A MORPHOLOGICAL STUDY OF NON-NEOPLASTIC LYMPHADENOPATHY

Niaz Mohammad Sulaiman Khan Khalil, Naseer Ahmad Chaudhry, Raza Malik, Rakhshindah Bajwa, Saeed Akhtar Khan and Jamil Ahmad

Department of Pathology,
Bolan Medical College Quetta,
Postgraduate Medical Institute, Lahore
and PMRC Islamabad and Lahore.

SUMMARY

A total of 200 lymph node specimens were studied. The age of these patients ranged from 2 years to 70 years. Maximum number of patients with lymphadenopathy (87 out of 200) 43% cases was in 10-19 years age group. Females (56.5%) presenting with lymph node enlargement were more affected than males (43.5%). The commonest presenting complaints were fever (67%). Cervical lymph nodes (83%) were the commonest site of involvement. Duration of lymph node enlargement ranged from 2-5 months in 143 out of 200 (71.5%). On histopathological examination, five morphological groups were highlighted: tuberculous lymphadenitis (50.5%) chronic non-specific lymphadenitis (43.5%), viral lymphadenitis (4%), fungal lymphadenitis (1%) and acute bacterial lymphadenitis (1%). The study also highlights the yield of mycobacteria on fluorescent staining as highly significant (P<0.001) as compared to Ziehl-Neelsen staining, hereby providing the superiority of fluorescent stain. In the present study, 8 out of 200 (4%) and 2 of 200 (1%) lymph node biopsies were found to have viral inclusions and fungal hyphae respectively. Two out of 200 (1%) lymph node biopsies were diagnosed to be acute bacterial lymphadenitis.

INTRODUCTION

Non-neoplastic lymph node lesions are more common as compared to neoplastic ones. Lymph nodes are usually involved in chronic disease such as tuberculosis, oxplasmosis, coccidioidomycosis, histoplasmosis, nocardia brasiliensis infection and suppurative granulomatous lymphadenitis.

Lymph nodes are also involved in acute bacterial disease such as Staphylococcal lymphadenitis and yersinia pseu- tuberculosis. Moreover lymphadeno-
A Morphological Study of Non-Neoplastic Lymphadenopathy

SITE OF LYMPH NODE BIOPSY OF PATIENTS WITH LYMPHADENOPATHY

<table>
<thead>
<tr>
<th>Site of Biopsy</th>
<th>No. of Cases</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>166</td>
<td>83.0</td>
</tr>
<tr>
<td>Axillary</td>
<td>18</td>
<td>9.0</td>
</tr>
<tr>
<td>Submandibular</td>
<td>6</td>
<td>3.0</td>
</tr>
<tr>
<td>Inguinal</td>
<td>5</td>
<td>2.5</td>
</tr>
<tr>
<td>Mediastinal</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>Mesenteric</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Anterior Chest</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Pre-auricular</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

TABLE - 1

Lymphadenopathy has been reported in cat-scratch disease.14

Mycotic involvement of lymph nodes have been studied with different features in different fungal infections. Robinson and Fogel17 reported a case of granulomatous lymphadenitis caused by coccidioides immitis which was diagnosed in the Eastern United States using staining techniques (Periodic Acid-Schiff and methenamine silver stain).

Persistent generalized lymphadenopathy is widely used as marker of asymptomatic human immunodeficiency virus infection.15

Lymph node enlargement may occur in disease caused by other viruses like Epstein-

Barr virus,16 Varicella zoster virus17 and herpes simplex virus.18

Mialiuskas and Leong18 reported localized herpes simplex lymphadenitis in 3 patients. Histopathological features were paracortical hyperplasia, follicular hyperplasia with diagnostic intranuclear inclusions. However, the diagnosis was finally confirmed by immunohistochemistry.

