

Cervical Lymphadenopathy: A Common Diagnostic Dilemma

Shahzad Ahmed Qasmi, Faran Kiani, Afaq Iqbal Malik, Jamil Salamatullah, Muhammad Omar Farooq, Muhammad Amjad Abassi

ABSTRACT

- Objective** To determine the diagnostic accuracy of fine needle aspiration cytology (FNAC) in cervical lymphadenopathy using histopathologic examination of the excised lymph node as gold standard.
- Study design** Cross sectional study.
- Place & Duration of study** Combined Military Hospital Rawalpindi in collaboration with Armed Forces Institute of Pathology (AFIP) Rawalpindi, from January 2007 to January 2008.
- Methodology** A total of 70 patients suffering from cervical lymphadenopathy were selected. After obtaining informed consent FNAC was obtained from the lymph node. Afterwards same lymph node was removed under local anesthesia for histopathology. All specimens were sent to AFIP for histopathology reporting. Sensitivity, specificity, positive and negative predictive values and diagnostic efficacy for both the modalities were calculated. Data was analyzed using SPSS version 10. Mean and standard deviation for age and gender were calculated.
- Results** Mean age of the patients was 38.14 +16.88 year. FNAC findings showed a sensitivity of 79.5%, specificity 47.61%, positive predictive value 78%, negative predictive value 50% and diagnostic efficacy 70%.
- Conclusions** FNAC appears well established method of diagnosis, as its results compared favorably in many respects with those obtained from traditional surgical biopsy.
- Key words** Fine needle aspiration, Cervical lymph node, Histopathology.

INTRODUCTION:

Lymph nodes are the most widely distributed and easily accessible component of lymphoid tissue. They are frequently examined for the diagnosis of lymphoreticular disorders.¹ Palpable lymph nodes are not always pathological but are presumed to reflect more frequent exposure to new antigens. It is generally agreed that the interpretation of lymph node cytology is one of the most difficult aspects of histopathology and yet a precise diagnosis is of paramount importance both to clinician and patient. The lymph nodes usually respond to a wide variety of stimuli and in some cases a reactive

condition may simulate a lymphoreticular neoplasm or vice versa. Therefore a critical appraisal of all the relevant histological and cytological evidence is of great importance in arriving at a diagnosis.

Majority of enlarged lymph nodes represent benign reactive or inflammatory process.² The clinician often has to decide when a tissue diagnosis is necessary to rule out malignancy.³ Histological examination of lymphoid tissue is traditionally considered the gold standard for diagnosis.⁴ An alternative to this is fine needle aspiration cytology which offers immediate preliminary diagnosis in the investigation of lymphadenopathy with minimal trauma to the patient at considerably low cost than surgical biopsy.⁵ The early use of FNAC can direct further testing and evaluation, saving time, expense and morbidity to the patient, besides reducing the anxiety.⁶ FNAC is a reliable tool of diagnosis in young patients presenting with peripheral lymphadenopathy, with

Correspondence:

Dr. Shahzad Ahmed Qasmi
Surgical department
Combined Military Hospital
Bahawalpur Cantt
E-mail: qasmi.shahzad@gmail.com

prolonged duration of illness and involvement of the cervical glands with multiple and matted appearance.⁷ FNAC is not only useful in the diagnosis of various lesions but can also help in deciding the appropriate management. The aspirated material can be used for appropriate histochemical and immune marker that facilitate the diagnosis.⁸ FNAC has minimal complications and can be repeated safely.⁹

Objective of this study was to determine the diagnostic accuracy of FNAC in cervical lymphadenopathy using histopathologic examination of the excised lymph node as gold standard. If FNAC turns out to be sensitive and specific in commonly seen clinical conditions with cervical lymphadenopathy, it can effectively replace excision biopsy as an effective and easy alternative.

METHODOLOGY:

This study was carried out in out patient department of combined military hospital Rawalpindi. Samples of histopathology and FNAC were sent to Armed Forces Institute of Pathology (AFIP) for analysis. Seventy patients regardless of gender, aged 12 to 60 year with clinical diagnosis of cervical lymphadenopathy referred to surgical OPD for lymph node biopsy, were included in the study. Patients with history of bleeding disorders and allergy to local anaesthetic were excluded. All these patients were included after a written consent. History and thorough clinical examination were carried out. These patients underwent FNAC which was followed by surgical excision biopsy of same lymph node.

