ABSTRACT

Background: Tuberculosis is a major public health problem in India and one of the main causes of lymphadenopathy. However, anti-tubercular treatment cannot be given only on clinical suspicion. Cytomorphology with acid fast staining proves to be a valuable tool in diagnosing these cases. Aim: To assess the role of FNAC in diagnosing tuberculous lymphadenitis and also to study the role of repeat aspiration cytology in patients with strong clinical suspicion of tuberculosis.

Research Methodology: FNAC were done by cytopathologist after taking a detailed clinical history regarding duration of swelling, site, size, consistency and mobility. The alcohol fixed smears were stained with Papanicolaou stain, air-dried smears stained with May-Grunwald Giemsa (MGG) and Ziehl-Neelsen (ZN) stain for Acid-Fast Bacilli (AFB).

Results: Out of 728 cases with lymphadenopathy of various aetiologies, 264 cases were diagnosed as tuberculous (TB) lymphadenitis. Four cytomorphologic patterns were observed: 1) Epithelioid granulomas with caseous necrosis: 142 cases (53.79%). 2) Epithelioid granulomas without caseous necrosis: 73 cases (27.65%). 3) Necrotising lymphadenitis: 38 cases (14.39%), and 4) Necrotising and suppurative lymphadenitis: 11 cases (4.17%). Ninety two cases were diagnosed as reactive lymphadenitis with activated histiocyte clusters and were advised a repeat aspiration after a course of antibiotics. Out of the 41 cases that turned-up for re-aspiration, 27 cases showed subsequent development of epithelioid granulomas, whereas the others continued to reveal features of reactive lymphadenitis.

Conclusion: FNAC is a reliable, rapid and cost-effective, outdoor diagnostic procedure requiring minimal instrumentation and is highly sensitive to diagnose tuberculous lymphadenitis and repeat aspiration, after 3–4 weeks helps in providing the correct diagnosis of early tubercular lesions.

Keywords: FNAC, Tuberculous lymphadenitis, AFB, Epithelioid granulomas.

INTRODUCTION

Tuberculosis (TB) remains a major public health problem worldwide, especially in the developing countries like India. About thirty percent of the tuberculous infections are extrapulmonary [1]. Peripheral tuberculous lymphadenopathy is the most common manifestation of extrapulmonary tuberculosis, mostly affects the cervical lymphnodes [1,2,3]. Since TB carries a high risk of morbidity and mortality and therefore accurate and timely diagnosis together with effective TB treatment is the mainstay of TB care and control.

Open biopsy has been traditionally the standard for the diagnosis of tuberculous lymphadenitis. However, it can be associated with significant morbidity as well as delay in diagnosis. Fine needle aspiration diagnosis of pulmonary and extra-pulmonary tuberculosis is becoming increasingly popular diagnostic tool because of its simplicity, rapidity and performance friendly nature [4,5,6]. Fine needle biopsy (FNB) avoids
the physical and psychological trauma occasionally encountered after open biopsy. It is convenient for the patient and the physician as well, useful for outpatients, and relatively painless [7]. FNB has been found to be a safe tool, a quick and inexpensive method of diagnoses with reasonable accuracy of 84.4–89.77% [8,9,10].

The present study was carried out to study the various cytomorphologic patterns in lymph nodes on FNAC and to evaluate the utility of re-aspiration cytology for detecting the subsequent development of granulomas.

MATERIALS AND METHODS

This prospective observational study was carried out at the department of pathology, Dr. Hedgewar Arogya Sansthan Hospital, from May 2009 to September 2010. FNAC was performed by cytopathologists on 728 patients who presented with peripheral lymphadenopathy. A detailed clinical history was elicited and a thorough physical examination was done along with relevant laboratory investigations and chest X-ray before subjecting the patients to aspiration. After taking proper consent, aspirations were done using 23 gauze needle with attached 10 ml disposable syringe. In all cases, alcohol fixed and air-dried smears were made: alcohol fixed slides were stained by Papanicolaou (PAP) method and air-dried smears were stained by May Grunwald-Giemsa (MGG). Special stain for acid fast bacilli (Z-N stain) was done in all cases where purulent or cheesy material was aspirated.

A detailed cytomorphologic patterns were studied. A repeat aspiration was advised after 3–4 weeks in those patients who were diagnosed as reactive lymphadenitis with activated histiocyte clusters.

RESULTS

Out of the 728 patients presented with peripheral lymphadenopathy, 264 cases were diagnosed as tuberculous lymphadenitis and 92 cases as reactive lymphadenitis with activated histiocyte clusters. The age of the patient ranged from 4 to 68 years with a median age of 32 yrs. The age group between 21–30 yrs was mostly affected (Table 1). The male: female ratio was 2:1. Among the various sites of lymph node involvements, cervical lymph nodes were the most common-137 cases (51.89%) followed by axillary, inguinal and supraclavicular nodes (Table 2).

