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USE OF CBNAAT X-PERT MTB FOR RAPID DIAGNOSIS OF TUBERCULOUS LYMPHADENITIS FROM FINE NEEDLE ASPIRATION CYTOLOGY SPECIMENS AT A TERTIARY CARE HOSPITAL

Pathology

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ABSTRACT

Background: Diagnosis of extrapulmonary tuberculosis is difficult. Tuberculous lymphadenitis is one of the most common extrapulmonary manifestation of tuberculosis.1 Cervical group of lymph nodes are commonly involved.2 Fine needle aspiration cytology can be used easily, safely for specimen collection of these cases. The cytology samples can be used for CBNAAT X-pert assay for rapid diagnosis of tuberculous lymphadenitis along with fluoroscence microscopy. The aim of the present study was to evaluate proportion of tuberculous lymphadenitis from FNAC specimens of all lymphadenopathy cases, to study diagnostic utility of CBNAAT X-pert MTB for diagnosis of tuberculous lymphadenopathy in patients with lymphadenitis and to correlate cytological findings with CBNAAT and fluorescence microscopy results.

Methods: The present study was included 45 cases of lymphadenopathy. Detailed history and physical examination was done followed by FNAC . Multiple smears were prepared from each aspirate for routine cytological examination and for evaluation by fluroscence microscopy. The cytology findings were correlated with CBNAAT and fluoroscence microscopy results.

Results: In the present study female preponderence was noted. Maximum number of cases were in 3rd decade. Tuberculous lymphadenitis was the most common cytological diagnosis found in 51.1 % cases, of which 33.3% were positive on CBNAAT and 20% cases were positive by fluorescence microscopy.

Conclusion: The most common cause of cervical lymphadenopathy is tuberculosis. The present study supports combined use of FNAC and CBNAAT for early diagnosis of tuberculosis.

KEYWORDS

Tuberculous lymphadenitis, FNAC, CBNAAT, Fluoroscence microscopy.

INTRODUCTION-

Tuberculosis is a leading public health problem worldwide. Tuberculous lymphadenitis is the most common extrapulmonary manifestation of tuberculosis and majority of cases have no active lung involvement.[3,4] Majority cases of extrapulmonary tuberculosis often present with lymphadenitis and may progress rapidly unless the infection is diagnosed and treated early. A diagnosis of tuberculosis is difficult in extrapulmonary infection as bacterial count is lower as compared with sputum specimens. Collection of extrapulmonary material often requires invasive procedures and it is not easy to obtain additional samples. But, in this new diagnostic era, attention has been devoted to new nucleic acid amplification diagnostic technology due to their sensitivity, specificity and rapidity. Fine Needle Aspiration Cytology offers a feasible and safe option for specimen collection. Conventional microbiological culture is not always available and takes longer period for inconclusive results.[5,6]

One of the latest techniques is Gene X-pert assay system, used to amplify Mycobacterium Tuberculosis specific sequence of the genes. X-pert assay detects Tuberculosis with high sensitivity of >97% and specificity of 99.2 %. WHO recommends Gene X-pert (CBNAAT) to be used as initial diagnostic test in patients suspected of having tuberculosis.[7]

The present study was aimed to evaluate proportion of tuberculous lymphadenitis from FNAC specimens of all lymphadenopathy cases, to study diagnostic utility of CBNAAT X-pert MTB for diagnosis of tuberculous lymphadenitis in patients with lymphadenitis and to correlate cytological findings with CBNAAT and fluorescence microscopy results.

MATERIAL AND METHODS-

The present study was prospective and observational. The Study was conducted in Dept. Of Pathology at tertiary care hospital for a period of 6 months after taking permission of Institutional Ethics Committee. All the FNAC specimens of lymphadenitis cases were included in the study. FNAC specimens were collected from patients by aspirating two passes of a 23-gauge needle attached to a 5-ml syringe. A separate prick was taken for CBNAAT test so as to obtain adequate quantity without hemorrhagic aspirate. It was added to the Falcon tube with normal saline in 2:1 ratio and subsequently processed for X-pert MTB testing.[1] Two to three smears were prepared from each aspirate, one is processed for routine H and E staining and other for evaluation by fluorescence microscopy. The CBNAAT test results were correlated with FNAC findings and fluorescence microscopy.

