HISTOPATHOLOGICAL STUDY OF PLEURA IN 50 CASES OF PLEURAL EFFUSION

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ABSTRACT

BACKGROUND

Pleural effusion is very common worldwide, which is broadly differentiated into exudative and transudative types depending upon various characteristics of fluid. This broad division further classified depending upon aetiology. Main cause of pleural effusion in developing countries including India is tuberculosis. Effusion due to malignancy is also common in India especially among elderly age group individuals. Diagnostic methods include pleural fluid analysis, thoracoscopic studies and pleural biopsy. Histopathological examination of the pleura is very much important in deriving the definitive diagnosis of the pleural effusion.

MATERIALS AND METHODS

50 random cases were selected and made to undergo pleural biopsy with Abrams punch biopsy needle after ruling out bleeding diathesis. Citrated pleural fluid was collected for cytological and biochemical analysis as well. Simultaneously, sample of pleura was sent for histopathological analysis. Based on the presence or nature of mesothelial lining, a reporting of normal pleura, inadequate for reporting, tuberculous or malignant was done. Sample was also sent for bacteriological studies. Four out of five transudates on biopsy showed normal pleura giving a specificity of 80%.

RESULTS

The age group ranged from 14 to 80 years. Male-to-female ratio was 3:1. Effusions were more frequent on right side as compared to left. Radiologically, all had pleural effusions and sputum for AFB was negative in all cases. Majority of the straw-coloured effusions were tubercular effusions, whereas most of malignant effusions were haemorrhagic. Two-third of these cases showed tubercular granuloma and a small number were found to have malignancy. A significant number (41%) showed nonspecific pleuritis.

CONCLUSION

A definitive diagnosis of tuberculosis or malignancy could be established in 16 (32%) cases by pleural biopsy alone, thus showing a sensitivity of 38%, which enhanced to 40% on combining histopathological and pleural fluid cytological examination.

KEYWORDS

Pleural Effusion, Histopathology.

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BACKGROUND

Pleural effusion is the most common manifestation of the pleural involvement. After routine haematological and radiological investigations, the diagnostic workup of patients with clinically significant pleural effusion usually begins with analysis of pleural fluid analysis after a thoracentesis. Then, on the basis of whether the fluid is transudate or exudate (according to Light’s Criteria), diagnostic insight is provided and further evaluation carried out.1 Pleural biopsy is helpful to reach an aetiological diagnosis of exudative pleural effusion particularly when malignancy is suspected or when results of detailed pleural fluid study are inconclusive, especially in a setup where thoracoscope is not available. The role of needle biopsy for diagnosis of pleural effusion is well-defined. Multiple pleural biopsies (closed or open) increase the diagnostic potential and subsequent investigations will disclose if these patients are bearers of malignant or granulomatous pleuritis. A significant percentage of pleural effusion remains undiagnosed. In such circumstances, the anatomical-pathological correlation of nonspecific chronic pleuritis should be taken into account mainly by the pneumologist who usually makes the clinical-pathological correlation and infer the final diagnosis. This study was undertaken to study histopathological changes of pleura in pleural effusion and to evaluate the efficacy of pleural biopsy as a diagnostic tool in pleural effusion.

MATERIALS AND METHODS

The present study was undertaken at Karwar Institute of Medical Sciences, Karwar, comprising of 50 cases of pleural effusions admitted during the period from August 2015 to
January 2017. The cases taken up for study were randomly chosen. Patients whose general conditions was not satisfactory for performing pleural biopsy or those who refused to undergo the procedure were omitted from the study. A detailed clinical examination was done in all patients and the clinical data was recorded according to the proforma. Routine investigations were done in all cases including chest x-ray/screening and sputum investigations. After ruling out any bleeding diathesis, pleural fluid aspiration and biopsy were done in all cases. Pleural biopsy was done using Abrams punch biopsy needle in the posterior scapular line in the 8th or 7th intercostal space depending upon the area of maximum dullness. A citrated sample of fluid was sent for cytological evaluation. Simultaneously, a sample was sent for bacteriological studies. The biopsied specimen was sent for histopathological study with 10% formalin.

