

## **Fine Needle Aspiration Cytology for Suspected Tuberculous Lymphadenitis: A Feasible Solution for a Diagnostic Dilemma in Sudan**

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### **ABSTRACT**

**Background:** Tuberculosis is a common health problem in Sudan. Tuberculous lymphadenitis is one of the most frequent causes of lymphadenopathy. In most of these cases sputum as well as other diagnostic routine tests are negative.

**Objective:** To evaluate the usefulness of fine needle aspiration cytology (FNAC) as a diagnostic tool for tuberculous lymphadenitis and to describe the cytomorphology of the smears.

**Material and Methods:** This is a prospective hospital-based study conducted in Khartoum during the period from February 2011 to January 2012. Eighty five patients with a clinical suspicion of tuberculous lymphadenopathy were included. Direct smears were prepared and stained with Diff Quick (DQ) and Ziehl-Neelsen (ZN) stains.

**Results:** of the 85 patients, 52 (61.2%) were females with 1.5:1 female to male ratio. The mean age was 31.6 years (range 2 - 70 years). The most frequent site involved was the cervical lymph node group, 58 (68.2%) cases. Seventy five (88.3%) smears showed necrotizing granulomatous lymphadenitis (with or without detected epithelioid cells), and 10 (11.7%) smears were non necrotizing granulomatous lymphadenitis, only epithelioid and inflammatory cells detected. Positive smears for acid fast bacilli (AFB) by ZN stain were observed in 40 (47%) cases.

**Conclusion:** FNAC is a simple and inexpensive method for diagnosis of tuberculous lymphadenitis, and can obviate the need for surgical excision. Combination of FNAC with ZN stain is valuable and recommended as first line diagnostic modality in suspected cases.

**Keywords:** Fine Needle Aspiration Cytology, Tuberculous lymphadenitis, Acid fast bacilli.

**T**uberculosis (TB) is a common infectious agent associated with high levels of morbidity and mortality, especially in developing countries.

Approximately, one-third of the world's population is currently infected with the TB bacillus<sup>1</sup>. As per a 2008 World Health Organization (WHO) report, TB is worldwide in distribution, but is particularly more prevalent in Asia and Africa and 9.2 million cases were detected and 1.7 million people lost their lives due to TB worldwide<sup>2</sup>. TB is a common health problem in Sudan and tuberculous lymphadenitis is one of the most frequent causes of lymphadenopathy. The estimated prevalence of TB in Sudan was 209 cases per 100,000 of the population with an estimated 50,000 incident cases during 2009<sup>3</sup>. Lung is the most common organ for TB infection, but isolated extra pulmonary organ involvement is well documented; common organs include lymph node, genital tract, long bones and joints, brain, and meninges,

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followed by peritoneum and other abdominal organs<sup>4</sup>.

Extra pulmonary TB represents a diagnostic dilemma and it is more difficult to diagnose than pulmonary TB. Tissue diagnosis, bacteriologic culture facility, and molecular biologic technique in form of polymerase chain reaction (PCR) are not available in the majority of both public and private health centers in Sudan.

The aim of this study was to assess the role of fine needle aspiration in the diagnosis of tuberculous lymphadenitis in combination with Ziehl-Neelsen (ZN) staining for detection of Acid Fast Bacilli in smears obtained by Fine Needle Aspiration (FNA).

#### **MATERIAL AND METHODS:**

This is a descriptive prospective study conducted in Total Lab Care (TLC) Diagnostic Centre and Faculty of Medical Laboratory Sciences – University of Medical Sciences and Technology (UMST), Khartoum, Sudan during the period from February 2011 to January 2012. A total of 85 cases with peripheral lymph node enlargement, who were clinically suspected to have tuberculous lymphadenitis were included in this study. Following clinical examination, palpable nodes were aspirated in the cytology department and direct smears stained with Diff Quick® (DQ) and Ziehl-Neelsen (ZN) stain to identify the acid fast bacilli (AFB). The diagnosis of tuberculous lymphadenitis was based on the morphologic features of smears based on two cytologic criteria; necrotizing granulomatous lymphadenitis, with or without detected epithelioid cells, and non-necrotizing granulomatous lymphadenitis where only epithelioid and inflammatory cells were detected.

Ethics committee approval was obtained and patients' informed consent was obtained.