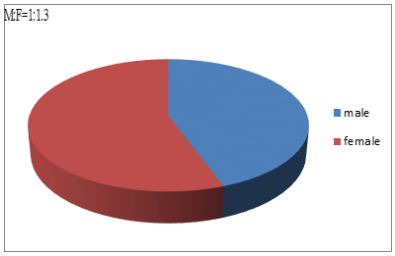
RESULT AND DISCUSSION-

In this 21st century, in new diagnostic era, FNAC has invaluable role in diagnosis of diseases. FNAC is an OPD based, minimally invasive, reliable and inexpensive method.[1] Lymphadenopathy is common clinical presentation of various diseases like lymphoma, tuberculosis etc. Among various lymph node groups, cervical group of lymph nodes is commonly involved. Incidence of extra pulmonary tuberculosis is in the range of 8.3% -13.1% of total tuberculosis cases. The diagnosis of extra pulmonary tuberculosis is difficult. Nowadays, FNAC is routinely used to diagnose tuberculosis in cases of tuberculous lymphadenopathy. To avoid biopsy for confirmation of tuberculosis, molecular diagnostic test like gene X-pert technique may be used as an adjunct to FNAC. Thus, extra pulmonary tuberculosis can be detected and confirmed at an early stage.

In the present study, total 45 cases of lymphadenopathy were studied. Maximum number of cases of lymphadenopathy were in the 3rd decade(26.7 %) followed by 2nd decade (20%). Mean age of presentation was 27.6 years of age.

Ligthelm et al (2011) found maximum number of cases in > 20 years of age in their study.[2] Singh et al (2017) also found maximum number of cases in 3rd decade.[8] Thus, Lymphadenopathy was commonly seen in children and young adults.

Chart No. 1 :Genderwise distribution : Male 20: Female 25



The present study showed slight female preponderence with M:F ratio as 1 :1.3. However, Krishnaswamy J et al (2017) found male preponderence in their study.[9]

In the present study of 45 cases, cervical lymphadenopathy (68.8%) was the common presentation followed by axillary Lymphadenopathy (13.3%) and postauricular lymphadenopathy (6.6%). Tadesse et al (2015) also noted cervical Lymphadenopathy (69.9%) as common presentation followed by axillary Lymphadenopathy (20.3%).[10]
In present study, 66.66% cases had only Lymphadenopathy as a clinical presentation. Remaining 33.33% cases had fever, weight loss, loss of appetite, hemoptysis, cough as the constitutional symptoms along with lymphadenopathy.

FNAC diagnosis of tuberculous lymphadenitis was found in 51.11 % cases (Fig. 1) followed by reactive lymphadenitis in 35.5% cases. Other minor causes of lymphadenopathy were acute suppurative lymphadenitis (6.66% cases) and neoplastic lymphadenitis (6.66% cases). However, Jawahar Krishnaswamy et al (2017) observed neoplastic lymphadenitis in 44% cases and tuberculous lymphadenitis in (40% cases) as a common FNAC diagnosis.[9]

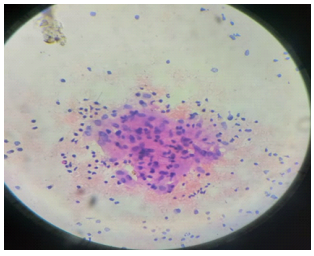


Figure 1: FNAC smear showing epithelioid cells, caseous necrosis and occassional giant cell (H and E stain 400X)

For early diagnosis, optimum combination of interventions should be used, so that case detection of extrapulmonary tuberculosis and MDR-TB should take place and so the present study helped in detecting each case of extrapulmonary tuberculosis presented as lymphadenopathy by using FNAC of lymph node and CBNAAT on FNAC material and fluroscence microscopy.

For CBNAAT testing, sample should non-haemorrhagic and adequate. It should be collected in Falcon tube provided by company. The present study recommends a separate prick for collection of sample for CBNAAT so as to obtain adequate material.

