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Original Article

Diagnostic Accuracy of Fine Needle Aspiration Cytology (FNAC) in Metastatic Lymphadenopathy

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Abstract

Objective: To determine the diagnostic accuracy of Fine needle aspiration cytology (FNAC) in metastatic lymphadenopathy, using histopathology of the same lymph node as a gold standard

Study Design: Cross sectional study

Setting: Department of Pathology, Pakistan Institute of Medical Sciences (PIMS), Islamabad

Duration of study: Samples were collected from 13th April, 2011 to 09th February, 2013

Methodology: After getting adequate clinical data, patients underwent FNAC. The slides were stained with Hematoxylin and Eosin (H&E), evaluated according to the set criteria and compared with histopathological slides

Results: All of the 54 cases were found to be lymph node lesions. Mean age was 45.17± 17.1 years. Male to female ratio was 1:1.08. Most of the smears were hypercellular. Most common metastatic tumor was Metastatic Squamous Cell Carcinoma (51.85%), followed by Metastatic Adenocarcinoma (7.41%). In 38 cases, the involved lymph node was found to be cervical, followed by supraclavicular lymph node which was involved in 9 cases. Axillary and inguinal lymph nodes comprised 4 and 3 cases respectively. A strong correlation was found between the diagnosis made by fine needle aspiration cytology and the final histopathological diagnosis. The sensitivity and specificity of FNAC came out to be 97.37% and 93.75% respectively with an overall diagnostic accuracy of 96.29%.

Conclusion: Fine needle aspiration cytology (FNAC) is a useful diagnostic test in metastatic lesions of lymph nodes because it is rapid, simple and inexpensive and has high diagnostic accuracy.

Key words: Fine needle aspiration cytology, FNAC, Lymph node, Lymphadenopathy, Metastasis.

Introduction

Lymph node is a common site of many primary and metastatic diseases. In an adult patient, the first presenting clinical sign of non-hematologic malignancy may be lymphadenopathy. Due to high prevalence of tuberculosis many cases of lymphadenopathy turn out to be infective in nature but still metastatic disease as a cause of cervical lymphadenopathy is not a rare finding.[1]

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Fne needle aspiration cytology (FNAC) is a safe, reliable, well tolerable, quick, economic and effective diagnostic technique.[2] It can be performed in the Out Patient Department (OPD), at patients' bedside or intra-operatively where an incisional biopsy may be risky. Nowadays the diagnosis of metastatic disease via FNAC is a well-established method.[3]

Diagnosis deciphered by FNAC has an impact on the overall management of patient and allows for appropriate early planning of treatment; however, sampling and interpretation errors may oc-

cur.[4] Although, FNAC is very handy in pre-operative assessment of patients but its interpretation requires solid knowledge of histology and awareness of certain limitations due to pathological variations in architecture and cellular patterns in different diseases.[5, 6]

Although open biopsy followed by histological examination of excised lymph node still remains the standard practice for diagnosing lymph node neoplasia, yet FNAC does constitute one of the most common indications for metastatic lymphadenopathy. FNAC can easily confirm the metastatic nature of disease and even provide clues to the site of primary tumor.[7]

The results of FNAC are comparable with those of tissue biopsies and in some situations the aspirate has equal characteristics of a micro-biopsy.[8] In a few instances, FNAC may even be superior to the other techniques in practice as multiple passes sample wider areas and there is better preservation of cells due to lack of artifacts emanating from tissue fixation, processing and cutting.

The sensitivity and specificity of FNAC in metastatic lymphadenopathy is 97.9% and 100% respectively, whereas the prevalence of metastatic lymphadenopathy is 35%.[9,10]

Our study was designed to evaluate the role of FNAC in accurately diagnosing metastatic lesions of lymph nodes in an environment like ours with limited resources.

Methodology

The study was conducted in the Department of Pathology, Pakistan Institute of Medical Sciences (P.I.M.S), Islamabad from 13th April, 2011 to 09th February, 2013. The total sample size of this cross sectional study was 54. The sampling technique used in the study was consecutive (non- probability).Patients of all ages and both sex, with clinical suspicion of metastatic lymphadenopathy in whom both FNAC followed by histopathological examination was done were included in the study. Cases in which aspiration material was unsatisfactory and cases with obvious inflammatory lesions were excluded. 21 one gauge needle was used in every case of FNAC. The slides were prepared after aspiration and fixed in 10% alcohol. After fixation the slides were stained by H&E. All FNAC slides were evaluated for the following cytomorphological parameters i.e. cellularity, cell type, cellular pattern, cellular atypia and background.

The surgically biopsied lymph nodes were fixed in 10% buffered formalin. After gross examination, entire or representative sections were taken followed by paraffin embedding, cutting and slide preparation and finally stained with H&E. Both histopathology and FNAC slides were examined under light microscope. A final diagnosis was recorded.

