

Original Article

Diagnostic Accuracy of Fine Needle Aspiration Cytology in Diagnosis of Tuberculous Lymphadenitis

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Abstract

Background: Tuberculosis is still a global health problem. Most common presentation of extrapulmonary tuberculosis is tuberculous lymphadenitis. In our setting, keeping huge burden of tuberculosis in mind, clinicians have to depend on pathological diagnosis of enlarged lymph nodes, i.e., cytomorphology with acid-fast staining in diagnosing these cases so that diagnosis and management of such cases can be initiated quickly. Fine needle aspiration cytology (FNAC) of lymph nodes has been a simple, rapid and cost-effective procedure for diagnosis of various causes of lymphadenopathies. **Objective:** To determine the diagnostic accuracy of fine needle aspiration cytology in providing a diagnosis of tuberculous lymphadenitis patients in Bangladesh. **Materials and Methods:** This cross-sectional study was done on 317 subjects in Bangabandhu Sheikh Mujib Medical University (BSMMU) in collaboration with icddr,b. After clinical examination, fine needle aspiration (FNA) was done. The FNA materials were processed for Papanicolaou staining (PAP stain), Ziehl-Neelsen staining and culture for the diagnosis of tuberculosis. Sensitivity, specificity, positive and negative predictive values of FNAC were determined where culture was taken as the gold standard. **Results:** Initially 351 clinically suspected tuberculous lymphadenitis patients were enrolled, but 34 cases were excluded due to diagnosis of malignancy. Among them 123 were male and 194 were female. Mean age was 27.91 ± 13.16 years. Among the subjects 95.9% presented with cervical lymphadenopathy, others presented with lymphadenopathy of axillary or other groups of lymph nodes. The results of cytomorphological diagnosis of TB were in 58.36% cases, and culture was positive in 23.3% cases. Sensitivity, specificity, positive predictive value and negative predictive value of cytomorphological diagnosis were 79.7%, 48.1%, 31.9% and 88.6% respectively. **Conclusions:** FNAC is an effective diagnostic method for tuberculous lymphadenitis. It can diagnose granulomatous inflammation as well as reactive and other disease conditions including malignancies, thereby providing more information about the patient's disease status.

Key words: Tuberculosis (TB); FNAC; Ziehl-Neelsen stain; Acid-Fast bacillus

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Introduction

Tuberculosis (TB) is thought to be one of the oldest human diseases and the history is almost as old as mankind.¹ The European kings of the middle ages imparted the royal touch to cure the “King’s evil” to which mycobacterial lymphadenitis referred.² Lymphadenopathy is one of the common clinical

problems with varied etiological considerations. The discovery and speedy diagnosis of enlarged lymph node is of great clinical importance. Fine needle aspiration cytology (FNAC) has become an important adjunct to the study of peripheral lymphadenopathy as a rapid, reliable and inexpensive method of making

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a diagnosis and is particularly relevant in developing countries like Bangladesh where facilities for surgical biopsy are insufficient. Tuberculous lymphadenitis is one of the most common causes of lymph node enlargement in developing countries.³ FNAC plays an important role in diagnosing tuberculous lymph nodes and prevents unnecessary surgery. Cytodiagnosis of tuberculosis depends on demonstration of epithelioid cells and caseous necrosis with or without Langhans giant cells. Bacteriological confirmation is required by Ziehl Neelsen (ZN) stain/culture for acid fast bacilli (AFB). Treatment of tuberculosis can be straightway started after FNAC diagnosis by correlation with clinical findings and other investigations. We wanted to see the diagnostic accuracy of fine needle aspiration cytology (FNAC) in diagnosis of tuberculous lymphadenitis in patients of Bangladesh. For this purpose we intended to see sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of cytomorphological test in comparison to culture.

