

Short Communication

Cytomorphological patterns in the Diagnosis of Tuberculous lymphadenitis

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ABSTRACT

The reliable diagnosis of tuberculous lymphadenitis by FNAC has important implications in a developing country like India. The aim is to study various cytomorphological patterns seen in tuberculous lymphadenitis and their correlation with AFB positivity. Fine needle aspiration cytology (FNAC) was performed on three hundred and twenty two patients with lymphadenopathy referred to the cytopathology section of pathology department, Sri Guru Ramdas Institute of Medical sciences and research Amritsar from August 2010 to July 2012. The patients with cytological diagnosis of tuberculous lymphadenitis were followed for their response to antitubercular treatment. A total of 322 FNACs were performed on patients with lymphnode lesions; out of which the most common (119) cytological diagnosis was tuberculous lymphadenitis. The most common pattern observed was (group II) presence of epitheloid granuloma with caseation necrosis which was seen in about half (50.5%) of the cases followed by smears with caseation necrosis only (group III) (27.7%) and smears with epitheloid granulomas only (group I) (21.8%). The overall AFB positivity was seen in 19.3% cases of tuberculous lymphadenitis. Maximum (30.3%) AFB positivity was seen in smears (group III) with only necrotic debris without granuloma and was least in group I (7.6%). While comparing Group I smears with that of group III using Fisher's exact test, the difference in AFB positivity between the smears was statistically significant as the two-tailed p value was 0.0496. Thus FNAC is safe, easy, quick reliable as well as conclusive for the diagnosis of tuberculous lymphadenitis when done along with Zeihl Neelsen stain for acid fast bacilli.

Keywords: FNAC, Tuberculous lymphadenitis, AFB

Introduction

In developing countries such as India, tuberculous lymphadenitis continues to be one of the most common causes of lymphadenitis. [1-3] Clinical diagnosis has pit falls and hence a morphological diagnosis is required before starting antituberculous therapy. Fine needle aspiration cytology (FNAC) avoids the physical and psychological trauma encountered after general anaesthesia, a surgical operation and hospitalisation. It is almost safe, cost effective and at the same time conclusive. [4]

The present study aims to determine the utility of fine needle aspiration cytology in the diagnosis of tubercular lymphadenitis. It also aims to identify various cytomorphologic patterns in tuberculous lymphadenitis along with their correlation with AFB positivity.

Material and Methods

FNAC was performed on three hundred and twenty two patients with lymphadenopathy referred to the cytopathology section of pathology

department, Sri Guru Ramdas Institute of Medical sciences and research Amritsar from August 2010 to July 2012. Under all aseptic conditions the lymph node was fixed and FNAC was done using sterilized 22 gauge needle attached to a 20ml sterile glass syringe using a Cameco syringe holder. The aspirated material was spread on several glass slides. One or two wet slides were fixed in 95 percent ethyl-alcohol and were stained with May Grunwald Geimsastain (MGG), and hematoxylin and eosin (H &E). The special stains like Ziehl Neelson stain was also done as required. The patients were followed up and clinical response of the treatment given following cytological diagnosis was recorded.

Result

The most common cause of lymphadenopathy diagnosed cytologically

was tuberculosis which was found in 119 (36.9%) out of 322 cases.

The tubercular lymphadenitis cases were studied in detail. The age group of the patients varied from 2 years to 70 years. The maximum number of patients was in second and third decade of life, the mean age was 32 ± 2 yrs. The most frequently involved group of lymph nodes in these cases were the cervical (65.5%) followed by axillary (19.3%), supraclavicular (15.1) and inguinal (3.3%) lymph nodes. Just over half (55%) of the patient had single lymph node enlargement; with rest having multiple matted lymph nodes. The size of most (73%) of the lymph nodes were between 2-5 cm in diameter and 9.6% cases had lymphnode more than 5 cm in size, while the rest were less than 2 cm.

The cytomorphological patterns identified in tuberculous lymphadenitis were divided into three groups. (Table 1)

Table 1 Smear pattern in Tuberculous Lymphadenitis

Group	Smear Pattern	No. of Cases	Percentage
I	Epithelioid granulomas without caseation necrosis	26	21.8
II	Epithelioid granulomas with caseation necrosis	60	50.5
III	Caseation necrosis without epithelioid granulomas	33	27.7

Group I: Epithelioid granulomas without caseation necrosis (Fig.1)

Group II: Epithelioid granulomas with caseation necrosis.