#### **RESULTS:**

In this study, 85 patients with peripheral lymphadenopathies were subjected to FNAC. Their ages ranged from 2 to 70 years (mean 31.6 years). They consisted of 33 (38.3%)

males and 52(61.2%) females with female to male to female ratio of 1: 1.5. The most frequent nodal site involved was the cervical lymph node group 58(68.2%), followed by supraclavicular 10 (11.8%), submandibular 9(10.6%), axillary 4(4.7%), and submental 4(4.7%). Seventy five smears (88.3%) showed necrotizing granulomatous lymphadenitis, with or without detected epithelioid cells, and 10 (11.7%) were non necrotizing granulomatous lymphadenitis where only epithelioid and inflammatory cells detected. Positive smears for acid fast bacilli (AFB) by ZN stain were observed in 40 cases (47%). Most, 33 (82.5%), AFB positive cases, were detected among the necrotizing granulomatous lymphadenitis group.

#### **DISCUSSION:**

Tuberculosis is a common health problem in Sudan with increasing morbidity and mortality. The presence of lymphadenopathy is the most common form of extra pulmonary TB. The histopathological analysis of the lymph node biopsy is usually conclusive, showing granuloma with caseous necrosis in majority of cases and still considered as the gold standard for diagnosis of tuberculous lymphadenitis in clinical practice<sup>5</sup>. Fine-needle aspiration (FNA) is a well-established technique for the diagnosis of lymphadenopathy, which occurs in a variety of diseases including reactive conditions, infections, and primary and metastatic malignancies. It is prudent to exclude tuberculous lymphadenitis in countries with high prevalence of TB among those with granulomatous lymphadenitis.

Our study showed female predominance (61.2% females and 38.3% males) which is comparable to a study from Pakistan reported that the male to female ratio was (1:2)<sup>6</sup>. This finding was in contradiction to other reports showing that men are more exposed to tuberculosis than women<sup>7,8</sup>. However, the infectious nature of the disease is unlikely to discriminate between gender, so these findings may reflect sampling bias rather than true differences. Cervical lymph nodes were involved in 58 (68.2%) of cases, this

observation is consistent with studies conducted by Polesky *et al*<sup>9</sup> and Wei YF *et al*<sup>10</sup> that reported cervical lymph node as the most common site of involvement in 57% and 72% of cases respectively. Our study also supports earlier reports that documented cervical lymph nodes as the commonest extra pulmonary site of tuberculosis<sup>11,12</sup>. In endemic countries it has been advocated that antituberculous therapy can be prescribed without prior histological proof if FNAC smear reveals background of caseous necrosis (eosinophilic granular material)<sup>13</sup>.

Fine needle aspiration cytology (FNAC) is safe, non-traumatic, repeatable and inexpensive diagnostic approach and useful in avoidance of unnecessary surgical excision in tuberculous lymphadenitis<sup>14,15</sup>.

In our study majority of cases (88.3%) showed necrotic eosinophilic granular material in the background, admixed with polymorphonuclear infiltration. Syncytial aggregates of epithelioid histiocytes and multinucleated giant cells were occasionally observed. Necrotizing granulomatous lymphadenitis as the commonest microscopic cytomorphological feature is also reported with less frequency by Rajeeff *et al*<sup>16</sup> and Gupta *et al*<sup>17</sup>.in 69% and 64.9% of cases respectively.

AFB positive smears were demonstrated in 40 (47%) of our patients, of which 82.5% were observed among necrotizing granulomatous lymphadenitis smears. Various studies report wide differences in positivity for AFB stained by the Ziehl-Neelsen (ZN) technique in aspirated lymph nodes with the majority of positive cases occurring in necrotizing lymphadenitis. A study from India reported significant association between AFB positivity and presence of necrosis and neutrophilic infiltration<sup>1</sup>. Metre MS and Jayaram G observed AFB positivity in 66% of aspirated material showed necrosis, and stress the importance of doing Ziehl-Neelsen staining in smears of all cases suspected of being tuberculous in etiology, particularly when purulent material is aspirated<sup>19</sup>. Samaila M and Oluwole OP almost reported the same frequency of AFB positivity (47.9%) among

Nigerian patients including the HIV seropositive ones<sup>20</sup>.

This study has many limitations. The small sample size may not allow generalizations to be made. The inter-observer differences in interpretation of cytomorphologic smears were decreased by allowing two cytopathologists to report on the smears. As a resource-limited country, no ancillary techniques were used to confirm the disease, however, the combination of clinical findings and other laboratory tests to FNAC diagnosis is expected to increase the accuracy of diagnosis. Dramatic response to antituberculous therapy, on follow-up, was also considered as a positive clue.

### CONCLUSION:

Fine Needle Aspiration Cytology is a simple, rapid, accurate, and cost-effective procedure that can be used in the diagnosis of tuberculous lymphadenitis in resource-limited countries such as Sudan. FNAC can obviate the need for surgical excision and allow physicians to start anti-TB drugs early. TB should be suspected in all lymphadenitis cases in Sudan and fine needle aspiration in combination with ZN stain is recommended as first line diagnostic modality for routine diagnosis of tuberculous lymphadenitis.

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