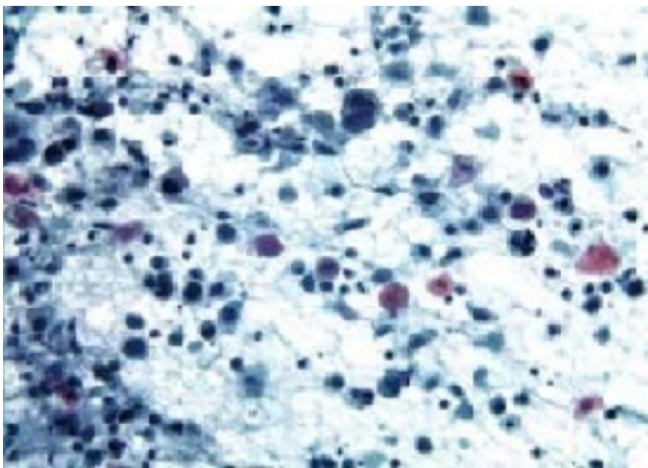
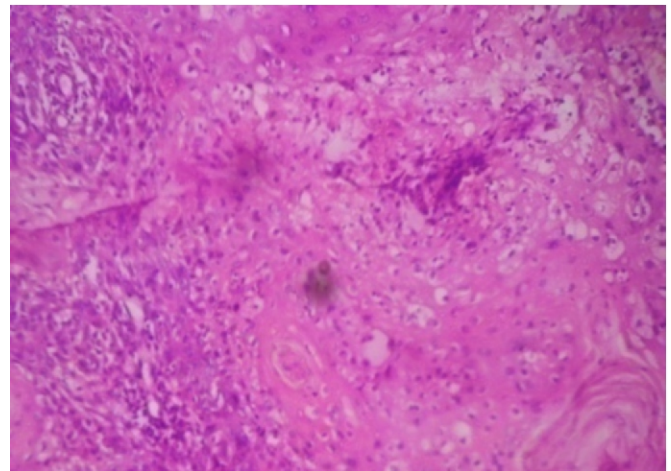
Out of 64 lymph node metastases, nasopharynx was the commonest primary site amounting to 22 cases (34%) followed by breast in 21 cases (33%). In 7 cases (11%) tongue was the primary site and in 3 cases (5%) esophagus. Oropharynx and larynx was primary in 2 cases each amounting to 3%. Primary from lung, parotid and perianal skin was noted in 1 case (1.5%) each. In 4(6.5%) cases primary couldn't be given on cytology. (Table-1)

**Table 1.** Distribution of primary sites in lymph node metastases given on cytology (n=64)

Sl.No	PRIMARY SITE	NUMBER OF CASES	PERCENTAGE (%)
1	NASOPHARYNX	22	34
2	BREAST	21	33
3	TONGUE	07	11
4	OESOPHAGUS	03	5
5	OROPHARYNX	02	3
6	LARYNX	02	3
7	LUNG	01	1.5
8	PAROTID	01	1.5
9	PERIANAL SKIN	01	1.5
10	UNKNOWN	04	6.5
	<b>TOTAL</b>	<b>64</b>	<b>100%</b>

**Table 2.** Analysis of discrepancies between clinicocytological and histopathological diagnosis of primary site (n=30)

Clinicocytological diagnosis of primary	Number of cases	Histopathological Diagnosis of primary	Number of cases
Invasive ductal carcinoma Breast	16	Invasive ductal carcinoma Breast	16
Squamous cell carcinoma Nasopharynx	05	Squamous cell carcinoma Nasopharynx	05
Squamous cell carcinoma Tongue	02	Squamous cell carcinoma Tongue	02
Squamous cell carcinoma larynx	02	Squamous cell carcinoma larynx	02
Malignant Melanoma Skin	01	Malignant Melanoma Skin	01
Unknown	02	Non Hodgkin Lymphoma	02
Unknown	02	Unknown	02
<b>TOTAL</b>	<b>30</b>		<b>30</b>

**Fig.1** Photomicrograph of metastatic squamous cell carcinoma in lymph node on cytology. (Pap stain. 40x)**Fig. 2** Photomicrograph of primary Squamous cell carcinoma nasopharynx on histopathology. (H&E stain. 10x)

Histopathological follow-up was available in 30 cases. Out of 30 cases, in 28 cases concordance was noted between cytological and histological diagnosis and 2 cases were discordant. (Table-2)

## DISCUSSION

The use of FNAC for the diagnosis of metastatic malignancies in the lymph node is a well established method.<sup>[7,8]</sup> FNAC not only confirms the presence of metastatic disease, but also gives the clue regarding the nature and origin of primary malignancy.<sup>[9]</sup> We have studied 64 cytologically diagnosed cases of lymph node metastasis. The commonest group of lymph node metastasis was cervical group followed by axillary group and inguinal group. These findings correlated with a study titled as FNAC - a handy

tool for metastatic lymphadenopathy done by Alam et al<sup>[10]</sup>, in which cervical group (72.2%) was the commonest metastatic group of lymph nodes followed by axillary group (9.5%). These findings were also correlated with the other studies done by Chhatray and Acharya<sup>[11]</sup>, Frable WJ et al<sup>[12]</sup> and Shamim S et al<sup>[11]</sup>.