Lymph node involvement by diseases characterised by immune cell activation have been reported, such as systemic lupus erythematosus16, reaction due to drugs20 angioimmunoblastic lymphadenopathy21 and rheumatoid arthritis.22

COMPARISON OF ZIEHL-NEELSEN STAINING IN CASES OF CHRONIC GRANULOMATOUS LYMPHADENOPATHY

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Ziehl-Neelsen positive</th>
<th>Ziehl-Neelsen negative</th>
<th>Not stained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caseous granulomatous</td>
<td>20</td>
<td>60</td>
<td>80</td>
</tr>
<tr>
<td>Lymphadenitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-caseous granulomatous</td>
<td>9</td>
<td>14</td>
<td>23</td>
</tr>
<tr>
<td>Lymphadenitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>74</td>
<td>103</td>
</tr>
</tbody>
</table>

P = Not significant

TABLE - 3

COMPARISON BETWEEN AURAMINE-RHODAMINE AND ZIEHL-NEELSEN IN CASES OF CHRONIC CASEOUS GRANULOMATOUS LYMPHADENOPATHY

<table>
<thead>
<tr>
<th>Group</th>
<th>Auramine-Rhodamine Positive</th>
<th>Auramine-Rhodamine Negative</th>
<th>Auramine-Rhodamine Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziehl-Neelsen</td>
<td>14</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>47*</td>
<td>13</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>19</td>
<td>80</td>
</tr>
</tbody>
</table>

*P<0.001 as compared to Ziehl-Neelsen stain

TABLE - 4
Many miscellaneous diseases involving lymph nodes have been reported, for example, kikuchi’s lymphadenitis, sinus histiocytosis with massive lymphadenopathy, lymph node infarction and lymph node inclusions. Peripheral tuberculous lymphadenopathy is the commonest form of extrapulmonary tuberculosis.

The present study was carried out to determine the frequency of various types of non-neoplastic lymphadenopathy and to study the morphological change in non-neoplastic lymphadenopathy.

**HISTOPATHOLOGICAL DIAGNOSIS OF PATIENTS WITH LYMPHADENOPATHY**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Chronic-specific lymphadenitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Bacterial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Granulomatous</td>
<td>101</td>
<td>50.5</td>
</tr>
<tr>
<td>b) Non-granulomatous</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>2. Viral lymphadenitis</td>
<td>8</td>
<td>4.0</td>
</tr>
<tr>
<td>3. Fungal lymphadenitis</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>II Chronic non-specific lymphadenitis</td>
<td>87</td>
<td>43.5</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

**TABLE – 5**

**TABLE – 6**

**COMPARISON OF FLUORESCENT (AURAMINE-RHODAMINE) STAINING IN CASES OF CHRONIC GRANULOMATOUS LYMPHADENOPATHY**

<table>
<thead>
<tr>
<th>Histopathological findings</th>
<th>Fluorescent positive</th>
<th>Fluorescent negative</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caseous granulomatous lymphadenitis</td>
<td>61</td>
<td>19</td>
<td>80</td>
</tr>
<tr>
<td>Non-caseous granulomatous lymphadenitis</td>
<td>15</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>27</td>
<td>103</td>
</tr>
</tbody>
</table>

P = Not significant
MATERIAL AND METHODS

A total of 200 specimens of the lymph nodes were collected from various hospitals, Lahore. Patients of all ages and both sexes were included in the study.

Clinical information regarding history, physical examination and relevant investigations were obtained from the patients and doctor incharge.

The specimens of the lymph nodes were collected irrespective of any specific sites for morphological study. The specimen were kept in labelled jars, containing 10% formol saline, after detailed gross examination of each specimens, all the sections were stained with Haematoxylin and Eosin (H&E) and reticulin stains. Whereas granulomatous lesions were stained with Ziehl-Neelsen, Auramine-Rhodamine, periodic acid-schiff, whereas, methenamine silver and Giemsa stains were used when required. In non-granulomatous lesions, Gram stain, Congo red and phyloxin-tartrazine stains were used.