The data was recorded and analyzed using Statistical Package for Social Sciences (SPSS) Version 17. A 2 x 2 contingency table was used to determine sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy.

Results

Age distribution of the study participants ranged from 19 to 85 years with a mean of 45.17 ± 17.1 years. Twenty six (48.15%) were males and 28 (51.85%) were females with a male to female ratio of 1:1.08. Most of the patients (24) were in 26-50 years age group.

Out of total 54 cases, 38 involved the cervical lymph node, followed by supraclavicular lymph node (9), axillary lymph nodes (4) and inguinal lymph nodes (3).

Fine needle aspiration cytology (FNAC) smears were reported in terms of two broad categories. All the diagnosed cases were either categorized as being metastatic carcinomas or reactive hyper-

plasia of involved lymph node, while the cases diagnosed as lympho-proliferative disorders or any inflammatory disorder were excluded.

The broad categories of histopathological and cytological diagnosis are shown in **Table 1.**

Table 1. Categories of final cytological and histopathological diagnosis

Categories	FNAC diagnosis Number of cases (%)	Histopathology diagnosis Number of cases (%)
Metastatic Carcinomas	38 (70.37%)	38 (70.37%)
Reactive Hyperplasia	16 (29.63%)	15 (27.78%)
Malignant Lymphoma	0 (0%)	1 (1.85%)
TOTAL	54 (100%)	54 (100%)

The final correlation between thehistopathological and cytological diagnosis was classified as either `100% correlation` or `lack of correlation`.(**Table 2**)

A strong correlation was found between the diagnosis made by Fine needle aspiration cytology and the final histopathological diagnosis, as shown in **Table 3**.

Table 2. Correlation between FNAC and histological diagnosis (n= 54 patients)

CORRELATION	FREQUENCY (%)
100% correlation	52 (96.23%)
Lack of correlation	2 (3.77%)
Total	54 (100%)

Table 3. Cyto-histopathological correlation of study cases (n= 54 patients)

FNAC	Histopathology	Number of patients
Malignant (Metastatic Carcinoma)	Malignant (Metastatic Carcinoma)	37
Benign (Reactive Hyperplasia)	Benign (Reactive Hyperplasia)	15
Benign (Reactive Hyperplasia)	Malignant (Metastatic Carcinoma)	1
Malignant (Metastatic Carcinoma)	Malignant (Malignant Lymphoma)	1
Total		54

In our study the sensitivity and positive predictive value of FNAC were found to be 97.37% while the specificity and negative predictive value were 93.75%. The overall diagnostic accuracy of FNAC was 96.29%.

Discussion

Fine needle aspiration cytology has decreased the need for excision or incision biopsy by reforming the diagnosis of lymph node diseases[11]. FNAC is performed as an outpatient departmental procedure and it gives quick results with the luxury of cost effectiveness[12]. The sensitivity and specificity of FNAC for metastatic lymphadenopathy is high with few pitfalls. According to contemporary studies by various authors, the sensitivity of FNAC for metastatic lesions to lymph nodes has varied from 97.9% to 100%, whereas the specificity has been found to be 100%. [13]

The age of current study group ranged from 19 - 85 years (mean 45.17±17.1), the most frequently affected age group was 26 - 75 years. A slight female predominance was seen with female patients being 28 which is 51.9% of total number of patients (n=54).

Our study was mainly focused around all the palpable lymph nodes in a patient with a clinical suspicion of lymph node metastasis. So our results showed that cervical lymph node was the most favored site of lymph node metastasis[13, 14] followed by supraclavicular lymph node. The less frequent sites of metastasis were axillary and inguinal lymph nodes. The most commonly seen metastatic tumor in the cervical lymph node was metastatic squamous cell carcinoma with 19 cases out of total 38 involved cervical lymph nodes (50%).

In this study the most commonly encountered metastatic carcinoma was metastatic squamous cell carcinoma, constituting 28 cases (51.9%). This

finding is in accordance with many other similar studies[14] followed by metastatic adenocarcinoma (Figure 1) and metastatic breast carcinoma (Figure 2) which comprised 7.4 % and 5.6 % of total respectively. There were just 2 cases of metastatic papillary thyroid carcinoma (Figure 3) and a solitary case of metastatic mucoepidermoid carcinoma was also seen. Metastatic squamous cell carcinoma was comparatively seen in a younger population than metastatic adenocarcinoma in our study. 17 out of total 28 cases of metastatic squamous cell carcinoma were seen in 51 – 75 years age group which comprises 60.71%. In comparison, the metastatic adenocarcinoma cases were predominantly seen in an older age group of 76 – 100 years (50% cases). A male preponderance was seen in metastatic squamous cell carcinoma

