Histopathology of lymph nodal tuberculosis – University Hospital experience

P JAYALAKSHMI, MRCPATH, AK MALIK, MD, HS SOO-HOO, PhD*

Department of Pathology and *Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur

Abstract

Fifty-nine cases of tuberculous cervical lymphadenitis were analysed histologically. Characteristic epithelioid cell granulomas were seen in all the cases with central areas of caseation necrosis in 96.6% (57/59) of these cases. The diagnosis of tuberculosis was further established by the demonstration of acid-fast bacilli (AFB) in the tissue sections in 29 cases. These AFB, although occasional, were found more frequently within the epithelioid cells as compared with other zones of the granuloma. There was no significant association between necrosis and bacillary content. We conclude that light microscopical assessment is still a useful screening method to diagnose tuberculosis in cases of cervical lymphadenopathy.

Key words: Cervical lymph node, tuberculosis, acid-fast bacilli.

INTRODUCTION

Tuberculosis is still a public health problem in Malaysia and is one of the ten major causes of death in Government hospitals. Extrapulmonary tuberculosis constitutes about 9.4% of the total number of cases of tuberculosis. Although tuberculous lymphadenitis is one of the most common forms of extrapulmonary tuberculosis, very few studies on the histopathology of this condition have been done. The purpose of our paper is to study the pathological spectrum of lymph nodal tuberculosis as encountered in the University Hospital.

MATERIALS AND METHODS

During the period January 1987 to July 1992, a total of 455 consecutive lymph node biopsies were received by the Department of Pathology. Of these 455 cases, 252 cases showed malignancy. A review of the remaining 203 cases of nonneoplastic lymph nodes was done. Ziehl-Neelsen staining for acid-fast bacilli (AFB) and Periodic acid-Schiff staining for fungal organisms, were done in all the cases. The diagnosis of tuberculosis was made on the criteria of well formed epithelioid cell granuloma with or without caseation necrosis and or demonstration of AFB. There were 63 cases of tuberculous lymphadenitis, 59 involving cervical group lymph nodes, 3 axillary group lymph nodes and 1 involving a hilar lymph node. Patients who had axillary tuberculous lymphadenitis were infants who developed lymphadenitis following BCG vaccination. We studied only cases of tuberculous cervical lymphadenitis. The pathological features noted included the nature of the granuloma, amount of necrosis, types of giant cells, presence of fibrosis and perinodal granulomatous inflammation. Necrosis was considered massive when caseation was present in more than 50% of the area of lymph node, submassive when it occupied less than 50% and focal when scattered microscopical foci were noted. Furthermore, histological analysis of all cases of tuberculosis involving the other organs in order to find the comparative frequency of tuberculous lymphadenitis was done.

Mycobacterial isolation at the time of undertaking biopsy was done in only 9 cases. Direct smear for AFB was made before the lymph node tissue was inoculated onto Lowenstein-Jensen medium. The latter was examined on alternate days for any growth. Clinical data was based on relevant information provided in the request form accompanying each biopsy.

RESULTS

Lymph node tuberculosis is the most common form of tuberculosis diagnosed histologically in the University Hospital (Table 1). The distribution of organ involvement in the order of frequency is given in Table 1. Tuberculous lymphadenitis constituted 13.8% of all cases of lymphadenopathy (Table 2).

The ages of patients ranged from 4 to 78 years with a mean of 32 years. There were 36 females
TABLE 1: Distribution of histologically diagnosed cases of tuberculosis by organ involvement between January 1987 and December 1992

<table>
<thead>
<tr>
<th>Site</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>63</td>
</tr>
<tr>
<td>Pleura</td>
<td>42</td>
</tr>
<tr>
<td>Bone and soft tissue</td>
<td>23</td>
</tr>
<tr>
<td>Lung</td>
<td>12</td>
</tr>
<tr>
<td>Genitourinary tract</td>
<td>12</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td>12</td>
</tr>
<tr>
<td>Skin</td>
<td>3</td>
</tr>
<tr>
<td>Vocal cord</td>
<td>2</td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>1</td>
</tr>
<tr>
<td>Breast</td>
<td>1</td>
</tr>
<tr>
<td>Pericardium</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>172</strong></td>
</tr>
</tbody>
</table>

and 23 males. Tuberculosis was suspected clinically in 47 patients, while in 4 patients a differential diagnosis of lymphoma was considered. An initial clinical diagnosis of lymphoma was made in 3 patients. Pyogenic infection and a branchial cyst was considered in 2 and 1 patient respectively.

Among the 9 cases from whom AFB culture was undertaken, *Mycobacterium tuberculosis* was grown only in 2 cases (22%). Atypical mycobacteria was isolated in one case. Even though the culture was negative in 6 cases, direct smear for AFB was positive in 2 cases.

TABLE 2: Lymph node pathology by rank order

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic tumour</td>
<td>139</td>
<td>30.6</td>
</tr>
<tr>
<td>Reactive lymphadenitis</td>
<td>115</td>
<td>25.3</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>113</td>
<td>24.8</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>63</td>
<td>13.8</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>25</td>
<td>5.5</td>
</tr>
<tr>
<td>Kikuchi's lymphadenitis</td>
<td>(8)</td>
<td></td>
</tr>
<tr>
<td>Dermatopathic lymphadenitis</td>
<td>(5)</td>
<td></td>
</tr>
<tr>
<td>Suppurative lymphadenitis</td>
<td>(4)</td>
<td></td>
</tr>
<tr>
<td>Non-specific</td>
<td>(4)</td>
<td></td>
</tr>
<tr>
<td>Castleman's disease</td>
<td>(2)</td>
<td></td>
</tr>
<tr>
<td>Histioctytosis-X</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>455</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

( ) = number of cases

DISCUSSION

Tuberculosis remains a major health problem in South East Asia. Tuberculous pleurisy is the commonest form of extrapulmonary tuberculosis. However, in our study the lymph node is the most frequent site of histologically-proven tuberculosis. This is probably due to the fact that, in some cases of tuberculous pleurisy, the diagnosis was based on culture of AFB without tissue diagnosis. Cervical lymphadenopathy is the most common form of...
FIG. 1: Epithelioid cell granuloma with Langhans’ giant cell. Haematoxylin and eosin x 250.