Group III: Necrotic debris without granulomas. (Fig. 2)

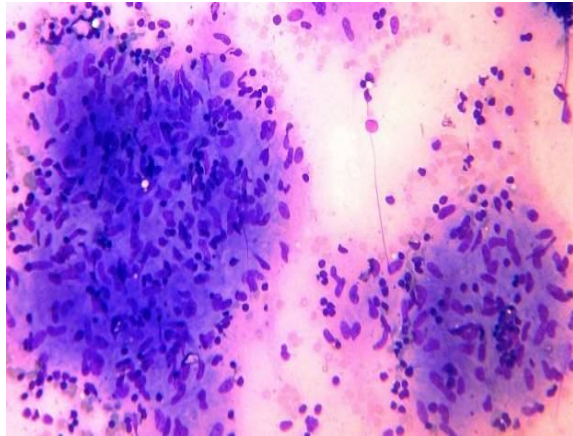


Fig. 1 Microphotograph showing variable sized granulomas composed of epithelioid cells and lymphocytes (MGGx400)

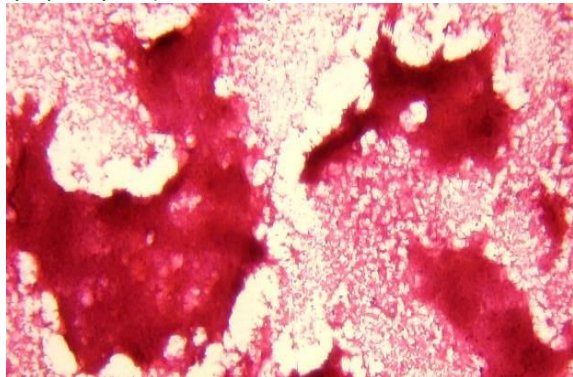


Fig. 2 Microphotograph showing irregular, acellular eosinophilic structures with well defined margins surrounded by clear halo. (H&E x400)

The most common (50.5%) pattern observed was presence of epithelioid granuloma with caseation necrosis.

In the hematoxylin and eosin (H and E) stained smears multiple irregular, homogenous, acellular, eosinophilic structures with well defined margins, surrounded by a clear halo could be appreciated which looked quite distinct from the surrounding eosinophilic debris. These were observed in twenty five percent of Group II and 30% of Group III smears

Ziehl-Neelsen (ZN) staining for tubercle bacilli was performed in all cases. The overall AFB positivity was 19.3%. Maximum AFB positivity (30.3%) was observed in Group III smears followed by Group II (18.3%) and lowest in group I smears (7.6%). (Table. 2) While comparing Group I smears with that of group III using Fisher's exact test, the difference in AFB positivity between the smears was statistically significant as the two-tailed p value was 0.0496.

Table 2 Relationship between the smear pattern and AFB positivity

Smear Pattern	Total No. of Cases	AFB Positive Cases	Percentage
Epithelioid granulomas without caseation necrosis (Group I)	26	02	7.6
Epithelioid granulomas with caseation necrosis (Group II)	60	11	18.3
Caseation necrosis without epithelioid granulomas (Group III)	33	10	30.3

Group III smears showed more number of tubercle bacilli as compared to Group I and Group II smears. In one patient ZN smears showed numerous acid fast bacilli (Fig. 3) which indicates an immunocompromised state but the immune status could not be ascertained as the patient was lost to follow up.

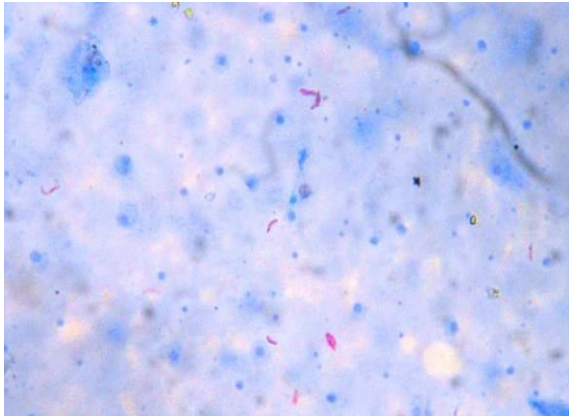


Fig. 3 Microphotograph showing scattered bright, straight or slightly curved rods of tubercular bacilli (ZN staining x1000)

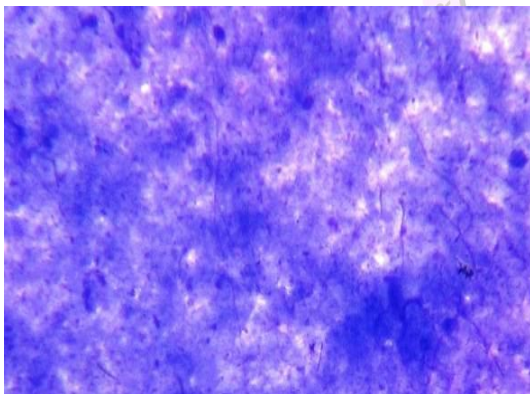


Fig. 4 Microphotograph showing acellular caseation necrotic debris (MGGx400)

In group III smears, which were negative for AFB, the diagnosis of tuberculosis was made on the basis of tubercular diathesis (Fig.4) and in correlation with clinical and laboratory parameters. All the patients showed improvement with anti-tubercular

treatment. In 10.2% of group III smears neutrophilic infiltrate was also seen.

Biopsy was done in four of the cases in which smears showed only necrotic material and were negative for AFB. Histopathological examination in these smears showed extensive areas of necrosis and few granulomas. All the patients were followed up clinically for at least six months and were seen to show improvement with anti-tubercular therapy

Discussion

Tuberculous lymphadenitis is one of the most common manifestations of extrapulmonary tuberculosis.^[5] The reliable diagnosis of tuberculous lymphadenitis by FNAC has important implications in a developing country like India with its limited resources and a very high prevalence of tuberculosis, FNAC can prove to be cost effective and easy tool in its diagnosis.