Fine needle aspiration cytology was performed with 22 gauge needle attached to a 10 ml syringe, without local anaesthesia. A minimum of two smears with a standard of four smears were prepared from each patient. One air dried smear was stained immediately with Hemacolor stain to see the adequacy of the aspirated material by the presence of lymphoid cells. The aspirate was repeated, if found inadequate. The alcohol fixed smears were stained with hematoxylin and eosin (H & E). All slides were seen by consultant histopathologists at AFIP.

Surgical excision biopsy was done under local anaesthesia. After infiltrating the area with 5 to 10 ml of 1% lignocaine with 1:1000000 adrenaline, incision was made in skin crease over the lymph node. Lymph node was gently dissected free of surrounding tissue and hemostasis was secured. Wound was closed in two layers. The biopsy specimen was immediately fixed in 10% buffered formalin. The sample was processed in an automatic

tissue processor for paraffin block preparation. From each block 2-3 micron thick sections were prepared by using rotatory microtome. All sections were then mounted on the slides and stained with routine H & E staining methods. All the slides were thoroughly screened and the diagnosis was confirmed by consultant histopathologist at AFIP.

The data was fed in Statistical Package for Social Sciences (SPSS) version 10. Descriptive statistics were used to calculate frequencies and means. Age of the patients was presented as Mean $\pm$ SD. The histopathological and FNAC diagnosis were presented as percentage. Histopathology of cervical lymph node was taken as diagnostic reference (Gold Standard). A 2 x 2 table was used to determine sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

RESULTS:

A total of 70 patients were included in the study out of which 48 were males and 22 females. The range of age was 15 – 70 year with a mean age of 38.14 $\pm$ 16.88 year. Out of 70 patients who underwent FNAC, 50 patients were diagnosed as having disease involvement of cervical lymph nodes. Out of these 50 patients, eleven were found disease free on histopathological examination of same lymph nodes. Twenty patients were found disease free on FNAC, out of which 10 were diagnosed as having disease on histopathology examination. Using FNAC in the diagnosis of cervical lymphadenopathy we found overall sensitivity of 79.5%, specificity 47.61%, positive predictive value 78%, negative predictive value 50% and diagnostic efficacy 70%. (Table I & II).

A total of 18 patients were diagnosed as having tuberculous lymphadenopathy on FNAC, out of which 15 were confirmed on histopathology, while 3 proved to have reactive hyperplasia. Four patients with tuberculous lymphadenopathy were not diagnosed on FNAC. Using FNAC in the diagnosis of tuberculous lymphadenopathy we found sensitivity of 78.95%, specificity 90.32%, positive predictive value 83.33%, negative predictive value 87.50% and accuracy 86% (Table III).

A total of 13 patients were diagnosed as having lympho-proliferative disorders on FNAC, out of which 5 were confirmed on histopathology while 8 patients had no disease on histopathology. Also 2 patients with lympho-proliferative disease were not diagnosed on FNAC. Using FNAC in the diagnosis of lympho-proliferative disease in cervical lymph nodes we found sensitivity of 71.42%, specificity 81.39%, positive predictive value 38.46%, negative predictive

Table I: 2 X 2 Table Format			
		Histopathology of Cervical Lymph Node	
FNAC		Disease	No disease
	Disease	True Positive (a) 39	False Positive (b) 11
	No disease	False Negative (c) 10	True Negative (d) 10

Table II: Accuracy of FNAC in Diagnosis of Cervical Lymphadenopathy (n=70).		
	Calculation based upon 2 x 2 table	Percentage
Sensitivity	$a / a + c \times 100$	79.5
Specificity	$d / b + d \times 100$	47.61
Positive Predictive Value	$a / a + b \times 100$	78
Negative Predictive Value	$d / c + d \times 100$	50
Diagnostic Efficacy	$a + d / a + b + c + d \times 100$	70

Table III: Percentages of Different Histopathological Types Accurately Diagnosed by FNAC			
Histopathology of Lymph nodes	Total Cases	Cases diagnosed by FNAC	% accurately diagnosed by FNAC
Tuberculosis	19	15	78.9
Lympho-proliferative disease	07	05	71.4
Meastatic carcinoma	20	19	95
Kikuchi's disease	01	00	00

value 94.59% and accuracy 80%.

FNAC accurately picked up 19 cases of metastatic carcinoma while one case was not diagnosed on FNAC but positive for metastatic carcinoma on histopathology. Thus FNAC was found 95% sensitive with 100% positive predictive value in case of metastatic carcinoma.