Maximum number of cases was in the age group of 50-70 years amounting to 54.6% followed by age group of 71-90 years constituting to 23.5%. Out of 64 cases, 38 (60%) were males and 26 (40%) were female patients. Male to female ratio was 1.4:1. These findings were similar to studies done by Wilkinson AR et al<sup>[13]</sup> in which out of 50 cases 60% were males and 40% were females. Males were also predominated in the study done by

Shamim S et al<sup>[1]</sup> in which 70% were male patients and 30% were female patients.

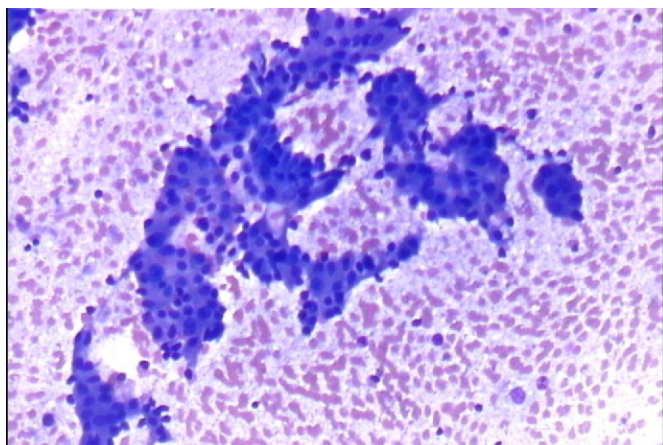
In our study nasopharynx was the commonest primary site followed by breast. In 7 cases (11%) tongue was the primary site and in 3 cases (5%) esophagus. Oropharynx and larynx was primary in 2 cases each amounting to 3%. Primary from lung, parotid and perennial skin was noted in 1 case (1.5%) each. Nasopharynx, larynx together with oral cavity was the commonest primary in our study. These findings were similar to studies done by Shamim S et al<sup>[1]</sup> in which oral cavity, pharynx and larynx constituted the commonest primary. These findings were also similar to Alam et al<sup>[10]</sup> study in which mouth and oropharynx constituted the commonest primary. But our findings differ from study done by Ghartinagar D et al<sup>[7]</sup> in which lung was the commonest primary followed by stomach, colon and rectum. Squamous cell carcinoma (56%) was most common microscopic variant in our study followed by infiltrating carcinoma breast (32.8%), poorly differentiated carcinoma in 4 cases (6.25%). These findings correlated to study done by Alam et al<sup>[10]</sup> in which 67% cases were squamous cell carcinoma followed by breast (11%) and adenocarcinoma. This finding also correlated with Wilkinson AR et al<sup>[13]</sup> study in which 40% cases were squamous cell carcinoma followed by breast in 20% of cases, 8% of thyroid carcinoma, 4% each of adenocarcinoma, and malignant

melanoma. However in our study, adenocarcinoma was seen only in 1.5% cases and also one each cases of malignant melanoma and anaplastic carcinoma thyroid was noted.

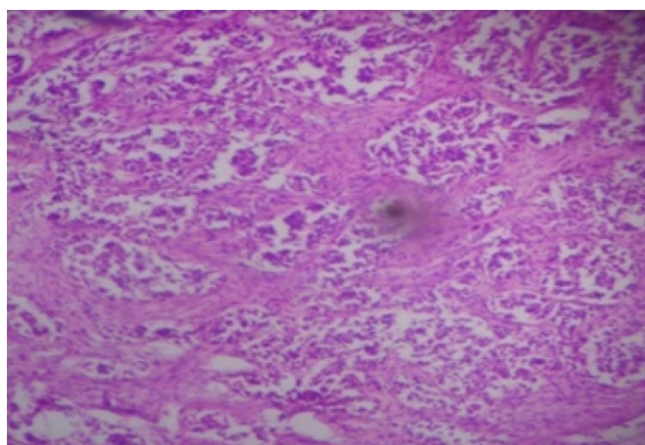
In our study cytological smears diagnosed as metastatic squamous cell carcinoma showed isolated cells/clusters of keratinizing malignant squamous cells with or without evidence of keratin formation. Cells also showed distinct cell borders, hyper chromatic nuclei with coarse chromatin. Eosinophilic keratinized cells were better appreciated by pap staining (Figure-1 & 2). Similar findings were seen in study done by other authors.<sup>[10,14,15,16]</sup> Also these patients presented clinically with hoarseness of voice, cough and difficulty in swallowing.

