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Management of pleural effusions; Experience from a single center thoracic surgery clinic

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Abstract
Background/Aim: The most common symptom in pleural effusion is shortness of breath, followed by pleuritic pain in the area accompanied by the pathology. Spesific treatment of pleural effusion can be determined after differential diagnosis.
Material-Method: We retrospectively evaluated 43 patients who were hospitalized in our thoracic surgery clinic between 2019-2020.
Results: In our study, 43 patients were evaluated for pleural effusion.The mean age of the patients was 57.76 years (18-88). In our study, pleural fluid of 15 patients was determined as transudate, and pleural fluid of 28 patients was determined as exudate.
Conclusion: Given the aging of the population and the consequent increasing prevalence of multiple morbidity, pleural effusions often have more than one cause. Thoracentesis can be performed for diagnostic purposes or to reduce the symptom of dyspnea in massive fluids [8,9]. In our study, 37 patients underwent tube thoracostomy while 6 patients did not. The biopsy procedure was performed with vats or imaging-guided fine needle biopsy methods. In our study, pleuridesis was applied to 21 patients.

Keywords: pleural effusion, malignant pleural effusion, effusions, pleural

Introduction

The most common etiologies of pleural effusion are congestive heart failure, cancer, pneumonia and pulmonary embolism. Pleural fluid puncture provides information to differentiate between transudate and exudate and remains the basis of further diagnostic studies
Lung cancer is the most common cause of malignant pleural effusion, followed by breast [1]. cancer.
The most common symptom in pleural effusion is shortness of breath, followed by pleuritic pain in the area accompanied by the pathology. No strong correlation was found between the amount of effusion and shortness of breath [2].
Congestive heart failure is the most common cause of bilateral pleural effusion.
Approximately 75% of patients with pulmonary embolism and pleural effusion have pleuritic chest pain [3].
Treatment of pleural effusion is primarily treatment of the underlying disease. However, tools such as video-assisted thoracoscopy (vats), placement of an indwelling pleural catheter, and pleurodesis can also be used.
Spesific treatment of pleural effusion can be determined after differential diagnosis.

Material-Method

We retrospectively evaluated 43 patients who were hospitalized in our thoracic surgery clinic between 2019-2020. Patients' age, gender, length of stay, comorbidity, side of pleural effusion, whether tube thoracostomy was performed or not, cytology results, biopsy results if it was performed or, pleural fluid culture results, LDH (Lactate Dehydrogenase), glucose, albumin and total protein analysis from pleural fluid results, exudate-transuda separation of the fluid, pathology results and whether pleuridesis was performed or not were recorded.

Results

In our study, 43 patients were evaluated for pleural effusion. 16 of the patients were female and 27 were male. The mean age of the patients was 57.76 years (18-88). The mean length of hospital stay of the patients was 9.37 days (1-28). Ten patients had no known primary disease or comorbidity. Thirty-three patients had primary disease and multiple comorbidities.
In our study, 10 patients had no clinical pathology that could be shown to cause pleural effusion. 9 patients had heart disease, 8 patients had non-respiratory malignancies, 7 patients had lung carcinoma, 2 patients had pneumonia, 2 patients had covid-19 pneumonia, 2 patients had chronic renal failure, 1 patient had rheumatoid arthritis, and 1 patient had thyrotoxicosis.

While pleural biopsy was not performed in 31 of the patients, video-assisted thoracoscopic surgery (vats) was performed in 9 patients and fine needle biopsy was performed in 3 patients with imaging. Of the effusions, 20 were in the left hemithorax, 20 were in the right hemithorax, and 3 were bilateral.
While tube thoracostomy was not applied in 6 of the patients, tube thoracostomy was performed in 37 of them. Cytopathological examination was performed from the pleural fluid of 26 patients.
No growth was detected in the pleural fluid culture of 39 patients, and growth was detected in the pleural fluid of 4 patients. Streptococcus constellatus was detected in one patient and gram-positive cocci in 3 patients.
Pleural fluid biochemistry of all patients was analyzed. Pleural fluid LDH, glucose, albumin and total protein values were measured and compared with simultaneous blood values. The fluid nature was determined as transudate in 15 patients and exudate in 28 patients. Twenty-one patients underwent chemical pleuridesis.