On the basis of cytomorphological analysis, TB lymphadenitis were categorised into 4 patterns (Table 3):

1. Epithelioid granuloma with caseous necrosis-142 cases (53.79%) which showed epithelioid granuloma, caseous necrosis with or without giant cells in a background of lymphoid cells (Fig.1).

2. Epithelioid granuloma without caseous necrosis-73 cases (27.65%) which showed only epithelioid granuloma with or without giant cells (Fig. 2).

3. Necrotising lymphadenitis-38 cases (14.39%) which showed degenerating epithelioid cells in a necrotic background.

4. Necrotising and suppurative lymphadenitis-11 cases (4.17%) which showed degenerating and viable neutrophils in a necrotic background.

A definitive cytologic diagnosis of TB lymphadenitis could be considered in the smears with the first two patterns, while the third and fourth could be dismissed as acute suppurative lymphadenitis in the absence of a positive ZN stain. Different patterns showed varied AFB positivity (Table 3). The necrotising lymphadenitis showed 94.74% AFB positivity while necrotising and suppurative lymphadenitis patterns showed 90.91% AFB positivity (Fig.3). The other two patterns i.e., epithelioid granuloma with caseous necrosis and epithelioid granuloma without caseous necrosis had AFB positive only in 48 (33.80%) and 11 (15.07%) cases respectively.

Apart from the above four patterns, the present study also showed a fifth cytomorphologic pattern in 92 cases, comprising of ill formed or suspicious
epithelioid cells without characteristic necrosis or giant cells. This pattern revealed tiny foci of activated histiocytes in a background of lymphoid cells in various stages of maturation. In such cases a follow-up re-aspiration was advised after 3–4 weeks to look for subsequent development of granuloma. But only 41 cases turned-up for repeat aspiration out of which 27 cases (65.85%) developed epithelioid granuloma, and AFB were seen in 10 cases. Fourteen cases (34.15%) still remained with reactive features.

**DISCUSSION**

Tuberculosis is a major public health problem in our country. The high rate of tuberculous lymphadenitis is due to low socioeconomic status, illiteracy, incomplete treatment, resistance and increased incidence of HIV. Tubercular lymphadenitis is a common manifestation of extrapulmonary tuberculosis and one of the main causes of lymphadenopathy. Mycobacterial infections are observed among late teens and young adults [11]. Due to high morbidity associated with the disease it affects the earning potential of the individual and their families. Considering the overall prevalence of tuberculosis in the Indian context, the presence of epithelioid cell granulomas is indicative of tuberculosis [12].

FNB has been very useful in the diagnosis of tuberculous lymphadenitis as it was discussed in numerous publications [9, 13–15]. Many authors described three cytomorphologic patterns [16,17]. Whereas some categorized cytologic features of tuberculous lymphadenitis into four groups: (1) epithelioid cell clusters with or without Langhans’s giant cells, without necrosis, (2) epithelioid cell clusters with or without Langhans's giant cells, with necrosis, (3) occasional epithelioid cells without characteristic of necrosis nor giant cells, and (4) necrosis without epithelioid cell clusters nor Langhans’s giant cells [18,19]. Our study also revealed four patterns similar to the study by Nayak et al [20].

The comparison between various cytomorphologic patterns by different authors is shown in Table 4. The present study showed that every age group of the population was affected by TB and the incidence of the disease was higher in males than in females. This is in correlation with the study by Gupta et al [20]. The cervical group of lymph nodes were the most commonly affected site (51.89%) which was similar to other studies [3,11,22]. The other affected sites were axillary and inguinal group of lymph nodes. These findings were similar to the study by Ng et al [23].

It is observed that there is an inverse relationship between granulomas and the presence of AFB [4,16,24,25]. Our study found higher AFB positivity in smears containing necrotic materials. It was similar to the study by Malakar et al [26]. TB lymphadenitis has unique stages as described by Jones et al [27]. The aspirates from stage one or two tuberculous lymphadenitis usually provide inflammatory cells as seen in reactive lymphadenitis. Thus, FNAC of these stages can only be non-specific reactive. Typical necrotic materials or tubercle bacilli can be seen in the advanced stages in which an abscess is readily formed in the core of the lymph node [8]. So aspirates from an early stage lymph node were the main cause of low sensitivity. If lymph node aspiration was done once in the early stage, the diagnosis is likely to be dismissed as a reactive node.

This study shows that re-aspirating after three or four weeks improves the diagnostic efficacy of FNAC. It is therefore necessary to follow the patients whose clinical findings are compatible with TB lesions.

**CONCLUSION**

To conclude, every case of peripheral lymphadenopathy needs to undergo Fine Needle Aspiration Cytology. This technique coupled with Ziehl-Neelsen staining for Acid Fast Bacilli is an excellent method for diagnosing tuberculous
lymphadenitis. It can even provide an important clue about the immune status of the patient. The study also included the significance of repeat aspiration cytology in patients with strong clinical suspicion of tuberculosis.