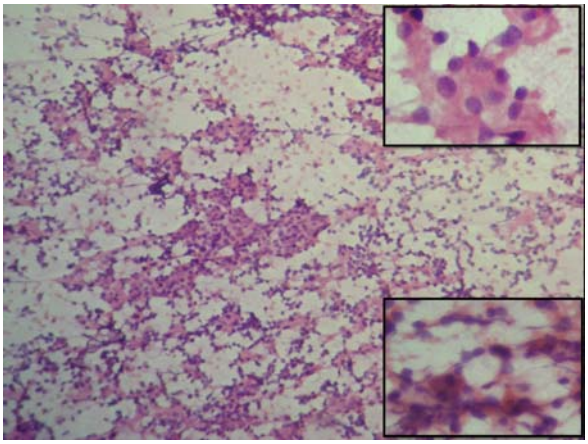

Figure 1 – FNAC smears of metastatic adenocarcinoma H&E x100. (Insets - Arrows show epithelial cells forming glands, H&E x400)

More than 57% cases of squamous cell carcinoma metastasizing to lymph nodes were seen in males (16 out of 28 cases)[15]. This could be due to the fact that tobacco is excessively used in many different forms in Pakistan and more in male population than females which leads to the squamous cell carcinoma of the head and neck region including oral cavity, pharynx, larynx and even esophagus. This fact is also noticed by several other studies from the same region.[16] Metastatic breast and papillary thyroid carcinomas were exclusively seen in female patients in our study.

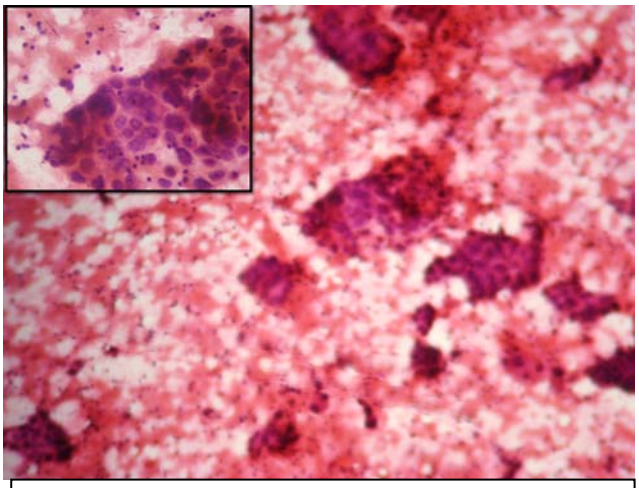

Figure 2 – FNAC smears of metastatic breast carcinoma H&E x100. (Inset - Arrow shows highly atypical mammary ductal epithelial cells against a background of lymphocytes and hemorrhage, H&E x400)

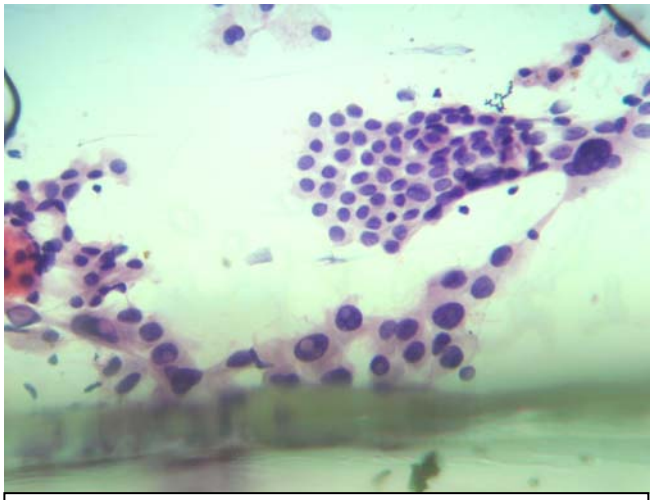

Figure 3 – FNAC smears of metastatic papillary thyroid carcinoma showing atypical thyroid follicular epithelial cells having nuclear grooves (arrows) and intra-nuclear inclusions (broad arrows) (H&E X 400)

FNAC was able to pick 37 of 38 metastatic carcinoma cases correctly. Out of these thirty seven

cases, 27 were of metastatic squamous cell carcinoma. These cases had 100% correlation with histopathology. The other tumors in the list with 100% correlation of FNAC and histopathology were metastatic adenocarcinoma, metastatic breast carcinoma, metastatic papillary thyroid carcinoma and metastatic mucoepidermoid carcinoma which comprised 4, 3, 2 and 1 case respectively.