Criteria for Histopathological Diagnosis
1. Adequate Pleura- The biopsy sample was considered to be adequate only when it showed mesothelial lining.
2. Inadequate Pleura- When mesothelial lining was not seen inadequate pleura was reported.
3. Tuberculous Pleuritis- It was reported when there was collection of epithelioid cells with or without a central caseation focus.
4. Malignancy- It was reported when the biopsy showed cells with hyperchromatic nuclei infiltrating between muscle bundles or the mesothelium. The cells could be anaplastic or differentiated.
5. Nonspecific Inflammatory Changes- It was reported when chronic inflammatory cells, viz. lymphocytes and plasma cells were seen with early evidence of fibrosis.
6. Acute Inflammatory Reaction- It was reported when acute inflammatory changes predominantly polymorphonuclear infiltration was seen.
7. Normal Pleura- It was reported when normal mesothelial lining was seen without any inflammatory changes.

RESULTS
Total number of patients studied were 50. The age group of patients ranged from 14 to 80 years. Maximum incidence of pleural effusion was in 31-40 age group, i.e. 15 (30%) cases. Total number of male patients were 38 (76%) and total number of female patients were 12 (24%). Location of effusion 26 patients had right-sided effusion, 22 patients had left-sided effusion and 2 patients had bilateral effusion (Figure 1). Physical appearance of pleural fluid was straw in color in 66% cases, haemorrhagic in 20% cases, clear in 8% cases and 6% cases had turbid pleural effusion (Figure 2). Out of 33 straw-coloured fluid, 2 were due to malignant effusions, 1 was due to CCF. Out of 10 haemorrhagic fluid, 2 were tubercular and 8 were malignant. Out of 3 turbid pleural fluid, 2 were in syphnumonie effusion and 1 in empyema. Clear fluid was found in CCF, nephrotic syndrome, cirrhosis with portal HTN, anaemia and hypoproteinaemia. The total protein content ranged from 1.5 gm% to 6.4 gm%. 41 (82%) cases had protein >3.0 gm%. 9 (18%) cases had protein <3.0 gm%. 22 cases of exudative effusions had cell count more than 1000/mm³, i.e. 44%. None of the transudates had cell count more than 1000 cells/mm³. Thus, it is obvious that the classification of exudates on the basis of cell count more than 1000/mm³ is not reliable. Lymphocytes were predominant (more than 50%) in 40 cases (80%). Neutrophils were predominant in 5 (10%) cases of which two were in pneumonia, 1 was in empyema and 2 in malignancy. Lymphocytic predominance was seen in 50 cases of tubercular effusions and 6 cases of malignancy and 1 case of CCF. No case had significant mesothelial cells in pleural fluid, i.e. more than 1% of cell count, but occasional cells were found in 5 cases. Out of 10 suspected cases of malignant effusion, only two cases proved positive for malignancy. In the remaining cases, no evidence of malignancy could be established even after repeated examination of pleural fluid. Smear for AFB was negative in all cases. Culture of the pleural fluid was positive in three cases among, which Staphylococci in one case with empyema, 1 case had Klebsiella and 1 had pneumococci. Histopathology of pleura showed adequate tissue sample was obtained in 39 cases, i.e. yield was 78%. Inadequate tissue in 11 cases (22%).

<table>
<thead>
<tr>
<th>Biopsy Diagnosis</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonspecific Pleuritis (NSP)</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>TB pleuritis</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Malignancy</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Acute inflammatory</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Normal pleura</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

*Table 1. Analysis of Biopsy Diagnosis of Adequate Pleura*

Out of the 16 cases of nonspecific pleuritis, tuberculosis formed 14 cases (87.5%) and malignancy formed 2 cases (12.5%).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>7</td>
<td>63.6</td>
</tr>
<tr>
<td>Malignancy</td>
<td>3</td>
<td>27.2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>9.0</td>
</tr>
</tbody>
</table>