ACKNOWLEDGEMENT
Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors, editors, publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

REFERENCES
16. Das DK, Pant JN, Chachra M et al. Tuberculous lymphadenitis: correlation of cellular components and necrosis in lymph node aspirate with AFB positivity and

Table 1: Cytomorphologic patterns of TB lymphadenitis in relation to age

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Age group (in years)</th>
<th>Epithelioid granuloma with caseous necrosis (Total 142)</th>
<th>Epithelioid granuloma without caseous necrosis (Total 73)</th>
<th>Necrotizing lymphadenitis (Total 38)</th>
<th>Necrotizing &amp; suppurative lymphadenitis (Total 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>0–10</td>
<td>25 17.61%</td>
<td>32 43.84%</td>
<td>4 10.53%</td>
<td>1 9.09%</td>
</tr>
<tr>
<td>2.</td>
<td>11–20</td>
<td>20 14.08%</td>
<td>23 31.51%</td>
<td>6 15.79%</td>
<td>2 18.18%</td>
</tr>
<tr>
<td>3.</td>
<td>21–30</td>
<td>54 38.03%</td>
<td>11 15.07%</td>
<td>12 31.58%</td>
<td>4 36.37%</td>
</tr>
<tr>
<td>4.</td>
<td>31–40</td>
<td>23 16.20%</td>
<td>2 2.74%</td>
<td>12 31.58%</td>
<td>2 18.18%</td>
</tr>
<tr>
<td>5.</td>
<td>41–50</td>
<td>13 9.15%</td>
<td>3 4.10%</td>
<td>2 5.26%</td>
<td>1 9.09%</td>
</tr>
<tr>
<td>6.</td>
<td>51–60</td>
<td>4 2.82%</td>
<td>1 1.37%</td>
<td>1 2.63%</td>
<td>1 9.09%</td>
</tr>
<tr>
<td>7.</td>
<td>61–70</td>
<td>3 2.11%</td>
<td>1 1.37%</td>
<td>1 2.63%</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 2: Sites of FNAC and number of cases

<table>
<thead>
<tr>
<th>S. No</th>
<th>Sites</th>
<th>Number of cases (Total = 264)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Cervical</td>
<td>137</td>
<td>51.89%</td>
</tr>
<tr>
<td>2.</td>
<td>Axillary</td>
<td>66</td>
<td>25%</td>
</tr>
<tr>
<td>3.</td>
<td>Inguinal</td>
<td>49</td>
<td>18.56%</td>
</tr>
<tr>
<td>4.</td>
<td>Supraclavicular</td>
<td>12</td>
<td>4.55%</td>
</tr>
</tbody>
</table>

Table 3: Cytomorphologic patterns with AFB positivity

<table>
<thead>
<tr>
<th>S. No</th>
<th>Cytomorphology</th>
<th>Total (%)</th>
<th>AFB positivity(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Epithelioid granuloma with caseous necrosis</td>
<td>142 (53.79%)</td>
<td>48 (33.80%)</td>
</tr>
<tr>
<td>2.</td>
<td>Epithelioid granuloma without caseous necrosis</td>
<td>73 (27.65%)</td>
<td>11 (15.07%)</td>
</tr>
<tr>
<td>3.</td>
<td>Necrotising lymphadenitis</td>
<td>38 (14.39%)</td>
<td>36 (94.74%)</td>
</tr>
<tr>
<td>4.</td>
<td>Necrotising and suppurative lymphadenitis</td>
<td>11 (4.17%)</td>
<td>10 (90.91%)</td>
</tr>
</tbody>
</table>

Table 4: Comparison between studies undertaken by various authors

<table>
<thead>
<tr>
<th>S. No</th>
<th>Study</th>
<th>Epithelioid granuloma with caseous necrosis</th>
<th>Epithelioid granuloma without caseous necrosis</th>
<th>Necrotizing lymphadenitis</th>
<th>Necrotizing and suppurative lymphadenitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ng et al [23]</td>
<td>18%</td>
<td>66%</td>
<td>7%</td>
<td>9%</td>
</tr>
<tr>
<td>2.</td>
<td>Das et al [16]</td>
<td>39.1%</td>
<td>25.3%</td>
<td>35.6%</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>Llatjos et al [17]</td>
<td>30.43%</td>
<td>17.29%</td>
<td>52.17%</td>
<td>-</td>
</tr>
<tr>
<td>4.</td>
<td>Present study</td>
<td>53.79%</td>
<td>27.65%</td>
<td>14.39%</td>
<td>4.17%</td>
</tr>
</tbody>
</table>

Fig.1. Photomicrograph of lymph node aspirate revealing Langhan’s giant cell along with abundant polymorphonuclear leukocytes (Pap X1000)
Fig. 2. Tuberculous lymphadenitis showing well-formed epithelioid cell granuloma (MGG X1000)

Fig. 3. Photomicrograph of AFB in a background of caseous necrosis (ZN stain X1000)