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GRANULOMATOUS LYMPHADENOPATHY: ROLE OF FNAC IN CONJUNCTION WITH BIOPSY, AFB & CB NAAT TEST AS A DIAGNOSTIC TOOL IN A TERTIARY CARE HOSPITAL OF WESTERN GUJARAT.

Pathology

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ABSTRACT

Background: Granulomatous lymphadenopathy is a common cause of peripheral lymph node enlargement, especially in regions endemic for tuberculosis. Fine Needle Aspiration cytology (FNAC) is the first line, rapid diagnostic technique for the initial evaluation of superficial palpable swellings. **Aims:** The aim is to study the clinico-pathological parameters that is of significance in diagnosing tuberculosis in granulomatous lymphadenopathies by FNAC & biopsy along with Ziehl-Neelsen (ZN) stain & CBNAAT. **Materials & Methods:** This is a retrospective study and a total of 100 patients belonging to all age groups and both sexes, presenting with palpable lymph nodes in our institute were included. This study was conducted over a period of 6 months with diagnosis of granulomatous, suppurative and necrotising lymphadenopathy on FNAC & biopsy by collecting the data. **Results:** Out of the 100 patients with palpable lymph nodes, 63 were female and 37 were male. The most affected age group was 11–20, which accounted for 29% of cases. Fine Needle Aspiration Cytology (FNAC) diagnoses showed chronic granulomatous lymphadenitis in 46 cases. AFB was positive in 20 cases. Cartridge-based Nucleic Acid Amplification Test (CBNAAT) results were positive in 26 cases. **Conclusions:** This article reviews the role of FNAC as well as biopsy in the diagnosis of AFB positive as well as negative granulomatous lymphadenitis and the value of histopathological correlation in a tertiary care hospital setting. CBNAAT helped in confirming the diagnosis of tuberculosis. Clinico-pathological correlation becomes essential in cases to establish accurate etiology and to guide therapy.

KEYWORDS

Granulomatous lymphadenitis, FNAC, AFB positive, CBNAAT , tuberculosis, lymph node, histopathology.

INTRODUCTION

Lymphadenopathy is a frequent clinical problem with a wide differential diagnosis. Granulomatous lymphadenitis is one of the most common causes in developing countries, with tuberculosis being the predominant etiology.[1]

FNAC has emerged as a frontline diagnostic procedure due to its simplicity, speed, and minimally invasive nature.[2] However, AFB negativity on FNAC complicates the diagnostic process. In these cases, clinico-pathological correlation, including histopathology and clinical data, becomes crucial for accurate diagnosis and appropriate management.

Global incidence of TB is 10.6 million and India alone accounts for 2.8 million cases. India contributes approximately around ~ 27% of TB cases in the world. [3] In India TB is the commonest cause of chronic lymph node enlargement comprising of two third of the cases of lymphadenopathy. [4] The most reliable criterions of demonstrating tuberculosis is by demonstrating AFB by ZN staining, fine needle aspiration cytology(FNAC), CBNAAT, polymerase chain reaction (PCR) or culture from aspirate. Tuberculous. lymphadenitis is the most common manifestation of extra-pulmonary tuberculosis and in countries like India with high disease burden and with limited resources the presence of epithelioid cell granuloma in FNAC is itself considered as evidence of tuberculous lymphadenitis[5].

FNAC is a simple, sensitive, specific, safe, accurate, repeatable and cost effective procedure in the diagnosis of lymphadenopathy.[6] Culture studies are a gold standard and polymerase chain reaction are very specific, still FNAC plays an important role in the initial diagnosis of TB and institution of therapy in AFB positive cases.[7] It has a specificity of 88 to 96 percent for diagnosing TB [8].

AIMS AND OBJECTIVES

- To evaluate the role of FNAC, Biopsy, Zn Staining & CBNAAT in diagnosing granulomatous lymphadenopathy in a tertiary care hospital.
- To emphasize clinico-pathological correlation of granulomatous lymphadenitis with help of FNAC, AFB, biopsy & CBNAAT.
- To assess diagnostic challenges and the role of ancillary tests in these cases.