*Table 2. Analysis of Biopsy Diagnosis of Inadequate Pleura*

Case distribution as per diagnosis showed that the study constituted of maximum number of tuberculosis cases with about 64% of cases 20% were due to tuberculosis, 4% of cases were due to supynemonie effusion, 4% of cases were due to congestive cardiac failure. Rest of the cases were due to empyema, anaemia, hypoproteinaemia, nephrotic syndrome, cirrhosis, portal hypertension, etc.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Cases</th>
<th>Positive by HPE</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>32</td>
<td>11</td>
<td>34.3</td>
</tr>
<tr>
<td>Malignancy</td>
<td>10</td>
<td>5</td>
<td>50.0</td>
</tr>
</tbody>
</table>

*Table 3. Analysis of Definitive Diagnosis Arrived by Histopathology alone in TB and Malignancy*
Mild pneumothorax was produced in six cases. None required intercostal tube, but resolved spontaneously. In one case, minimal local surgical emphysema occurred.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Surgical emphysema</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>7</strong></td>
<td><strong>14</strong></td>
</tr>
</tbody>
</table>

*Table 4. Complications of Pleural Biopsy*

Right-sided effusions were found in 26 (52%), left sided in 22 (44%) cases and bilateral effusion 2 (4%) of cases. Levallan et al found right-sided effusions in 51%, left-sided in 45.3% and bilateral in 4.75, so also Poe et al found right-sided effusion in 53.65 and left-sided effusion in 44% of cases.

The results of predominance of right-sided effusions is similar to above studies.

**Clinical Diagnosis on Admission**

In the present study, out of 50 cases, 32 cases were due to tubercular effusion (64%) and in 10 cases (20%), malignant effusion was suspected. Among the studies conducted in India, the incidence of tuberculosis was 65% in studies by Thiruvengadam, 57.5% by Chouti and 74.6% by Rajkondawar. The high incidence of tuberculosis found in the present study is consistent with similar other Indian studies.

**Investigative Findings**

The haemoglobin ranged from 2.5 gm to 5 gm indicating a mild degree of anaemia. This was probably attributable to their low socioeconomic status. Also, many had round worm and Ancylostoma infestations. Four cases had radiological evidence of pulmonary tuberculosis. Berger et al found associated parenchymal involvement in 18 cases out of 42 tuberculous pleurisy (37%). Sibley found this association in 15% of TB cases. One case showed mass lesion in the corresponding side of effusion and one case showed evidence of collapse consolidation of upper lobe among the 10 malignant cases. None of the cases tested positive for sputum AFB. But, Herbert Berger demonstrated tubercle bacilli in sputum or gastric contents in 12 (30%) out of 40 cases. Ten of these patients had visible pulmonary lesions on their chest roentgenograms. Mantoux test was not done in the present study because it is positive in more than 30% of the Indian population above the age of 30 years since tuberculosis is endemic in our country. This finding is confirmed by Thiruvengadam et al (1965) and Levine et al (1967). Specific gravity estimations were also not done as they have been documented to be often quite inaccurate as it is dependent on many factors like temperature changes, hydrometric variation and other factors and is not reliable.
Lymphocytic predominance was found in over 80% of cases and polymorphs predominant in less than 11% of cases. Lymphocytic predominance was found in equal proportions of tubercular and malignant effusions. But in addition, RBCs were found in penty in malignant effusions.

Malignant Cells
In the present study, only 2 cases (20%) showed positive findings of malignant cells. Light et al found 77% positivity, and in some studies, it is documented that the percentage of positivity increases with multiple examinations. But, in present study, multiple examinations yielded no better results.

Pleural Fluid Culture
This was positive in three cases. Staphylococcus aureus was cultured from patient diagnosed as emphysema. Klebsiella and pneumococci were cultured from two cases with parapneumonic effusions.

AFB could not be cultured because of its long duration and laborious procedure. None of the pleural fluid samples were positive for AFB stain either.

Benjamin P.K. et al (1970) had 25% positivity and Sibley had 70% positivity of pleural fluid for AFB culture and AFB stain combined together.

