

## Research Article

# Our Closed Pleural Biopsy Results in Our Patients With Pleural Effusion

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### Abstract

**Objective:** We retrospectively analyzed patients who underwent closed pleural biopsy for diagnostic purposes among our patients who were followed up in our clinic for the last 5 years due to pleural effusion.

**Material and Method:** Of the 155 patients who underwent closed pleural biopsy in our clinic between January 2015 and January 2020, 125 patients whom we could contact were included in the study. Postero anterior lung (PAAG) radiographs and lateral chest radiographs were examined. Pleural fluid amount according to the PAAG graph; It was defined as minimal (fluid that closes the costophrenic angle and does not erase the entire diaphragm), medium (fluid covering less than 2/3 of the hilus) and massive (fluid covering more than 2/3 of the hemithorax).

**Results:** When the complaints of our cases were evaluated; The most common complaint was the shortness of breath with 35 (28%) people, while 24 (19.2%) people had cough and 21 (16.8%) chest pain, respectively. A statistically significant difference was observed in the complaints of the patients in terms of the amount of dyspnea and fluid ( $p = 0.04$ ). When the biopsy pathology results of our patients were examined, 43 (34.4%) patients were malignant, 29 (23.2%) patients had nonspecific inflammation, 28 (22.4%) patients had chronic inflammation and 25 (20%) patients had granulomatous inflammation.

**Conclusion:** Considering its low cost, easy use in experienced hands, and low complication rates, and its applicability with local anesthesia, closed pleural biopsy should always be considered as a first-line

diagnostic tool in the diagnosis of exudative pleural effusion.

**Keywords:** Closed pleural biopsy; Thoracentesis; Pleural effusion

## **1. Introduction**

Fluid accumulation in the pleural space; It is a common clinical condition with many diseases in its etiology. Chest diseases and thoracic surgery have an important place in clinical practice due to difficulties in etiological diagnosis. Etiological distribution of pleural effusions; The geographical region where the study is conducted varies according to the characteristics of the community, hospital and clinic and the diagnostic methods used [1].

Since pleural effusion (PE) can be seen during the course of different diseases, many invasive and noninvasive tests are used in diagnosis. However, despite the diagnostic tests used today, some of the PEs cannot be diagnosed [2]. In cases where thoracentesis is insufficient, the second alternative diagnostic method is closed pleural biopsy. Diagnosis value in malignant cases is between 38-87% [3]. However, there may be cases in approximately 20% of cases that both methods are insufficient for diagnosis. In these cases, it is reported that up to 96% diagnosis can be achieved with Video Assisted Thoracoscopic Surgery (VATS) [4]. The first endoscopic examination of the pleura was performed in 1866 and closed biopsy needles have been used since the early 1950s [5]. Closed pleural biopsy can be performed at the bedside with local anesthesia. Thoracentesis is 39-75%, closed pleural biopsy is 40-87%, VATS is 80-100% successful in determining the etiology of PE [6]. In this study, we retrospectively analyzed the patients

who were hospitalized in our clinic for 5 years due to PE or who were sampled from the outpatient clinic and then underwent diagnostic pleural biopsy for diagnostic purposes. Demographic features of the cases, remarkable features in fluid analysis, diagnostic methods other than thoracentesis, their contribution to the final diagnosis and the final diagnoses obtained were evaluated.

## **2. Method**

The files of 823 patients who had PE in Afyonkarahisar Health Sciences University Medical Faculty Hospital Chest Diseases Clinic between January 2015-January 2020 were reviewed retrospectively. According to the Light criteria, out of 155 patients whose results came from exudate 125 patients whom we could contact were included in the study.

Demographic features, application complaints, physical examination findings of all cases were recorded. PAAG and lateral chest radiographs taken in the application were examined. Pleural fluid amount according to the PAAG graph; It was defined as minimal (fluid that closes the costophrenic angle and does not erase the entire diaphragm), medium (fluid covering less than 2/3 of the hilus) and massive (fluid covering more than 2/3 of the hemithorax). Placement of the pleural fluid was classified as unilateral (right or left hemithorax) or bilaterally. All patients were asked for pleural fluid culture and acid-resistant bacillus staining (ARB). Adenosine deaminase (ADA) was requested from patients with clinical suspicion. All cytology and pathology reports were recorded retrospectively from the hospital information system. Closed pleural biopsies (with Abrams needle), which were applied for etiological diagnosis, were evaluated.