Discussion

The most common causes of pleural effusion are congestive heart failure, cancer, pneumonia, and pulmonary embolism. A delayed diagnosis may be associated with higher morbidity and mortality. Given the aging of the population and the consequent increasing prevalence of multiple morbidity, pleural effusions often have more than one cause. In our study, the patients had multiple morbidities.
Medications can also cause pleural effusion. Some of the identified causes are nitrofurantoin, dantrolene, methysergite, amiodarone, interleukin-2, procarbazine, methotrexate, clozapine, phenytoin and beta blockers.
A number of rarer diseases can almost always be associated with an exudative type of pleural effusion.
Pleural effusion ("polyserositis") is present in 30-50% of patients with systemic lupus erythematosus. Pleural effusion is also common in patients with granulomatosis with polyangiitis (Wegener's disease), rheumatoid arthritis, and Langerhans cell granulomatosis [3]. 21% of patients suffering from idiopathic and familial pulmonary hypertension have mostly unilateral pleural effusion [4].
In our study, 10 patients had no clinical pathology that could be shown to cause pleural effusion. 9 patients had heart disease, 8 patients had non-respiratory malignancies, 7 patients had lung carcinoma, 2 patients had pneumonia, 2 patients had covid-19 pneumonia, 2 patients had chronic renal failure, 1 patient had rheumatoid arthritis, and 1 patient had thyrotoxicosis.
Some patients complain of a dry cough, which can be explained as a manifestation of pleural inflammation or lung compression due to a massive effusion. Pleural effusions can also significantly impair sleep quality [5].
Approximately 75% of patients with pulmonary embolism and pleural effusion complain of pleuritic chest pain [3].
The most common complaints of the patients included in our study were dyspnea, cough and chest pain.
One of the more common causes of unexplained pleural effusion is pulmonary embolism. Pleural effusion is present in 20-55% of patients with pulmonary embolism. The frequency of pleural effusion in pulmonary embolism is related to the severity of the embolism and the occurrence of pulmonary infarction. These patients are usually characterized by a marked discrepancy between the not too much effusion, and the accompanying severe dyspnea [6].
In our study, there was no patient diagnosed with pulmonary embolism among the causes of unexplained effusion.
Bintcliffe *et al.* states that 70% of 126 patients with pleural effusion actually had a single cause while 30% of them had more than one cause [7].
Patients with multiple morbidities constitute this group of patients. In our study, 30% of the patients had multiple morbidity. If a pleural effusion is suspected, a chest X-ray should be taken. [8].
Postero-anterior view reveals effusions with a volume of 200 mL or greater, lateral view reveals effusions with a volume of 50 mL or greater. Thoracic ultrasound is very useful in detecting fluid [9].
Thoracic tomography reveals pleural effusions that cannot be seen on conventional chest X-rays. It can distinguish pleural fluid from pleural tissue proliferation and provides clues to potential causes of effusion (pneumonia, cancer, pulmonary embolism).
In our study, anterior and lateral chest radiographs were performed to all patients. Contrast-enhanced or non-contrast thorax tomography was performed for patients who could not be adequately evaluated in terms of differential diagnosis with chest X-ray and thoracic ultrasound.
Thoracentesis can be performed for diagnostic purposes or to reduce the symptom of dyspnea in massive fluids [8, 9]. If the pleural effusion is extensive and causes respiratory or cardiac decompensation, prompt thoracentesis or pleural drain placement is required.
In our study, patients with massive pleural fluid, symptomatic and no pathology to prevent lung expansion (eg, central mass obliterating the main bronchus, etc.) were first applied diagnostic puncture and evaluation, and then thoracentesis and/or tube thoracostomy performed.
In chronic pleural effusions, recurrent catheter thoracostomy, tube thoracostomy or draining thoracentesis procedure were performed. In pleural effusions in which self-limited submassive fluid was detected on chest X-ray or thorax tomography, surgical intervention was usually performed under imaging guidance.
In a patient with pneumonia, effusion may be punctured to rule out pleural empyema [10, 11]. There is a possibility of empyema development in parapneumonic effusions. Fluids detected during the pneumonia treatment or in the post-pneumonia period were punctured for diagnostic purposes under sterile conditions and empyema was excluded.