MATERIALS AND METHODS

Study Design: Retrospective observational study.

Setting: Department of Pathology, Tertiary Care Teaching Hospital.

Study Period: Records reviewed from : 6 months data was collected.

Study Population:
All patients who underwent FNAC of peripheral lymph nodes during the study period & were reported as having granulomatous lymphadenitis.

Inclusion Criteria:
- FNAC smears showing epithelioid cell granulomas with or without necrosis.
- FNAC smears showing extensive caseation type necrosis without proper granuloma.
- Availability of material for Zn staining.
- Cases with available histopathology (biopsy) reports for correlation.
- Complete clinical records available for review.

Exclusion Criteria:
- Inadequate or hemorrhagic smears.
- Cases with proven malignancy on cytology or histopathology.
- Incomplete records.

Data Collection:
- Retrieval of FNAC slides and reports from pathology archives.
- Review of cyto-morphological features: presence of epithelioid cell clusters, Langhans-type giant cells, necrosis, background inflammatory cells.

- ZN-stained smears assessed for AFB positivity/negativity.
- Clinical data collected from hospital records: age, sex, site of lymphadenopathy, relevant history (fever, cough, weight loss, TB contact).
- Histopathology reports of lymph nodes reviewed for final diagnosis and granuloma characterization (caseating versus non-caseating).

Procedures:
- FNAC performed using a 23/24G needle under aseptic precautions.
- Smears stained with May–Grünwald–Giemsa (MGG), Papanicolaou, and Ziehl–Neelsen (ZN) for AFB.
- Detailed clinical history recorded.
- Biopsy and histopathological examination performed in selected cases for confirmation.

Definition Of AFB-Negative Cases:
Granulomatous / necrotic cytomorphology on FNAC without demonstrable acid-fast bacilli on ZN staining.

Definitions of AFB-Positive Cases:
Demonstrable acid-fast bacilli on ZN-stained smears.

CBNAAT (Cartridge Based Nucleic Acid Amplification Test):
Cartridge-based nucleic acid amplification test (CBNAAT) assay is a real-time polymerase chain reaction (PCR) cartridge-based assay for the simultaneous detection of Mycobacterium tuberculosis complex and rifampicin resistance from biological specimen samples within two hours. Its sensitivity is around 30-40%

RESULTS
Total lymph node FNACs performed: 100

Table No 1 Showing Age & Gender Distribution In Total Cases (n=100)

Age	Male	Female	Total
0-10	6	9	15
11-20	12	17	29
21-30	5	19	24
31-40	6	9	15
41-50	4	5	9
51-60	4	3	7
61-70	0	1	1
Total	37	63	100

Above table shows that females were more compared to male with F:M ratio of 1.7:1

Maximum patients were in the age group of 11-20 years

Table No. 2 Showing FNAC Diagnosis In All Cases (n=100)

Diagnosis	No of cases
Reactive lymphadenitis	24
Necrotizing lymphadenitis	20
Chronic granulomatous lymphadenitis	46
Suppurative Lymphadenitis	10

Above table shows that maximum number of cases were of granulomatous lymphadenitis (46%) followed by others.

Table No. 3 Showing Histopathology Diagnosis In Suspected Tuberculosis Cases On FNAC (n=52)

Diagnosis	No of cases
Necrotizing lymphadenitis	10 (19.2%)
Chronic granulomatous lymphadenitis	35 (67.3%)
Suppurative Lymphadenitis	7 (13.5%)

We received biopsy for 52 cases out of which diagnosis of chronic granulomatous lymphadenitis was seen in 35 cases. (67.3 %)

AFB Stain Results:
Ziehl-Neelsen (ZN) staining for Acid-Fast Bacilli (AFB) is a key component of diagnosing TB. The study found below given result from out of 76 cases excluding reactive lymphadenitis.
* 20 cases were AFB-positive.
* 56 cases were AFB-negative.

CBNAAT Results:
CBNAAT is a rapid molecular test. The study found below given result from out of 76 cases excluding reactive lymphadenitis.
*26 cases were CBNAAT positive.
*50 cases were CBNAAT negative.

