

# CAUSES OF LYMPHOCYTIC EXUDATIVE PLEURAL EFFUSION AS REVEALED BY PERCUTANEOUS PLEURAL BIOPSY: Experience From Peshawar

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## ABSTRACT

**Objective:** To find out the causes of lymphocytic exudative pleural effusion as revealed by percutaneous pleural biopsy, in Peshawar.

**Type of Study:** It was a retrospective study.

**Place & Duration:** The study was conducted on patients admitted in the Pulmonology Department, Khyber Teaching Hospital Peshawar and Medical A unit, Lady Reading Hospital Peshawar during January to December 2003.

**Methods:** A total of 74 patients, aged 17-79 years with mean age 46 years, of either sex, with lymphocytic exudative pleural effusion, were enrolled in this study. They underwent closed pleural biopsy with Abram's needle in standard way. An average of three biopsy specimens were obtained in each patient, which were examined histopathologically. A retrospective analysis of the histopathological reports was carried out, to find out the aetiology.

**Results:** In 71.62% patients, definite histopathological diagnosis was possible whereas in 28.38% no definite diagnosis could be made. Among the definite diagnosis group, 52.71% were tuberculosis and 18.91% were malignancy.

**Conclusion:** Among diagnosed patients, tuberculosis and malignancy were the most common causes of lymphocytic exudative pleural effusion in our setup.

**KEY WORDS:** Pleural Biopsy, Exudative Pleural Effusion, Tuberculosis, Mesothelioma

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## INTRODUCTION

Lymphocytic exudative pleural effusion is one of the most common medical problems. It has a wide spectrum of etiologies like tuberculosis, malignancy, rheumatoid pleurisy, fungal pleurisy, sarcoidosis and even parasitic diseases such as echinococcus granulosis<sup>1-4</sup>. Therefore, to find out the underlying cause in any particular patient, proper diagnostic workup includes clinical examination, X-Rays, pleural fluid analysis and pleural biopsy; the latter is the investigation of choice in such cases. The diagnostic yield of pleural biopsy has been reported from 50% to 75% in different studies<sup>3,4,6</sup>. De Francis and coworkers first pioneered pleural biopsy in 1955, and this was followed three years later by introduction of Abrams and

Cope pleural biopsy needles<sup>7-9</sup>. Diagnostic yield of pleural biopsy depends upon patient population, biopsy technique, number of biopsy specimens, the expertise of operator and histopathological analysis<sup>4</sup>. This study was carried out to find out the causes of lymphocytic exudative pleural effusion, as revealed by percutaneous pleural biopsy, in our set-up (Peshawar).

## PATIENTS AND METHODS

Records of 74 patients, admitted in Pulmonology Department of Khyber Teaching Hospital Peshawar and Medical-A Unit of Lady Reading Hospital Peshawar from January to December 2003 were examined. These patients had undergone pleural biopsy to find out the underlying cause of their lymphocytic pleural effusion. The data was analyzed to find out total number of patients, age distribution, gender distribution and histopathological diagnosis as revealed by biopsy (definitive / inconclusive diagnosis).

**Pleural Biopsy:** Prior to pleural biopsy the procedure was explained to the patient and informed written consent was taken. The patient, he/she was asked to be seated on a couch, leaning forward with arms across the chest placed on shoulders, to easily access the posterior chest wall. Biopsy site was selected two intercostal spaces below the fluid level demonstrated on physical examination. Local infiltration of 2% lignocaine was used to anes-

thetize skin, subcutaneous tissue, muscle and parietal pleura. Skin incision was made with pointed surgical blade parallel to ribs. Two to four, on average three, biopsy specimens were obtained in each patient using Abrams pleural biopsy needle in standard way, and placed in 10% formaldehyde. In cases of large effusion, therapeutic drainage was also performed. Biopsy site wounds were sealed with sterilized dressing technique afterward. In three patients, seepage of pleural fluid from pleural biopsy site had to be controlled with one or two stitches of silk. A check chest X-ray, and homodynamic monitoring was done in every case to look for complications. Biopsy specimens were sent for histopathological analysis to know the underlying cause of effusion

## RESULTS

The study-group included 74 patients, with male to female ratio of approximately 2:1. Mean age of the patients was 46 years. Depending upon the results, the patients were divided into two groups:

- Group I comprised those patients who had definite histopathological diagnosis.
- Group II comprised those patients who had inconclusive histopathological report.