In our study, 37 patients underwent tube thoracostomy, while 6 patients underwent diagnostic puncture or were followed up only radiologically. Effusion was detected bilaterally in three patients, in the left hemithorax in 20 patients, and in the right hemithorax in 20 patients.

Patients with bilateral pleural effusion do not always need a diagnostic or therapeutic thoracentesis; instead, the underlying disease should be treated first. Thoracentesis can be applied for relief of symptoms and for differential diagnosis in bilateral symptomatic patients. In our study, bilateral effusions were detected in 3 patients, 2 of these patients had heart failure and one of them had chronic kidney failure. Because these 3 patients were symptomatic, tube thoracostomy was applied to the hemithorax that has excessive effusion.

The risk of iatrogenic pneumothorax after thoracentesis is 0.61–6.0%. Close observation of the patient for 1-4 hours is recommended after the intervention.

Puncture of pleural effusions under ultrasonic guidance plays an important role in the diagnostic evaluation of smaller effusions of unknown origin, especially in intubated and ventilated patients [12].

In our study, 37 patients underwent tube thoracostomy while 6 patients did not. While diagnostic puncture was performed in 4 of these 6 patients, 2 patients were followed up radiologically.

Post-procedure complications like pneumothorax, hemothorax, etc. were not detected in any of the patients who did not undergo tube thoracostomy or who underwent diagnostic puncture.

Urgent puncture or drainage placements should be performed at an INR (international normalized ratio) setting of less than 1.5. An up-to-date chest X-ray should be available and the intervention should be accompanied by ultrasonography.

If an infectious cause for the pleural effusion is suspected, pleural fluid pH should be tested by an appropriate method. Acidosis in pleural fluid; seen in complicated pleural infections, tuberculosis, rheumatoid arthritis, and malignant effusions

The sampled fluid is aliquoted for microbiological (5 mL), biochemical (2-5 mL), and cytological (20-40 mL) analysis. Blood culture vials increase sensitivity for the detection of bacterial pathogens, especially anaerobes. Sending pleural fluid in blood culture bottles is not recommended for detection of Mycobacterium tuberculosis [13].

The macroscopic appearance of the fluid may provide clues for diagnosis. Milky fluid is typical for chylothorax, pus is evidence of empyema, and serohemorrhagic fluid is more common in malignancies.

Determining whether a pleural effusion is a transudate or an exudate determines its further evaluation and treatment [14].

To distinguish between the two possibilities, lactate dehydrogenase (LDH) and protein are measured. this measurement can accurately tell the difference between transudate and exudate in 93-96% of cases [8, 15].

In the evaluation of pleural effusion, if the ratio of protein concentration in the effusion to serum protein concentration is>0.5, the ratio of lactate dehydrogenase (LDH) concentration is >200 IU, and the ratio of LDH concentration is>0.6, an exudative pleural effusion can be mentioned.

In our study, pleural fluid of 15 patients was determined as transudate, and pleural fluid of 28 patients was determined as exudate. Albumin, total protein, glucose and LDH were analyzed from pleural fluids.

In microbiological examination, growth was detected in 4 patients. Gram positive cocci were grown in three patients and streptococcus constellatus in one patient.

Among patients with malignant effusions, acidosis of the effusion fluid is correlated with shorter survival; these patients usually have more extensive disease and a lower chance of successful pleurodesis [16].

If the pleural fluid pH is less than 7.2, prompt insertion of a pleural drain is recommended, even if the effusion is clearly of parapneumonic origin. In our study, all patients with malignant effusion needed tube thoracostomy.

The glucose concentration in the pleural fluid is the same as in the blood under normal conditions. Low glucose concentration in the pleural fluid; detected in empyema, tuberculosis, malignancy, and rheumatoid arthritis [8].

One in two patients with acute pancreatitis has a pleural effusion with a high concentration of amylase [8]. In our study, pleural glucose/blood glucose levels were not found to be low in only 11 patients, but this rate was low in other patients.