Materials and Methods

This cross-sectional study was conducted over July 2013 to May 2015 in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU) in collaboration with International Centre for Diarrhoeal Diseases and Research, Bangladesh (icddr,b). Three hundred fifty one subjects who were clinically suspected to have tuberculous lymphadenitis were included purposively, but 34 were excluded due to diagnosis of malignancy. Subjects who had history of taking anti-TB drugs within 60 days of sample collection, lymphadenopathy due to suspected malignancies and inadequate sample (aspirated material) were excluded from the study. Samples were collected by trained doctor at the Department of Pathology, BSMMU from enlarged lymph nodes by FNA. Consent was taken and information was collected by using a structured questionnaire by the researchers. Papanicolaou staining (PAP stain) and microscopy were done at the Department of Pathology, BSMMU. Ziehl-Neelsen staining for AFB was also done. Culture was done at the Tuberculosis

Laboratory. Biosafety and confidentiality were maintained. Data were tabulated and then analyzed by SPSS Version 17.0. Sensitivity (SEN), specificity (SEP), positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess the performance of diagnostic tests.

Results

A total of 351 clinically suspected tuberculous lymphadenitis patients were initially enrolled in the study. But 34 cases were excluded because of a diagnosis of malignancy-like non-Hodgkin lymphoma, metastatic squamous cell carcinoma, metastatic adenocarcinoma etc. Finally 317 cases were included in this study for evaluation. Age of the patients ranged from 5 to 75 years with mean 27.91 ± 13.16 years. The most commonly affected age group was the 3rd decade of life (34.4%) followed by the 4th decade (21.8%). Patients below 30 years were 60.6% and below 20 years were 26.2%. Male were 123 and 194 were female with male female ratio 1:1.58. Most of the cases (95.9%) presented with cervical lymphadenopathy while others presented with lymphadenopathy of axillary or other groups of lymph nodes. Fever and cough were the most common associated symptoms. Past history of tuberculosis was present in 11.7% cases, and 18.3% cases had history of contact with TB patients. The FNA materials of lymph nodes of all 317 patients were processed for cytomorphology and culture for the diagnosis of tuberculosis.

Cytological diagnosis of TB was positive in 185 (58.4%) cases and culture was positive for TB in 74 (23.3%) cases. Among 74 culture positive cases 59 (79.7%) were FNAC positive while 15 (20.3%) were FNAC negative (Table I). Sensitivity, specificity, positive predictive value and negative predictive value of cytomorphological diagnosis were 79.7%, 48.1%, 31.9% and 88.6% respectively. Percentage of agreement of cytomorphological diagnosis of TB with culture was 0.183 [*Kappa test*]. Performance of ZN stain for AFB against culture as gold standard is shown in Table II. Sensitivity, specificity, positive predictive value and negative predictive value of ZN stain for AFB were 17.6%, 98.4%, 76.5% and 79.7% respectively.

Table I: Performance of cytomorphological diagnostic test against culture as gold standard

		Culture			p value
		Positive	Negative	Total	
Cytomorphological diagnostic test	Positive	59 (79.7%)	126(68.1 %)	185 (58.4%)	<0.001
	Negative	15 (20.3%)	117 (48.1%)	132 (41.6%)	
	Total	74 (100%)	243 (100%)	317 (100%)	

p value was reached by Pearson Chi-square test

Table II: Performance of ZN stain for AFB against culture as gold standard

		Culture			p value
		Positive	Negative	Total	
Z N stain (AFB)	Positive	13 (17.6)	4 (1.6)	17 (5.4)	<0.001
	Negative	61 (82.4)	239 (98.4)	300 (94.6)	
	Total	74 (100)	243 (100)	317 (100)	

p value was reached by Fisher's Exact test

Discussion

In this study, sample size was smaller than calculated sample size due to time limitation. Several conditions like fungal, bacterial and viral adenitis can present with similar cytologic features like tuberculous lymphadenitis. In this scenario, additional laboratory tests may be essential to identify the cause of adenopathy for a definitive treatment. ZN staining, culture and some other tests can be done on the aspirated material to confirm diagnosis. This present study tried to find sensitivity, specificity, positive predictive value and negative predictive value of FNAC to see and compare the usefulness, reliability and diagnostic accuracy of FNAC for investigating patients with suspected tuberculous lymphadenitis.