Histopathological results of pleural biopsy along with sex distribution are mentioned in table-I.

Table-I: Distribution of histopathological lesions on pleural biopsy (n = 74)

Lesions	No. of Patients	Sex-distribution		
		Lesions	Males	Females
Definitive diagnosis	53 (71.62%)	Tuberculosis	25 (33.78%)	14 (18.92)
		Mesothelioma	07 (9.46%)	01 (1.35)
		Adenocarcinoma	03 (4.06%)	0 (-)
		Metastatic disease	01 (1.35%)	0 (-)
		Lymphoma	01 (1.35%)	01 (1.35%)
			37 (50.00%)	16 (21.62%)
Inconclusive diagnosis	21 (28.38%)		12 (16.22%)	09 (12.16%)
GRAND TOTAL	74 (100.00%)		49 (66.22%)	25 (33.78%)

*GROUP-I* comprised 53 (71.62%) patients with male to female ratio of approximately 2:1. The mean age was 49 years. The most common aetiology was Tuberculosis (52.71% patients) followed by Malignancy (18.91% patients).

*GROUP II* comprised 21 (28.38%) patients, with male to female ratio of approximately 1.5:1. The mean age was 44 years.

## DISCUSSION

Pleural effusions are classified as either exudative or transudative depending on the concentration of protein and LDH in the pleural fluid. Exudative pleural effusion has at least one of the following three properties:

- 1) Pleural fluid/serum total protein ratio > 0.5
- 2) Pleural fluid/serum LDH ratio > 0.6
- 3) An absolute value of pleural fluid LDH > 200 IU

Exudative pleural effusion may be neutrophilic or lymphocytic: Tuberculosis<sup>3,4,10,11</sup>, malignancy<sup>10,11</sup>, lymphoma<sup>11</sup>, sarcoidosis<sup>12</sup>, and rheumatoid pleurisy<sup>3,4</sup>, are the common causes of the latter type. According to Light RW et al<sup>13</sup>, when exudative criteria are met by LDH alone, fluid leukocyte count is virtually never diagnostic, the diagnosis of malignancy or parapneumonic effusions should be considered. Diagnostic yield of pleural fluid analysis alone has been reported to be low. Javed A, et al<sup>3</sup> reported 8% diagnostic yield of pleural fluid analysis in their 150 patients. Similarly Collin TR, et al<sup>5</sup> reported 18% diagnostic yield of pleural fluid analysis in their 125 patients. Therefore, percutaneous pleural biopsy must be complemented to pleural fluid analysis to find out the aetiological cause of lymphocytic exudative pleural effusion, as suggested by Sahn SA, et al<sup>14</sup> and Goldman L, et al<sup>15</sup> as well.

A wide range of diagnostic yield of pleural biopsy has been reported in literature. Fishman AP, et al<sup>1</sup> reported 40% diagnostic yield of pleu-