The N-terminal pro-B-type natriuretic peptide is a sensitive biomarker for heart failure. Even if an effusion is of the exudative type, a high N-terminal pro-B level explains that the cause is congestive heart failure.

A negative N-terminal pro-B finding in the blood almost certainly excludes congestive heart failure as the cause of the pleural effusion [17].

The blood cell count in the pleural fluid does not definitively identify the cause of the effusion, but may further narrow the differential diagnosis.

In effusions caused by parapneumonic effusion, empyema, and pulmonary embolism, a high neutrophil concentration is often observed in the acute phase [8]. Lymphocyte cell majority is more common in prolonged pleural effusions, congestive heart failure, tuberculosis, or malignant etiology.

Microbiological identification of a pathogenic organism in a non-purulent parapneumonic effusion is successful in only 25% of cases [18]. Microbiological examination gives a large number of false negative findings. If tuberculous pleuritis is suspected, microbiological examination and culture should be performed [13]. In our study, growth was detected in the pleural fluid culture at a rate of 9.3%.

In approximately 50% of lung cancers [19] and 60% of all cancers [8], malignant pleural effusion can be cytologically confirmed. The histopathological type with the highest probability of positive tumor diagnosis in

pleural fluid is adenocarcinoma. In our study, malignant cells were detected in pleural fluid cytology at a rate of 11.62%.

There is no routine measurement of tumor markers from fluid or serum in the etiologic classification of pleural effusions. In 25% of patients with lung carcinoma with pleural effusion, malignant cells were detected in the pleural fluid.

On the other hand, 28.5% of all patients with malignancy were found to have malignant cells in the pleural fluid. In our study, 12 (27.9%) of 43 patients were diagnosed by pleural biopsy.

The biopsy procedure was performed with vats or imaging-guided fine needle biopsy methods. The patients who underwent pleural biopsy were patients whose differential diagnosis could not be reached from pleural cytology and who did not have a known diagnosis before.

Because of its high efficacy, talc is the preferred pleurodesis agent [20]. Tetracycline and bleomycin are still used, but less effective [19]. In our study, pleuridesis was applied to 21 patients. Sterile talc and tetracycline were used as chemical agents. If video-assisted thoracoscopy is performed for a diagnostic indication and the neoplastic origin of the effusion is confirmed, pleurodesis can be performed in the same session [21].

Another method used in patients with recurrent malignant pleural effusion is the placement of an indwelling pleural catheter. This provides long-term treatment of the effusion with little deterioration in quality of life. It is a safe and gives a chance for outpatient treatment. In case of insufficient lung expansion or hydropneumothorax after drainage of the malignant effusion, specific surgical procedures can be performed.

For patients who achieved adequate lung expansion after drainage of the malignant effusion, talc pleurodesis combined with a pleural catheter has demonstrated a higher success rate than catheter alone [22].

For the diagnosis of malignant pleural changes, tomography-guided needle biopsy of the pleura is significantly more sensitive compared to the previously widely practiced Abrams needle biopsy procedure [8]. In our study, imaging-guided fine-needle biopsy was performed instead of Abrams needle biopsy.

Pleural effusion in a patient with cancer is associated with a poor prognosis, however, it varies considerably. Patients with hematological malignancies or pleural mesothelioma live on average almost one year, while patients with lung cancer have the worst prognosis with a median survival time of only 2-3 months [23].

Conclusion

Pleural effusions can be seen during the course of many malignant or benign diseases. Thoracic surgeons also have a role to play in elucidating the etiology of the effusion.

When faced with effusions of unknown origin, diagnostic surgical interventions provide rapid results and provide early treatment. The probability of cytological diagnosis with thoracentesis is lower than with pleural biopsies.

The diagnosis rates of tube thoracostomy are significantly increased by performing pleural biopsy with videothoracoscopy. The videothoracoscopic appearance also includes a preliminary idea for the disease. Vats application accelerates diagnosis and treatment as it gives the chance of chemical pleurodesis without terminating tube thoracostomy for patients diagnosed with malignant effusion.

In suitable patients, performing pleural fluid sampling and pleural biopsy with vats instead of waiting for the pathology result of diagnostic thoracentesis accelerates the diagnosis and treatment.

Conflicts of interest

The authors declare no conflict of interests.

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