FIG. 2: Histology showing granuloma of varying sizes. Haematoxylin and eosin x 125.
lymph node tuberculosis noted in our analysis and this finding was similar to other studies.\textsuperscript{6,7} The preponderance of cervical node tuberculosis could be possibly the result of lymphoid tissue in the tonsils, adenoids and Waldayer's ring facilitating an easy entry to \textit{mycobacteria}.\textsuperscript{6}

Tuberculosis of lymph nodes can present at any age. It was observed most frequently in the third decade of life in our study as in other published reports.\textsuperscript{3,4} We have also found that tuberculous \textit{lymphadenitis} is more commonly seen in females, a similar experience recorded by others.\textsuperscript{2,10} The reason for this is not clear.

Although several studies on the role and utility of fine needle aspiration cytology in establishing the diagnosis of tuberculous lymphadenitis have

\begin{table}[h]
\centering
\caption{Correlation between presence of necrosis and acid-fast bacilli}
\begin{tabular}{|c|c|c|}
\hline
\textbf{Caseation} & \textbf{Acid-fast bacilli} \\
\hline
Present  & Positive & 27 \\
        & Negative & 27 \\
\hline
Absent   & Positive & 2 \\
        & Negative & 3 \\
\hline
Total    & 29 & 30 \\
\hline
\end{tabular}
\end{table}

been published,\textsuperscript{11,12,13} surprisingly only two publications elucidated the histopathological aspects of lymph nodal \textit{tuberculosis}.\textsuperscript{2,3} Among the various pathological features of tuberculosis analysed in our study, a number of interesting observations have emerged. The two histological features which are useful in the diagnosis of tuberculosis are variation in the size of the granulomata and the presence of caseation necrosis. None of the cases in the present study had granuloma of uniform size. Sarcoidosis has to be ruled out in the presence of isomorphic granulomata. Caseation necrosis is an important microscopical feature noted in 57 out of 59 cases in the study. However, there was no correlation between necrosis and \textit{AFB} demonstration (p=1.0), unlike in an earlier study by Das \textit{et al}.\textsuperscript{11} In the latter study, \textit{bacilli} were seen more frequently in those cases with caseation necrosis. We have specifically looked at the different zones of the granuloma for the detection of \textit{AFB} and they were more frequently observed in the epithelioid cells compared to necrotic area. This is perhaps due to the fact that \textit{bacilli} in the necrotic area are either highly fragmented or completely disintegrated and thus not identifiable in routine Ziehl-Neelsen stained sections. The

\begin{table}[h]
\centering
\caption{Bacillary content versus different zones of the granuloma}
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Site of bacilli} & \textbf{No.} & \textbf{Bacillary content} & \\
\textit{---} & \textit{Scanty} & \textit{Numerous} \\
\hline
Epithelioid cells & 13 & 11 & 2 \\
Borderzone & & & \\
\textit{(Epithelioid cells/necrosis)} & 6 & 6 & 0 \\
Caseation necrosis & 8 & 7 & 1 \\
Epithelioid cells and necrosis & 2 & 1 & 1 \\
\hline
Total & 29 & 25 & 4 \\
\hline
\end{tabular}
\end{table}
overall AFB positivity of 49% in our study is similar to other published data.\textsuperscript{14,15}

Culture of the lymph node was undertaken only in nine cases. \textit{Mycobacterium tuberculosis} and atypical mycobacteria were grown in culture only in 2 and 1 case respectively. The reason for the low yield was probably due to the small number of live bacilli in the lymph node. The positive yield for AFB in the literature varies from 18% to 90%.\textsuperscript{16,17} Fibrosis in the lymph node was seen in 19 cases indicating chronicity. However in all these cases caseation necrosis was also present suggesting activity.

\textbf{Mycobacterial lymphadenitis} in the cervical region can be confused with many other conditions clinically which include malignancy, infections and reactive conditions. The histological differential diagnosis is granulomatous lymphadenitis due to sarcoidosis, foreign body granuloma and fungal infection. Clinical features as well as microscopic findings such as noncaseating granulomata in the absence of AFB suggest sarcoidosis. Fungal infection is diagnosed by the identification of the organisms in the Periodic acid-Schiff stain. Where history and tuberculin test are noncontributory and culture techniques are not easily available, a histological assessment of the excised lymph node is a simple diagnostic tool. In our study AFB were seen only in 49% of biopsies, even after a careful search. In the majority of these cases (89%), only an occasional bacillus was found. We recommend that bacilli should be looked for especially in the epithelioid cells and in the borderzone (interface of epithelioid cell and necrosis) of the granulomas to further substantiate the diagnosis of tuberculosis. Ideally culture must be undertaken not only for detection of AFB but also subclassification of the various types of mycobacteria especially the atypical forms. Such an effort is imperative in view of rising incidence of HIV infection in Malaysia.

\textbf{Acknowledgement}

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\textbf{REFERENCES}


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