Diagnostic methods were investigated. Due to the examination of the records retrospectively, the data of the patients were determined by telephone, which will be used for scientific purposes, so that their identity information is kept confidential.

### 3. Results

Of the 125 patients included in our study, 85 (68%) were male and 40 (32%) were female. The average age was  $63.12 \pm 16.868$  (minimum 18, maximum 89) years. 79 (63.2%) of our patients were smoking and 64 (81%) of the smokers were male and 15 (19%) were female. There was no statistically significant difference between smoking and gender in terms of pleural effusion (PE) development ( $p > 0.05$ ).

When the complaints of our cases were evaluated; the most common complaint was 35 (28%) people with shortness of breath, 24 (19.2%) people with cough, 21 (16.8%) people with chest pain, 16 (12.8%) people with weight loss, 14 (11%), 2) people had hemoptysis, 11 (8.8%) people had fever and 4 (3.2%) people had hoarseness. There was a statistically significant difference between dyspnea and fluid amount ( $p = 0.044$ ). When the amount of fluid in PAAG at the time of application was evaluated, 59 (47.2%) patients were submassive, 43 (34.4%) patients were massive and 23 (18.4%) patients had minimal pleural effusion. When the direction of the pleural fluids of the patients was evaluated, 114 (91.2%) were unilateral and 11 (8.8%) were bilateral. When fluid side was taken into consideration, the pleural effusion of 75 (60%) patients was in the right and 50 (40%) in the left pleural space. Pleural fluid distributions by gender are given in Table 1. 120 (96%) of the sampled pleural fluids were evaluated as exudate, 4 (3.2%) as empyema and 1 (0.8%) as transudate. Of the patients subject to evaluation, 13 (10.4%) had a fluid image containing

septal in PAAG. As a result of invasive procedures in our cases, 3 (2.4%) people developed pneumothorax. When pleural fluid cytology of the cases included in our study was evaluated; It was evaluated as benign in 93 (74.4%) patients and malignant in 32 (25.6%) patients. ARB was positive in 5 (4%) of our patients. Of these, 2 (1.6%) patients were evaluated as positive in the culture result. 29 (23.2%) patients included in the study were also asked for ADA levels and were evaluated as an average of  $25.77 \pm 23.508$  (min 0 max 145). When respiratory function tests (PFT) of our patients were evaluated, 47 (37.6%) patients were restrictive, 10 (8%) patients were obstructive, and 21 (16.8%) patients had mixed respiratory disorders. Normal respiratory test findings were observed in 47 (37.6%) patients. Biopsy pathology results of our patients were malignant in 43 (34.4%) patients, nonspecific inflammation in 29 (23.2%) patients, chronic inflammation in 28 (22.4%) patients and granulomatous inflammation in 25 (20%) patients. When pleural fluid malignancy rates were evaluated according to gender, a statistically significant difference was found in the rate of malignant cytology in male gender ( $p = 0.012$ ). Pathological diagnoses are shown in Table 2. When biopsies taken from patients were evaluated, 43 (34.9%) patients were diagnosed with malignancy. When malignancy diagnoses are evaluated; 22 (17.6%) adenoca, 6 (4.8%) unknown carcinoma metastasis, 5 (4%) malignant mesothelioma, 5 (4%) extrathoracic metastases, two of which are lymphoma metastasis, 4 (3.2%) squamous cell cancer and 1 (0.8%) small cell lung cancer. It was found that 37 (29.6%) of our diagnosed patients died within 3 years of diagnosis. In patients diagnosed with malignancy, there was a statistically significant difference in the mortality rate after diagnosis compared to other diagnoses ( $p > 0.05$ ).