ral biopsy in their patients. Baum GL et al.<sup>16</sup> reported 51% diagnostic yield of pleural biopsy in their meta analysis of 14 studies including 2893 patients. However, in case of tuberculosis, diagnosis was based on histopathological and microbiological analysis. In patients whose histopathology could not confirm diagnosis, culture of tissue fragments increased the potential for confirmatory diagnosis upto 60% of cases. Khurram M et al<sup>4</sup> reported 49% diagnostic yield of pleural biopsy in their 120 patients. In our series, diagnostic yield of pleural biopsy was 71.62% that is comparable with 69% diagnostic yield of another local study by Javaid A, et al<sup>3</sup> in their 150 patients. In 28.38% of our patients, histopathological diagnosis was inconclusive, also comparable with the international and local literature<sup>1,3,4,14,17,18</sup>, in such scenario repeat biopsy is advisable<sup>4</sup>. To improve the diagnostic yield of initial biopsy, it has been suggested to take four or more biopsies<sup>3</sup> and from the lowest pleural margin<sup>19</sup>. Kirsch et al<sup>20</sup> also reported that the sensitivity of pleural biopsy is highest when more than six specimens are obtained, which on average contain more than two specimens of parietal pleura. We obtained two to four, on average three, biopsy specimens in each patient in standard way.

According to Shah NH et al<sup>21</sup> in Pakistan, the main indication for pleural biopsy is to diagnose or exclude tuberculosis and malignancy. Tomlinson SR, et al<sup>6</sup> reported diagnostic yield of 74% and 57% for tuberculosis and malignancy respectively in their review of 1893 pleural biopsies. In our series, tuberculosis was the most common cause, found in 52.71% patients followed by malignancy in 18.91% patients on pleural biopsy, comparable with other local studies. Khurram M, et al<sup>4</sup> reported 64.40% diagnostic yield for tuberculosis and 13.55% for malignancy in their 120 patients. Javaid A, et al<sup>3</sup> reported 45% diagnostic yield for tuberculosis and 24 for malignancy in their 150 patients. Tubercle bacilli have been notoriously difficult to culture from pleural fluid, with a positive culture in only 31.5% patients<sup>2</sup>. Therefore, diagnosis of tuberculosis pleural effusion is most often established by histological

examination of pleural biopsy. In our country, all lymphocytic exudative pleural effusions are presumed to be due to tuberculosis and many clinicians prescribe such patients anti-TB drugs without going for any further investigations. This approach needs to be given up, as at least 1/3rd of such effusions are caused by malignancy, as found in our series as well as other local literature<sup>3,4</sup>. Our reported diagnostic yield of 18.91% for malignancy is comparatively low as compared to international studies<sup>22,23</sup>, which suggest diagnostic yield ranging from 30% to 70%. This may be due to high prevalence of tuberculosis in our country, making frequency of malignancy relatively low.

Inconclusive histopathological report in terms of chronic non-specific inflammation or acute on chronic inflammation is not uncommon. Capelozzi VI, et al<sup>24</sup> reported chronic non-specific inflammation in 34% of their 164 patients. Similarly Abu-Shams K, et al<sup>25</sup> reported chronic non-specific inflammation in 33% of their 216 patients. Khurram M, et al<sup>4</sup> reported chronic non-specific inflammation in 51% of their 120 patients. In our series, chronic non-specific inflammation was found in 28.38% of 74 patients that is comparable with 31% chronic non-specific inflammation in another local study by Javaid A, et al<sup>3</sup> in their 150 patients.

It has been mostly emphasized that pleural biopsy should be performed in the presence of pleural effusion but Nider AI, et al<sup>26</sup> demonstrated the safety and feasibility of this procedure in the absence of pleural fluid.

The common complications of pleural biopsy include site pain, vasovagal reaction, seepage of pleural fluid, site hematoma, pneumothorax, and pulmonary edema<sup>3</sup>. Other less common complications are transient fever, subcutaneous emphysema, tumor seeding and air embolism<sup>27</sup>. Tumor seeding following pleural biopsy appears to be more common in mesothelioma<sup>28,29</sup>. We didn't come across any major complications in our series illustrating the safety of the procedure. Therefore it should be a routine diagnostic procedure in patients with exudative pleural effusion.

## CONCLUSIONS

Tuberculosis and malignancy are the only diagnosed causes of lymphocytic exudative pleural effusion in our set-up. It was of no help in about 29% of cases. Closed-needle pleural biopsy helps us to differentiate between malignancy and tuberculosis. It should be a routine complimentary diagnostic procedure in patients with exudative pleural effusion.

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