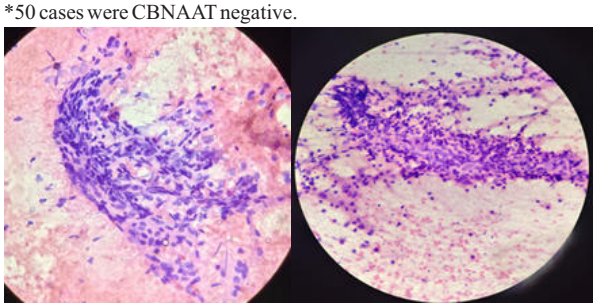

Fig 1. **Fig 2.**

Fig. 1 & 2 Showing Well-formed Granuloma Consisting Of Lymphocytes, Epithelioid Cells With Necrosis.

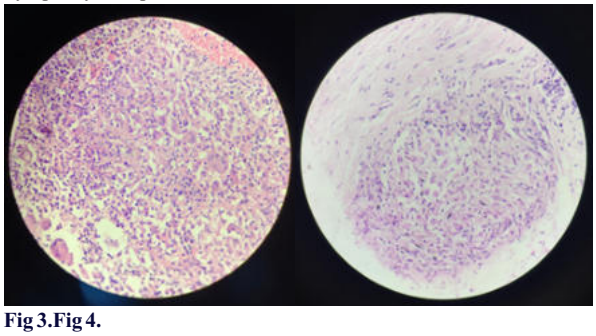

Fig 3.Fig 4.

Fig. 3 & 4 Showing Histopatholgy Section Of Lymph Node Showimg Granuloma Formation Consisting Of Lymphocyte, Epithelioid Cells And Giant Cells(in fig. 3)

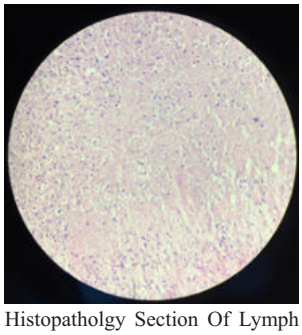

Fig. 5 Showing Histopatholgy Section Of Lymph Node Showimg Necrosis Along With Lymphocytes.

DISCUSSION

Overview Of Pathogenesis
TB pathogenesis involves a dynamic interplay between Mtb and the host immune system. The outcome-latent infection, active disease, or clearance-depends on bacterial virulence, host immunity, and environmental factors. Granuloma formation includes infected macrophages recruit other immune cells (T cells, dendritic cells, neutrophils). A granuloma forms-a structured aggregate of macrophages, epithelioid cells, ,multinucleated giant cells and lymphocytes surrounded by fibroblasts[9].

Granulomatous Lymphadenitis Overview
Granulomas are structured collections of epithelioid histiocytes, often with multinucleated giant cells. They represent a chronic inflammatory response to a persistent antigen [10].

Common Causes:
- Infectious: Tuberculosis, fungal infections, atypical mycobacteria.
- Non-infectious: Sarcoidosis, foreign body reactions, cat scratch disease[11].

FNAC Features
Cytological findings:
- Epithelioid cell clusters.
- Langhans-type giant cells.
- Necrosis, especially caseous necrosis.
- ZN stain for AFB[12].

Challenges in AFB-Negative Cases
AFB negativity does not exclude tuberculosis. Reasons include:
- Low bacillary load.
- Sampling error.
- Technical limitations.

Diagnostic Implications:
- High index of suspicion is essential.
- Reliance on clinical features and epidemiology.
- Radiological support.
- Need for histopathology[13].

Histopathology Correlation
Histopathology remains the gold standard, particularly in AFB-negative cases.

Findings:
-Tuberculous: Well-formed granulomas with caseous necrosis.
-Suppurative: Collection of neutrophils(pus) with necrosis.
-Necrotizing: Extensive necrosis without granuloma.

AFB may be detected on tissue sections even when cytology is negative[14].

Diagnostic Approach to AFB-Negative Granulomatous Lymphadenitis
- Cytological evaluation: necrosis suggests TB.
- Clinical history and imaging.
- Tuberculin skin test or IGRA.
- Histopathology for confirmation.
- Microbiological culture, PCR if available[15].