Cytological smears diagnosed as infiltrating ductal carcinoma breast showed cells arranged in cohesive groups of various sizes. The cell groups were either arranged in ball like clusters, papillary fragments or acini with central lumina. Cells showed eccentric nucleus with prominent nucleoli and evidence of mucin production in the form of cytoplasmic vacuolation which correlated with the findings mentioned by other authors.<sup>[17]</sup>(Figure-3 & 4) Most of these patients clinically presented with lump in the breast.

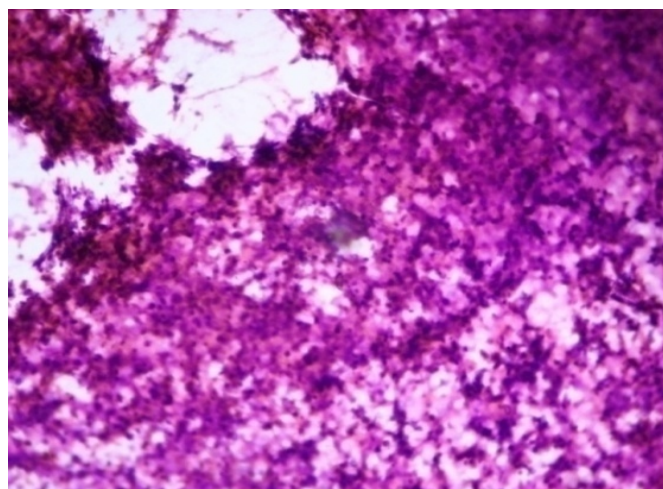
Cytological smears from metastatic melanoma showed large pleomorphic cells with prominent nucleoli and intracellular or



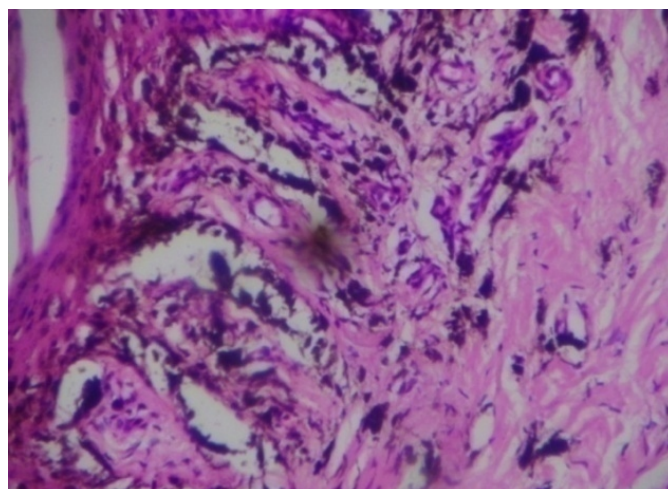
**Fig. 3** Photomicrograph of metastatic carcinoma breast in lymph node on cytology. (MGG stain 20x)



**Fig. 4** Photomicrograph of primary ductal carcinoma of breast on histopathology (H&E stain 10x)



**Fig. 5** Photomicrograph of metastatic malignant melanoma in lymph node on cytology (H & E stain .20x)



**Fig. 6** Photomicrograph of primary malignant melanoma of skin on histopathology. (H&E stain.10x)

extracellular melanin. The presence of fine, granular melanin pigment in the cytoplasm was helpful in identifying melanoma. This patient presented with inguinal lymphadenopathy. Cytological diagnosis of metastatic malignant melanoma was given after thorough clinical examination. Patient also gave history of perennial growth for which excision was done and histopathology of which revealed features of malignant melanoma. (Figure 5 & 6) In 4 cases of cervical lymphadenopathy, cytology showed large pleomorphic cells in sheets and clusters with high nuclear cytoplasmic ratio, prominent nucleoli and scant to moderate cytoplasm.<sup>[10]</sup> In these cases primary couldn't be detected even after thorough clinical examination and patients were presented with only cervical lymph node enlargement. Hence diagnosis of metastatic poorly differentiated carcinoma was given. Out of 4 cases, in 2 cases histopathological follow-up was available. In these cases on histopathology, differential diagnosis of poorly differentiated carcinoma and Non Hodgkin lymphoma was given (Figure 7 & 8). For these cases IHC markers such as CK7 and CK 20 was done which were negative and hence concluded as Non Hodgkin lymphoma. Thus a systematic clinicomorphological approach can frequently help to narrow down the list of differential diagnosis to a few likely primary tumor sites that can be confirmed.

### CONCLUSION

FNAC is a rapid, safe and cost effective technique in determining the primary site. Thus thorough clinicocytological evaluation is effective diagnostic method to detect the primary tumor with cost effective diagnostic procedures.

Cytology evaluation along with proper clinico-radiological correlation is quite useful in diagnosing metastasis with good degree of certainty. To conclude, in developing countries FNAC is a cheap, quick and reliable method to assess primary site in metastatic lymphadenopathy.

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