In this study 317 patients with suspected tuberculous lymphadenopathy were enrolled. The patients were referred to the Department of Pathology, BSMMU for FNAC of their enlarged lymph nodes. The aspirated material was used for cytological examination (with Pap stain), detection of AFB (with ZN stain) and culture (with Lowenstein–Jensen [LJ] medium). The age range of the patients was from 5 to 75 years. In our study 26.2% patients were below 20 years and 60.6% were below 30 years. Majeed & Bukhari⁴ found that 47% patients' age was 20 years or below and in 62% cases it was below 30 years. Bezabih et al⁵ also found that in 69% cases age was below 30 years. These results suggest that tuberculosis is more commonly seen in young population.

In this study male female ratio was 1:1.58. This may be due to poor nutritional status and decreased immunity of female. Other studies also found female predominance.^{4,6,7} However, Bezabih et al⁵ found slight male predominance. In this study cervical lymph node involvement was found most commonly (95.9%) followed by axillary lymphadenopathy. Other similar studies also found cervical lymphadenopathy in the majority of cases followed by axillary lymphadenopathy.^{4-6,8,9} Cytomorphological diagnosis of TB was made when there was presence of epithelioid cells singly or in clusters (granuloma) with caseous necrosis. FNA has become the first-line diagnostic technique in endemic areas, where the mere presence of epithelioid cell/granuloma indicates tuberculosis until proven otherwise. The reported sensitivity from endemic areas ranges from 97% to 100% and the specificity ranges from 88% to 100%.¹⁰⁻¹² But in non-endemic areas sensitivity and specificity of FNAC were found low. Ellison et al¹³ reported a sensitivity of 25% and a positive predictive value of 65% in USA. Knox et al⁶ found sensitivity of cytology 38% in a non-endemic area. In this study sensitivity, specificity, positive predictive value and negative predictive value of FNAC were 79.7%, 48.1%, 31.9% and 88.6% respectively. In the present study, FNAC gave a relatively low sensitivity (79.7%) in comparison with other endemic areas. A study in Egypt reported the overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of FNAC of cervical lymph nodes 90.9%, 67.2%, 82.6%, and 81.3% respectively.¹⁴ Another study in Ethiopia found sensitivity, specificity,

PPV, and NPV of FNAC 81%, 50%, 54.2%, and 78.6% respectively.¹⁵ In the present study, like some other studies from endemic areas, FNAC has a relatively low sensitivity, specificity, positive predictive value and negative predictive value. Cytological diagnosis of tuberculosis and culture negative results in this study could be due to nontuberculous causes of epithelioid cell/granuloma or it might be that viable mycobacteria were not present in adequate amount to allow for growth in the culture medium. Simultaneous diagnosis of tuberculosis in cytological examination and negative results in culture were common findings in this study. Possible explanation of it may be due to suppressive inflammation where granuloma and/or caseous necrosis identification was difficult due to the inhibitory effect of prior broad spectrum antibiotic.^{10,16} Cytomorphology is an expression of immune response which may exist even in other conditions such as sarcoidosis, fungal infection, leprosy, foreign body granuloma etc. Or it might be that patients with cytological diagnosis of tuberculosis, but negative culture in various stages of disease was possibly due to nonexistence of viable mycobacteria in the lymph node.

In summary, our study shows that tuberculosis is currently the commonest cause of cervical lymphadenopathy. FNAC is an important diagnostic method in evaluation of etiology of cervical lymphadenopathy. Moreover, FNA is quite a useful diagnostic test even where lymph node biopsy is not possible. A negative FNA or ZN test does not rule out tuberculous adenitis and FNAC is still useful in diagnosis of tuberculosis even when ZN is negative. However, modern techniques like Xpert MTB/RIF (Xpert) test that is PCR could be included as a diagnostic method and a large multicenter randomized study can be done to confirm the findings.

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