RESULTS

A total of 200 lymph node specimens were studied. Maximum number of patients with lymphadenopathy 87 out of 200 (43.5%) were in 10-19 years age group (Fig. 1). In the present study significantly greater (P<0.01) number of females (113 out 200) presented with lymph node enlargement (Fig. 2). The common presenting symptom was fever (Fig. 3). Cervical lymph nodes (166 out of 200, 83%) were the commonest site of biopsy involved in these patients (Table 1).

The investigations carried out on these patients were haemoglobin estimation, erythrocyte sedimentation rate and X-ray chest (Fig. 4).
A Morphological Study of Non-Neoplastic Lymphadenopathy

Presenting Complaints of Patients with Lymphadenopathy

Fig. 3

Investigation of Patients with Lymphadenopathy

Fig. 4

JPNI Vol. 14 (2) 52-60
On microscopic examination of 200 lymph node biopsies, chronic specific lymphadenitis was significantly (P<0.01) commoner as compared to chronic non-specific lymphadenitis (Table 2). Granulomatous lesions (103 cases, 51.5%) were the commonest (Table 3 and 4).

Fluorescent staining of histopathological sections from 103 chronic granulomatous lymphadenitis gave positive results in 76 out of 103 (73.78%) cases, however Ziehl-Neelsen staining was positive only in 29 out 103 (28.15%) cases (Tables 3 and 5).

However, the yield of mycobacteria on fluorescent staining was highly significant (P<0.001) as compared to Ziehl-Neelsen staining, thereby proving the superiority of fluorescent stain.

In the present study, 8 out of 200 (4%), and 2 out 200 (1%) lymph node biopsies were found to have viral inclusions and fungal hyphae respectively (Fig. 5).

Viral intracellular inclusions were detected by utilizing phloxintartrazine stain. Fungal hyphae were, however, identified on periodic acid schiff and methenamine silver stain.

In our study, 2 out of 200 (1%) lymph node biopsies were diagnosed to be acute bacterial lymphadenitis. Gram positive cocci were detected on Gram stain of histological sections (Table 6).

**DISCUSSION**

Enlargement of lymph nodes as a primary pathology in all age groups is encountered frequently in the surgical outpatients department. A total 200 lymph node specimens were studied. Maximum number of patients with lymphadenopathy, 87 out of 200 cases (43.51%) were in 10-19 years of age, these findings were comparable with those of Ahmad who studied 80 patients with lymphadenopathy in Mayo Hospital Lahore, and reported 26 out 80 cases (32.5%) in 11-20 years of age group. In the present study significantly greater number of females, 113 out of 200 cases (P<0.001) presented with lymph node enlargement. Krishnaswami et al studied 265 patients with lymphadenopathy in India. Out of these 265, 148 were found to be females. Ahmad also reported lymphadenopathy in females, 42 out of 80 cases in his study in Lahore.

The common presenting symptoms of our patients were fever, weight loss, productive cough and sore throat. Nearly all workers found the same complaints in their patients with lymphadenopathy.

The investigations carried out in most of our patients showed moderate anaemia and raised erythrocyte sedimentation rate. Those were the typical laboratory finding reported by other workers as well.

On microscopic examination specific cause of lymphadenitis was found in 113 out of 200 cases (56.5%). The findings are comparable to the study by Dandapat et al.

In the present study, granulomatous lesions 103 out of 200 cases (51.5%) were the commonest. The same were the findings of Dandapat et al and Krishnaswami et al.

Fluorescent staining of histopathological sections from 103 chronic granulomatous lymphadenitis revealed Mycobacteria in 76 out of 103 (73.78%) cases. Different studies quote an incidence of demonstration of Mycobacteria on fluorescent stain varying from 55.76% to 74.35%.

In our study Mycobacteria on Ziehl-Neelsen staining was positive only in 29 out of 103 (28.15%) cases. Different studies quote frequency of demonstration of Mycobacteria on Ziehl-Neelsen staining, varying from 16.27% to 37.5%.