The one case of metastatic squamous cell carcinoma (Figure 4) which was missed by FNAC and labelled as reactive hyperplasia of lymph node was of a 59 year old male patient with an enlarged left cervical lymph node. A careful review of the slide later on showed that these were in fact well differentiated squamous cells with slightly eosinophilic nuclei and mild dysplasia. This highlights the thorough examination of all the slides and that in doubtful cases, a repeat FNAC if performed could have helped in reaching the correct diagnosis.

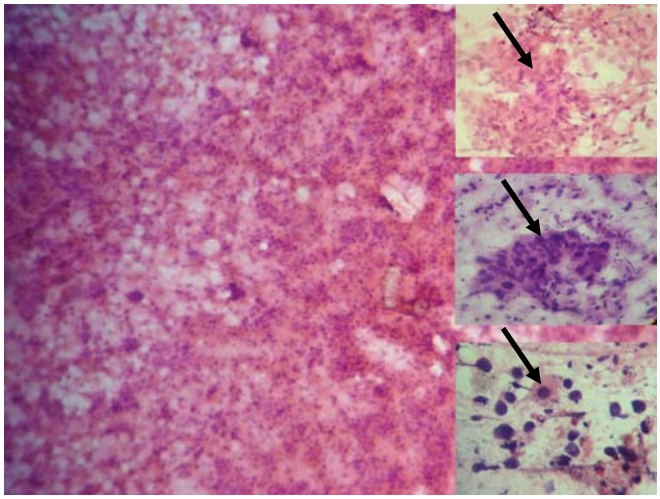

Figure 4 – FNAC smears of metastatic squamous cell carcinoma, H&E x100 (Inset – Arrows show atypical metastatic squamous cells, H&E x400)

The other case in which there was discrepancy between FNAC diagnosis and histopathology was of a 61 year old female patient with a right cervical lymph node with a strong clinical suspicion of metastatic lymphadenopathy. She also had a recent history of weight loss as well but the lymph node enlargement was for more than 6 months. This case was misdiagnosed as metastatic poorly differentiated carcinoma. On subsequent histopathology, the lymph node lesion turned out to be a malignant lymphoma which was also confirmed by performing immunohistochemistry (IHC) on sections from the same lymph node. The difficulty in correctly labeling this lymph node on FNAC as being a malignant lymphoma rather than a metastatic carcinoma was mainly because of the poor differentiation of malignant cells which always poses difficulty in identifying these as of epithelial origin or not. The population of lymphocytes in the smears from this patient were incorrectly taken as a background of benign lymphocytes against which malignant cells were seen. Perhaps a more detailed history of the patient along with relevant investigations could have helped in reaching the correct diagnosis but nevertheless, this was a difficult case.

The other notable diagnosis in this study was of reactive hyperplasia of the involved lymph nodes which although having a clinical suspicion of metastatic disease were indeed correctly diagnosed on FNAC in 15 of 16 cases with a high percentage of 93.65% correct diagnosis.

In our study the overall sensitivity and specificity of FNAC was found to be 97.37% and 93.75% respectively, with the diagnostic accuracy of 96.29%. These findings are compatible with those made by Qasmi SA et al. who found sensitivity of FNAC in metastatic lymphadenopathy to be 95%.[15] Similarly, Sheahan et al. found the specificity of FNAC in metastatic lymphadenopathy to be 95%[17] which is also compatible with the result of our study. Finally, Fazal-I-Wahid et al. found the diagnostic accuracy of FNAC in metastatic lymphadenopathy to be 94.73%[18] which is also

comparable to what we found in our study. Similar diagnostic accuracies are also reported in various other studies.[11, 17]

The complications of lymph node FNAC are rare.[19] One risk is minor bleeding which may occur in the lesion or under the skin. This only causes mild discomfort or a minor bruise and is generally limited if firm pressure is applied to the aspirated site. Serious complications such as infections or significant bleeding are extremely rare. In our study however, none of the patients developed any complications. Finally, a few authors have also commented upon the risk of implantation during FNAC and suggested clearly that in their experience they did not observe any tumor cell implantation in FNAC needle tract[20] and hence the procedure's safety is further emphasized.

Conclusion

FNAC of the lymph node has a very useful role in diagnosis of lymph node metastasis. It is safe, time saving as well as cost-effective diagnostic tool.

Cytology slides should always be carefully interpreted by a trained cytopathologist to avoid misdiagnosis.

Particular attention to subtle morphologic changes may help in reaching the right diagnosis.

Repeat FNAC can easily be done where the initial diagnosis is not clear or when the cellularity is low, and it should always be evaluated with other clinical findings and relevant investigations.

FNAC can differentiate between non neoplastic and neoplastic lesions; moreover it can even separate the benign lesions from the malignant ones.

Therefore FNAC plays a significant role in the management of patients and can reduce many unnecessary surgeries.

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