Histopathology of Pleura (Pleural Biopsy)
Adequate tissue could be obtained in 38 (78%) cases. Of these, 11 cases (22%) showed tubercular pleuritis, 5 cases (10%) showed malignant cells, 16 (32%) showed nonspecific pleuritis, 2 (4%) showed acute inflammatory changes and in 4 cases the pleura was normal.

The diagnostic yield in our study using Abram’s pleural punch biopsy was 78%. Biopsy was repeated on only 2 occasions where one showed evidence of malignancy and the other was reported as inadequate pleura.

According to J.C. Suri et al,9 yield of first biopsy was 60.87%. However, this rose to 72.83% and 90.48%, following the second and third biopsies, respectively. On combining cytology and biopsy, the diagnostic yield rose to 94%.

In the present study, 5 cases (50%) were diagnosed to be malignant and this rose to 60% combining biopsy and cytology findings.

Only 11 cases showed positive findings of tuberculosis of 32 cases of tubercular effusions. The sensitivity being 34%.

Five cases showed biopsy findings suggestive of malignancy out of 10 malignant effusions giving a sensitivity of 50%.

### Table 8. Comparing the Sensitivity of the Biopsy Procedure with Various Authors

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of Cases</th>
<th>Instrument</th>
<th>M</th>
<th>TBP</th>
<th>NSP</th>
<th>NP</th>
<th>IAP</th>
<th>Yield</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donohoe et al</td>
<td>78</td>
<td>VS</td>
<td>8</td>
<td>10,2%</td>
<td>22</td>
<td>28,2%</td>
<td>29</td>
<td>37,1%</td>
<td>1</td>
</tr>
<tr>
<td>Mestitz et al</td>
<td>200</td>
<td>Abr</td>
<td>33</td>
<td>71</td>
<td>92</td>
<td>-</td>
<td>4</td>
<td>196</td>
<td>98</td>
</tr>
<tr>
<td>Legghat et al</td>
<td>20</td>
<td>Abr</td>
<td>12</td>
<td>-</td>
<td>7</td>
<td>-</td>
<td>1</td>
<td>19</td>
<td>85</td>
</tr>
<tr>
<td>Carpenter et al</td>
<td>47</td>
<td>Crp</td>
<td>13</td>
<td>1</td>
<td>26</td>
<td>3</td>
<td>4</td>
<td>43</td>
<td>91</td>
</tr>
</tbody>
</table>
Complications
In the present study, complications occurred in 7 patients (14%). In 6 cases, there was minimal pneumothorax, which did not require intercostal drainage. In one case, there was surgical emphysema. The complications encountered during pleural biopsy are comparable with those occurring with thoracentesis.\textsuperscript{10,11,12} According to Anthony S. Floreni,\textsuperscript{10} the most frequent complication of pleural biopsy is pneumothorax, which occurs in 3 to 20% of the time. There were no major complications seen during the present study.

CONCLUSION
Histopathological study of pleura is a useful tool in the aetiological diagnosis of pleural effusions particularly in exudative pleural effusions such as tuberculosis and malignancy. Closed pleural biopsy using the Abram’s pleural punch biopsy needle is a simple, effective and safe procedure. Nonspecific inflammatory changes does not rule out tuberculosis or malignancy. Hence, histopathological findings should be correlated with other investigative procedures to arrive at the aetiological diagnosis of pleural effusions. Pleural biopsy is of limited value in transudative effusions and may help in excluding other coexisting disease.

REFERENCES

| Niden et al | 44 | Copr | 16 | 4 | 20 | 3 | 1 | 43 | 97 |
| Hampson et al | 118 | Abr | 25 | 24 | 65 | - | 4 | 114 | 96 |
| Thiruvengadam et al | 100 | Abr | 17 | 33 | 4 | - | 5 | 94 | 94 |
| Suri et al | 155 | Cope | 18 | 86 | 15 | - | 25 | 129 | 83 |
| Ratnakar and Maiya | 25 | Abr | 1 | 15 | 6 | - | 3 | 22 | 84 |
| Present study | 50 | Abr | 5 | 11 | 16 | 4 | 12 | 38 | 76 |

Table 9. Summary of Previously Reported Needle Biopsies