As the rate of smoking and cigarette packet years of patients included in the study increased, there was an increase in pleural fluid massivity rate and malignancy rate and it was statistically significant (p = 0.013).

Liquid Amount	Women (n)	Men (n)	Total (n)
Minimally	6	17	23
Submassive	16	43	59
Massive	18	25	43
<b>Fluid Localization</b>			
Right	25	50	75
Left	15	35	50
<b>Liquid Cytology</b>			
Benign	24	69	93
Malign	16	16	32

**Table 1:** Distribution of pleural fluid by sex.

DIAGNOSIS	Women (n)	Men (n)	Total (n)
Chronic Inflammation	1	27	28
Malignancy	18	18	36
Malignant Mesothelioma	2	3	5
Lymphoma	0	2	2
Granulomatous Inflammation	11	14	25
Nonspecific	8	21	29
Total	40	85	125

**Table 2:** Pathological diagnoses in pleural effusion sampling.

#### 4. Discussion and Conclusion

Abnormal fluid accumulation is defined as PE as a result of disturbed balance between fluid production and absorption in the pleural cavity [7]. In the case with effusion, a detailed history and physical examination should be performed first, and when more than 1 cm of fluid is detected on the lateral decubitus

radiograph, fluid should be sampled by performing thoracentesis, except in cases where there is obvious heart failure. When it is considered as a clinical complaint; pleurisy constitutes 4% of all applications to the chest diseases outpatient clinic [8]. When analyzed by gender, in the study of Güngör A et al. 76 (59%) of 128 cases were male and 52 (41%) were

female. The mean age of the patients was  $39 \pm 12$  (15-74) years [9]. In our study, 85 of 125 patients (68%) were male and 40 (32%) were female. The average age of the patients included in the study was  $63.12 \pm 16.868$  (18- 89) years. There is a similarity to the studies in the literature in terms of average age and population.

The most common complaints are dyspnea, cough, and pleuric chest pain [8]. In another study conducted in patients with PE, the most common complaints were chest pain (74.2%), cough (62.5%) and shortness of breath (27.3%), respectively [9]. In our study, the most common symptoms of admission were dyspnea 35 (28%), 24 (19.2%) cough, 21 (16.8%) chest pain, 16 (12.8%) weight loss. 14 (11.2%) people had hemoptysis, 11 (8.8%) people had fever, and 4 (3.2%) had hoarseness. Closed pleural biopsy has been accepted as a valuable method for the diagnosis of exudative pleural effusion [10]. In our study, the results of closed pleural biopsy were analyzed by age, gender, smoking habits and effusion degree, effusion color, disease duration, and pulmonary function tests. In unilateral effusions, a significant correlation was found in terms of pleural biopsy positivity compared to bilateral pleural effusions ( $p < 0.05$ ).

ADA activity has been used for tuberculosis pleurisy since 1978 for diagnostic purposes. It is an enzyme of the purine destruction pathway that reflects proliferation and differentiation, especially in lymphocytes. It has a diagnostic value for tuberculosis. This marker may show false positive results in rheumatoid diseases, chronic lymphocytic leukemia, lymphoma and empyema [11-13]. In the study conducted by Akyıldız L et al. In 19 patients with TB pleurisy, they found the mean ADA level to be  $62 \pm$

$23.7$  IU / L [9]. Similarly, ADA level was examined in our study and the mean was found  $25.77 \pm 23.508$  IU / L. The reason for the low mean ADA level is the low number of cases with TB pleurisy in our study. For the definitive diagnosis of tuberculosis pleurisy, Mycobacterium tuberculosis (Tbc) must be isolated in tissue or pleural fluid or granulomas must be shown in the tissue [14]. However, it is not always possible to diagnose in this way. Tuberculosis pleurisy is seen in the young age group. It exists as a one-sided pleurisy that is exudate and is generally rich in lymphocytes and has high ADA levels. It is accepted that treatment can be started without biopsy in these patients [9].