In our study, however the yield of mycobacteria on fluorescent staining was
FIG. 5
SCHEMATIC REPRESENTATION OF NON-NEOPLASTIC LYMPHADENOPATHY

200
H&E
RET

103 Granulomatous
PAS

97 Non-granulomatous
PT stain

2 PAS + ve
(Fungal granuloma)
AR - ve
ZN - ve

101 PAS - ve
AR
ZN

8 PT + ve
(Viral lymphadenitis)

89 PT - ve
Gram stain

84 AR + ve
ZN + ve
(Tuberculous
lymphadenitis)

17 AR - ve
ZN - ve

17 Giemsa - ve
(Granulomatous
lymphadenitis)

Positive for
micro-organism

Negative for
micro-organism

2 + ve for
Gram + ve Cocci
(Acute acteral
lymphadenitis)

87 (Chronic non-
specific lymphadenitis)

Key:
H&E = Haemotoxylin and Eosin stain
RET = Reticulin stain
PAS = Periodic-Acid Schiff stain
PT = Phloxine-Tartrazine stain
AR = Auramine-Rhodamine stain
ZN = Ziehl-Neelsen stain
highly significant (P<0.001) as compared to Ziehl-Neelsen staining, thereby proving the superiority of fluorescent stain. The superiority of Auramine-Rhodamine stain over Ziehl-Neelsen technique is demonstrated by other workers as well.32-33

Tuberculous lymphadenopathy is the commonest morphological findings in our study. In 101 cases the histopathological diagnosis was consistent with tuberculous lymphadenitis giving an overall 50.5% in 200 lymph node specimens.

There were 2 out of 200 (1%) cases of fungal lymphadenitis in our study. Fungal hyphae were seen on periodic acid-schiff and methenamine silver stains.

Robinson and Fogel7 diagnosed a case of granulomatous lymphadenitis caused by Coccidiodes immitis by using periodic acid-schiff (PAS) and Gomori methenamine silver stains for fungi.

In our study, 2 of 200 (1%) lymph node biopsies were diagnosed to be acute bacterial lymphadenitis. Gram positive cocci were detected on Gram stain of histological sections. Ahmad2 also reported 4 out of 63 (6.34%) cases of acute lymphadenitis in his study in Lahore. Brook54 studied 33 out of 40 cases of cervical lymphadenopathy with history of recurrent non Streptococcal tonsillitis. Diagnosis was made on the basis of culture.

In the present study we found 8 out of 200 (4%) cases of viral lymphadenitis. Viral inclusions were seen on phloxin-tartrazine stain. Mean age is 21.37 years.

Mialiauskas and Leong18 reported localized herpes simplex lymphadenitis in 3 patients. Histopathological features were paracortical hyperplasia, follicular hyperplasia with diagnostic intranuclear inclusions. However, the diagnosis was finally confirmed by immunohistochemistry.

In the present study, 87 out of 200 (43.5%) cases of chronic non-specific lymphadenitis were found. Similarly Hussain and Jaferey28 reported 8 out of 55 (14.5%) cases in paediatric age group in Karachi. In another study Krishnaswami et al29 reported 75 out of 265 (28.3%) cases in India. Dandapat et al1 reported 58 out of 192 (30.21%) cases in India. Ahmad2 also reported 16 out of 63 (25.39%) cases in Lahore.

Thus on conclusion this study highlights, five morphological groups, tuberculous lymphadenitis (50.5%), chronic non-specific lymphadenitis (43.5%), viral lymphadenitis (4%), fungal lymphadenitis (1%) and acute bacterial lymphadenitis (1%). It is noted that tuberculosis is an important differential diagnosis of cervical lymphadenopathy and cervical lymph node biopsies should be sent for histological as well as for microbiological examination.

REFERENCES