The most frequent cytological pattern seen in our study was the presence of epitheloid cell granuloma with caseation necrosis, seen in half (50.5%) of the cases. Bhattacharya et al^[6] and parsoon et al^[7] also found this cytomorphological pattern to be the commonest present in 69.4% and 44.2% of cases respectively in their studies. The presence of epitheloid granulomas without necrosis was the least common pattern in the present study and was seen in 18.3% cases. Das et al^[8] and Bhattacharya et al^[6] in their studies reported this smear pattern in 25.3% and 17.7% patients respectively.

Although granulomas without caseation necrosis may be seen in other conditions like leprosy, mycoses and sarcoidosis etc^[9] in India, however, the overall prevalence

and incidence of tuberculosis being very high, finding epithelioid cell granulomas is highly indicative of tuberculosis unless proved otherwise.^[10]

Eosinophilic structures in hematoxylin and eosin stained smears were present in 25% of the cases showing epithelioid granulomas with caseation necrosis and 30% of the smears showing necrotic material only; however, no immunologic staining for tubercular antigen were done to prove the same. Pandit et al reported the presence of certain eosinophilic structures amidst the necrotic debris in hematoxylin and eosin stained smears in cases of tuberculous lymphadenitis. These structures were multiple, pink, homogenous, irregular and acellular with well defined margins and were surrounded by a clear halo. The authors proposed that these structures represented degenerating granulomas as immunoperoxidase staining revealed the presence of tuberculous antigen. They concluded that these eosinophilic structures may be particularly helpful in cases where only necrosis is present in the absence of granulomas and AFB.^[10] Arora et al reported that these structures were not specific for tuberculosis and could also be seen in necrotic lesions of cysticercosis. They also suggested that these could represent artefacts of acellular necrosis.^[11] Thus, the significance of these structures is debatable.

The overall AFB positivity 19.3% was seen in the present study. The AFB positivity is variable in different studies ranging from 7.4% to 55.2%.^[3, 6, 7, 8, 12] AFB negative cases revealing only epithelioid cell granulomas without necrosis should be clinically correlated with microbiological assessment. Similarly, atypical cells should

be ruled out in smears showing necrosis only without epithelioid cell granulomas and AFB negativity and material should be submitted for culture.

Microbiological assessment is necessary in AFB negative cases to confirm the diagnosis of tuberculosis. It is known that for tubercle bacilli to be demonstrated microscopically, their number should be 10,000 to 1,00,000/ml of material. Hence absence of AFB in smears showing an otherwise characteristic cytological picture should not weigh against the diagnosis of tuberculosis.^[6]

Paul et al considered the smears with only acellular necrotic material devoid of granuloma or AFB to be diagnostic of tuberculous lymphadenitis on the basis of presence tubercular diathesis; which is a characteristic necrotic background comprising of eosinophilic granular material containing nuclear debris a similar connotation to tumor diathesis present in the cytological picture of malignant tumors. In their follow up study, the cytodiagnosis of these cases was found to be clinically correlative with all patients responding well to antitubercular treatment.^[2] In the present study, in the smears showing necrotic material without granulomas and AFB, the diagnosis of tuberculous lymphadenitis was suggested on the basis of tubercular diathesis (39.3%cases) in correlation with clinical and laboratory parameters. Follow up showed that all the patients improved with anti-tubercular treatment.

Smears with only necrotic material showed the maximum number of AFB whereas smears with granulomas without associated necrosis showed the least AFB positivity in the present study. This inverse

relationship between AFB positivity and the number of granulomas was seen in other studies also. [6, 7, 12] The association of increased AFB positivity in necrotic smears compared to smears with granulomas only without necrosis seen in our study was statistically significant ($p=0.0496$). The smears containing epithelioid granulomas without necrosis showed the least AFB positivity as the cell mediated immunity of the patient is able to mount a granulomatous response against tubercle bacilli. The smears containing only necrotic material, in contrast, show maximum AFB positivity because of a compromised immune status of the patient and thus lack of a granulomatous response. [6]

The accuracy of FNAC in the diagnosis of tuberculous lymphadenitis in various studies has been reported to range from 76.7% to 89.7%. [4, 13, 14] when compared with subsequent histopathological diagnosis. In our study, biopsy was done in only four patients and on follow up all the patients responded well to treatment given after FNAC based diagnosis. The histological diagnosis was consistent with the cytological opinion in all 4 cases.

FNAC can be performed as outpatient department procedure in superficial lymphadenopathy cases. The procedure is safe, well accepted by patients, very cost-effective and requires minimum instrumentation in comparison to excision biopsy. Therefore even in most remote areas, FNAC can be used for diagnosing tuberculous lymphadenopathy. Coupling FNAC with Z-N staining increases the diagnostic accuracy. Diagnostic accuracy can be further increased by submitting

some material obtained by FNAC for culture.

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