This study retrospectively analyzed 100 patients with palpable lymph nodes to evaluate the role of various diagnostic techniques in granulomatous lymphadenopathy. The results from the tables provide key insights into the demographics, diagnoses, and diagnostic challenges encountered.

The study included a total of 100 patients, with a notable gender disparity: 63% were female and 37% were male. The age distribution showed that the highest number of cases were in the 11–20 age group (29% of cases), followed by the 21–30 age group (24% of cases). This suggests that granulomatous lymphadenopathy, and by extension, tuberculosis (TB) which is the most common cause, disproportionately affects younger individuals in this study population. This demographic pattern aligns with the general epidemiology of TB in endemic regions like India, where TB is the leading cause of chronic lymph node enlargement.

Fine Needle Aspiration Cytology (FNAC) was the primary diagnostic tool used for initial evaluation. The FNAC diagnoses for the 100 cases were as follows

*** Chronic granulomatous lymphadenitis: 46 cases.** The presence of epithelioid cell granulomas, with or without necrosis, is the defining cytological feature for this diagnosis. Given that TB is the most common cause of granulomatous lymphadenitis in India, a large proportion of these cases are likely to be tuberculous.

*** Necrotizing lymphadenitis: 20 cases**. This category includes cases with extensive caseation-type necrosis but without well-formed granulomas. In high-prevalence areas for TB, extensive necrosis on FNAC is highly suggestive of a tuberculous etiology, even in the absence of a distinct granuloma.

*** Suppurative lymphadenitis: 10 cases**. This indicates a pus-forming inflammatory process. While often associated with bacterial infections, it can also be a feature of tuberculous lymphadenitis.

*** Reactive lymphadenitis: 24 cases**. These are likely non-specific inflammatory responses.

Histopathological examination via biopsy was performed in a subset of cases, totaling 52 patients. This is crucial because histopathology is considered the gold standard for diagnosis, especially when FNAC results are inconclusive. This data underscores the role of biopsy in confirming and refining diagnoses, particularly in cases where FNAC findings may be ambiguous.

Role of Ancillary Tests: AFB Stain and CBNAAT. The article emphasizes the use of ancillary tests to overcome the limitations of FNAC.

AFB Stain Results:
Ziehl-Neelsen (ZN) staining for Acid-Fast Bacilli (AFB) is a key component of diagnosing TB. The study found that:
* 20 cases were AFB-positive. The presence of AFB on ZN stain provides a definitive diagnosis of tuberculous lymphadenitis.

* 56 cases were AFB-negative. (reactive LN cases were excluded) This highlights a major diagnostic challenge. The reasons for AFB negativity can include a low bacillary load, sampling error, or technical limitations. For these cases, clinico-pathological correlation and further testing are essential.

Cartridge-based Nucleic Acid Amplification Test (CBNAAT) is a rapid molecular test that can detect Mycobacterium tuberculosis complex DNA. The results show 26 positive cases while rest were negative. While this result generally rules out active TB, it's possible for a negative result to occur with very mild or early infections, or if the bacterial load is too low (below the detection limit) to be found by the test. Therefore, a negative CBNAAT should be considered alongside other clinical symptoms and potentially further testing to confirm a diagnosis.

CONCLUSION
The study effectively illustrates the diagnostic algorithm for granulomatous lymphadenopathy in a high-prevalence setting. FNAC serves as a sensitive, rapid, and cost-effective first-line tool. When FNAC shows granulomas and is AFB-positive, a diagnosis of tuberculous lymphadenitis can be made with high certainty. However, in the vast majority of cases in this study that were AFB-negative, a more comprehensive approach is required. In these instances, the combination of clinical history, histopathology, and molecular tests like CBNAAT becomes indispensable for an accurate diagnosis and to differentiate TB from other etiologies like reactive LN, sarcoidosis or fungal infections. The study's findings support the conclusion that a multidisciplinary approach, integrating FNAC, biopsy and molecular testing is essential for optimal patient care.

Early diagnosis with institution of AKT helps in complete recovery of patients with less side effects.

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