Due to high prevalence of tuberculosis in India, it is mandatory to assess all lymphadenopathy cases by molecular diagnostic test, so we should not miss even a single case of Tuberculous Lymphadenopathy. Recently WHO recommends CBNAAT to be used as the initial diagnostic test in patients of suspected extrapulmonary tuberculosis.[10] Cultures for tuberculosis take longer time period, need trained technical personnel and also require biosafety precautions while collecting the material.[11]

Atypical presentation of tuberculosis poses diagnostic challenge as acid fast bacilli can be detected in purulent aspirates without granulomas, necrosis or epithelioid cells. In such cases, definitive diagnosis needs histopathological examination, but with the use of CBNAAT on FNAC material we can diagnose tuberculosis and we can avoid lymph node biopsy.

Table No. 5: Correlation of FNAC with CBNAAT and Fluores cence microscopy

FNAC diagnosis		CBNAAT		Fluorescence microscopy	
		Positive	Negative	Positive	Negative
Tuberculous lymphadenitis	23(51.1%)	15(33.33%)	8(17.78%)	9 (20%)	14(80%)
Reactive lymphadenitis	16(35.5%)	1(2.22%)	15(33.33%)	0	16(35.5%)
Acute suppurative lymphadenitis	03(6.66%)	0	3(6.66%)	0	3(6.66%)
Neoplastic lymphadenitis	03(6.66%)	0	3(6.66%)	0	3(6.66%)
Total	45(100%)	16(35.55%)	29(64.45%)	9(20%)	36(80%)

The above table depicts that among 51.1 % cases of FNAC proved tuberculosis cases, 33.33% cases were CBNAAT positive and 20% cases were positive on fluorescence microscopy(Fig. 2). However, 17.78% cases were negative on CBNAAT and 80% cases were negative on fluorescence microscopy among the FNAC proved tuberculosis cases. Similar observations were found by Sunil Kumar et al (2018). FNAC proved tuberculosis in 51.04% cases, CBNAAT diagnosed 49.1% cases and fluorescence microscopy detected 39.7% cases.[12]

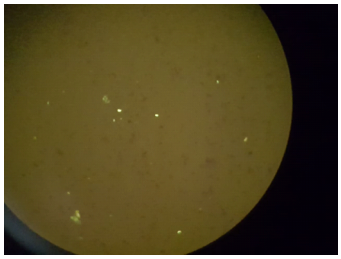


Figure 2: Fluoroscence microscopy showing fluoroscent tuberculous bacteria

35.5% cases showed features of reactive lymphadenitis on FNAC but one case was CBNAAT positive and having constitutional symptoms of tuberculosis, treatment of tuberculosis was started for that case, considering sensitivity and specificity of CBNAAT technique and constitutional symptoms. All cases diagnosed as acute suppurative lymphadenitis (6.66%) and neoplastic lymphadenitis (6.66%) were negative on both CBNAAT testing and on fluorescence microscopy.

Tuberculous lymphadenitis was diagnosed on FNAC in 51.1% cases whereas CBNAAT was positive in 33.3% cases and fluorescence microscopy was positive in 20% cases.

The study done by Singh K. G. et al showed FNAC was positive in 82.4% cases. However, CBNAAT was positive in 77.19% of tuberculous lymphadenitis cases. Thus CBNAAT did not diagnose more cases of tuberculous lymphadenitis than FNAC[7]. Similar observation was noted in the present study.

However, in the present study, one case was diagnosed as reactive lymphadenitis which showed CBNAAT positivity and patient has started treatment for same. Thus, CBNAAT is significant for diagnosis of tuberculous lymphadenitis especially in FNAC negative cases.

As culture for tuberculosis is difficult to perform and takes long duration, FNAC along with CBNAAT may be used simultaneously to diagnose tuberculosis in cases of lymphadenopathy.

CONCLUSION :

This study supports the fact that tuberculosis is still a common cause of cervical lymphadenopathy in India. It is mandatory to do CBNAAT of FNAC samples of all lymphadenopathy cases for rapid diagnosis of tuberculous lymphadenitis regardless of the clinical diagnosis.

Though CBNAAT is the highly specific for diagnosis of tuberculosis, still FNAC of lymph nodes remains a good diagnostic tool for tuberculous lymphadenopathy and it's importance can not be overlooked especially in Indian settings. Combined use of FNAC and CBNAAT gives a maximum diagnostic yield and increase the rate of detection of tuberculosis and MDR-TB which will reduce mortality and morbidity due to tuberculosis.

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