DISCUSSION

FNAC is defined as using a fine needle to remove sample of cells from suspicious mass for diagnostic purposes.¹⁰ Fine needle aspiration cytology has revolutionized the diagnosis of cervical lymphadenopathy, decreasing the morbidity of excision or incisional biopsy of lymph node.¹¹ Cervical lymphadenopathy is a common problem faced by health care professionals.¹² FNAC is an outpatient procedure that is cost effective and results are obtained quickly.¹³ It offers immediate preliminary diagnosis in the investigation of lymphadenopathy with minimal trauma to the patient at a considerably lower cost than surgical biopsy.^{5,14,15} FNAC has also

been advocated as a useful method in comparison to more expensive surgical excision biopsies in developing countries with limited financial and health-care resources.¹⁶

The similarities of cells and cell patterns that may pose differential diagnostic problems with malignant lymphomas include reactive hyperplasia, which is a common finding in patients undergoing FNAC. Stani and Nasuti et al and Nada had 23%, 32% and 54.2 % patients diagnosed as having reactive hyperplasia respectively.¹⁷⁻¹⁹ In our study reactive or benign lymphadenopathies were diagnosed on cytology in of 20 (28.5%) cases with enlarged lymph nodes of the head and neck region.

Tuberculosis (TB) is a widely prevalent disease in our part of the world. Bailey et al and Al Nousairy showed in their studies that TB is the most common disease in developing countries affecting the cervical lymph nodes.^{20,21} FNAC is reliable tool for diagnosing this pathology.²² Although it is an effective mean for the diagnosis of cervical tuberculous lymphadenitis,

it still poses a certain degree of false negative and false positive.²³ In places where mycobacterial infections are prevalent, and other granulomatous diseases uncommon, a diagnosis of tuberculous lymphadenitis can be made with some confidence when granulomatous changes are present cytologically.¹⁹ However, patients with pyogenic tuberculous lymphadenitis may not necessarily exhibit such a picture. Moreover, FNAC of advanced tuberculous lymphadenitis may frequently display changes that are incompatible with nonspecific reactive hyperplasia.^{24,25} That is why it is always stressed that in a clinically suspected case, especially if the aspirate contains pus, a bacteriological examination should be tested for acid-fast bacilli and a culture made to improve the diagnostic accuracy.^{25,20} In our study 38% (19) patients were diagnosed as having chronic caseating granulomatous inflammation, whereas Qaiser et al gave a figure of 26.6%.³ Two cases diagnosed as having abscess on FNAC turned out to be of tuberculous etiology on histopathology. This trend is due to the fact that only adequate aspirates were included in our study discarding inadequate aspirates. Manitchotpisit had shown sensitivity and specificity of 48% and 87.5% respectively in the diagnosis of cervical tuberculosis on FNAC.²³ Our study confirms these findings.

Lympho-proliferative disorders are traditionally difficult to diagnose accurately on FNAC. Out of 70 cases in our study 10% (7) cases were diagnosed as lymphomas and this is the third most common disease in patients undergoing FNAC, which is supported by Qaiser et al who gave a figure of 10.56%.³ Sensitivity and specificity of FNAC in diagnosis of lymphoma has been traditionally low but with increasing expertise and availability of immuno-histochemistry this limitation of FNAC has been overcome to a certain extent. Accuracy of FNAC in diagnosing lymphomas has been reported in the range of 85% by Das DK.²⁶ Accuracy of FNAC in diagnosing lymphoma in our study was 80%, a figure close to the findings of above mentioned studies. Although in our study the sensitivity and specificity in diagnosing lymphomas is high but the exact diagnosis and type was made on excisional biopsy. One of the reasons for not completely diagnosing lymphomas is that immuno-histochemistry was not applied on cytology in our laboratory.

FNAC has the highest degree of specificity and sensitivity for diagnosis of metastatic malignancies. In our study 19 cases were diagnosed as having metastatic carcinoma on FNAC. One case of

metastatic adenocarcinoma was missed on FNAC which was picked by histopathology. Eighteen out of the 19 cases positive on FNAC were metastatic squamous cell carcinoma except one supraclavicular lymph node that was a metastatic adenocarcinoma. Squamous cell carcinoma is the commonest malignancy presenting in the cervical lymph nodes, metastasizing from upper aerodigestive tract a fact validated in our study.

In our country where resources are limited and diagnostic investigations are not widely available, FNAC has proven to be a very important tool in the armament of the treating physician.

CONCLUSIONS:

FNAC of cervical lymphadenopathy has a reasonably good sensitivity with good diagnostic yield. Although it is not a replacement for open biopsy, it can help to establish a workable diagnosis and reduce the number of total open biopsies.

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