Cansız et al. In his study, it was reported that tuberculosis-related chylothorax-induced pleurisy and high ADA level [15]. In our study, ADA level was requested from 29 patients. Biopsy results were reported as granulomatous and nonspecific in 54 patients, and ADA level was found above 40 U / L in 15 patients. Anti-tuberculosis treatment was started for these patients and response was received. The limitation in our study is that ADA was not requested from all patients. Therefore, it is difficult to determine the ADA level and diagnostic rate in the entire population. Therefore, more detailed studies are needed.

In recent studies in the etiology of pleural effusion in our country; Liquids related to tuberculosis and malignancy are higher [16]. Bayrak et al. Found malignancy (37%), granulomatous inflammation (21%), empyema and parapneumonic effusions (18%) in their studies [17]. Another study reported the frequency of pleurisy as tuberculosis (29%), malignancy (27%) and congestive heart failure (CHF) (13%) [18]. In our study, malignancy was detected in

43 (34.4%), nonspecific inflammation in 29 (23.2%), chronic inflammation in 28 (22.4%) and granulomatous inflammation in 25 (20%). The rate of those diagnosed with malignancy (20 patients) in the female patients included in our study did not differ statistically from the men diagnosed with malignancy (23 patients) ( $p = 0.479$ ).

Closed pleural biopsy described by Cope and Abrams is an alternative method that began to be used to obtain pleural tissue in the mid-20th century without the need for a surgical procedure [19, 20]. The procedure has invasive complications. The frequency of complications is between 4-8% in the literature [21]. In one study, 566 pleural biopsies were examined and reported complication rates of 7-8% [22]. In our study, 3 patients had partial pneumothorax after closed pleural biopsy, and 1 patient had pain and sensory loss in the biopsy region after biopsy. Complications were observed in 4 people (3.2%) in total. It has been reported in the literature that pneumothorax can be seen even in Covid-19 pneumonia without invasive intervention [23].

Malignancies are the most common cause of exudative pleural effusions over the age of 60 years [24]. Impairment of lymphatic system integrity between the parietal pleura and mediastinal lymph nodes, the spread of tumors through proximity or hematogenous way causes pleural fluid formation [25, 26]. Mesothelioma varies according to the geographical region [27]. The most common primary causes in a series in which 2040 malignant pleural effusion was evaluated; Lung (38%), breast (17%), lymphoma (12%), unknown primary (11%) genitouriner system (9%), gastrointestinal system (7%) have been reported as malignancies [27]. In our study, primary lung

cancer was the most common with 27 patients, extrathoracic metastasis with 6 patients and malignant mesothelioma with 5 patients. In malignant effusions, pleural fluid cytology contributes to the diagnosis by 66% [28]. Negative results are associated with tumor type (such as mesothelioma, sarcoma, lymphoma), tumor margin in the pleural space, and the experience of the cytologist [8]. When pleural fluid cytology was evaluated, 32 of 43 cases pleural fluid cytology was evaluated as malignant. Among these, the fluid of 2 of the 4 malignant mesothelioma cases was benign and the quality of the pleural fluid of one of the 2 lymphoma cases was benign.

Closed pleural biopsy was analyzed in terms of age, gender, smoking habits and effusion grade, side of effusion, life span, types of diagnosis and hospital admission complaints.

## **5. Limitations of the Study**

1. Radiographic findings such as pleural thickening, nodule, mass and sequelae changes were not included in the analysis.
2. The albumin, protein, LDH and glucose values of the liquids were not included in the study since they were differentiated from exudate to transudate before,
3. They are excluded from the analysis, which can affect test performance indicators.

In conclusion, closed pleural biopsies are an effective method for diagnosing intrathoracic malignancies in patients with pleural effusion. Provided by adequately trained pulmonologists, blind pleural biopsy is well tolerated by patients with poor general condition, short life expectancy, and concomitant diseases. Given the

low cost, easy availability and low complication rates, closed pleural biopsy should always be considered as the first diagnostic tool in exudative pleural effusions.

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No financial support has been received for this study.

### Conflict of Interest

The authors declared that there were no conflicts of interest between them.

### Ethical Approval

It was taken from Afyonkarahisar Health Sciences University Clinical Research Ethics Committee on March 6, 2020 with the number 2020/129.

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