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Characteristics of patients with transudative efusion followed in an university hospital

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ABSTRACT

Aim: To determine the etiological causes, radiological and laboratory features of transudative pleural effusions and to observe the clinical course after therapeutic thoracentesis.

Material and Method: The files of patients with transudative effusion who underwent therapeutic thoracentesis by the Interventional Radiology Department between 01.01.2012 and 30.11.2012 were retrospectively reviewed. Pleural effusion (PE) anatomical features were evaluated with Postero anterior (PA) chest X-ray and Thorax Ultrasonography (USG). Demographic and clinical features, pleural effusion analysis results, presence and rates of complications were analyzed.

Results: As a result of pleural fluid analysis, our study group consisted of 60 transudative pleural effusion cases, 36 (60%) women. The mean age was 71.23±2.36 years. Patients using diuretic therapy in cases with pleural effusion were statistically significantly higher than patients who did not ($p<0.05$). The most common etiologic causes were Congestive heart failure (CHF) and the accompanying disease hypertension (HT). Fifty (83.3%) of the pleural effusions were unilateral and 39 (65%) of them were right-sided ($p<0.05$). Diagnostic and therapeutic thoracentesis of our cases was performed by the radiologist under the guidance of thorax USG, and pneumothorax was observed in only one case (1.7%). In our 2-month clinical follow-up, the presence of recurrent pleural effusion was not detected in any of the cases.

Conclusion: In cases with persistent transudative pleural effusion, therapeutic thoracentesis can be considered in cases where fluid resorption is not at the desired level despite effective treatment.

Keywords: Pleural effusion, thorax USG, thoracentesis, transuda

INTRODUCTION

Pleural diseases are common medical problems with more than 50 known causes, including diseases confined to the pleura or lungs, systemic diseases, organ dysfunctions and drugs (1).

Two basic mechanisms play a role in the formation of pleural effusion (PE); increased fluid formation and/or decreased fluid resorption. Pathological pleural fluids constitute 4% of patients admitted to internal medicine clinics (2).

While the main cause of exudative fluids may be malignancy, infections, or iatrogenic or trauma, transudative fluids are usually caused by congestive heart failure (CHF), chronic renal failure (CRF) or hypoalbuminemia (3).

Light criteria have been used since 1970 in the separation of pleural fluids. Puncture of the fluid in the pleural space consisting of visceral and pariaetal leaves can be done under the guidance of thorax ultrasonography (USG) (3).

While thoracentesis may not be required for effusions in the pleural space, which are usually bilateral, etiologically clear, and which we expect to regress with the treatment of the underlying disease, therapeutic thoracentesis may be considered in cases where we cannot obtain the desired results with unilateral effective treatment (4).

In transudative effusion, there is no pleural disease or pleural involvement of a disease. Problems leading to increased pulmonary or systemic hydrostatic pressure or decreased plasma oncotic pressure lead to transudative pleurisy. Transudative fluids are often the result of systemic problems. For this reason, in the case of detecting a transudate fluid, further investigation may not be necessary in terms of lung disease (5,6).

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There are conflicting results about which effusions to intervene and what the results are in these cases of transudative PE (7,8).

Our aim in this article; to determine the etiological causes, radiological and laboratory features of persistent transudative pleural effusions, which can cause difficulties for clinicians, and to observe the clinical course in their follow-up after therapeutic thoracentesis.

MATERIAL AND METHOD

This retrospective study was approved by the Baskent University Clinical Researches institional review board and produced from thesis (Date: 28.02.2012, Decision No:12/32). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Our study included 169 patients who underwent therapeutic thoracentesis by the Interventional Radiology Department of a University Medical Faculty Hospital between 01.01.2012 and 30.11.2012. Patients with exudate as a result of the fluid analysis performed according to Light's criteria and who only underwent sampling thoracentesis were excluded from the study, 60 patients with transudate were included in the study. File contents of patients with transudative pleural effusion were reviewed retrospectively. The amount of pleural effusion was determined by direct chest radiographs. Patients with transudative pleural effusion who were referred from different departments of our hospital and underwent therapeutic thoracentesis by the Department of Interventional Radiology were followed up in terms of their two-month course following the thoracentesis procedure. As clinical follow-up parameters, pleural fluid analysis results of the patients, additional diseases, medical treatments they use regularly, symptoms at admission, the radiological imaging used to determine the pleural fluid, the localization of the fluid, the number of times thoracentesis was performed, the amount of fluid drained, the presence of complications and their rates were evaluated.

The Light criteria are used to differentiate transudate-exudate in pleural fluids (3). Accordingly, if the ratio of pleural fluid protein to serum protein is greater than 0.5, the LDH (lactate dehydrogenase) ratio is greater than 0.6, or the pleural fluid LDH value is greater than 200 IU, or the pleural fluid < LDH value is 2/3 of the upper limit of serum LDH. Presence of one of the criteria of being higher than ≥ indicates that the liquid is exudate. Transudates do not have any of these criteria. With the Light criteria, it is possible to distinguish between transuda and exudate in approximately 99% of cases (9).

Statistics: Categorical Data were analyzed with one-way Chi-Square test and two independent ratio z-tests. Numerical data are expressed as mean±standard deviation and minimum and maximum values. The $p<0.05$ level was considered statistically significant. The data were evaluated in the SPSS statistical package program (Version 17, Chicago IL, USA).

RESULTS

Sixty cases who underwent therapeutic thoracentesis between 01.01.2012 and 30.11.2012 and were evaluated as transudate as a result of pleural effusion were included in our study. It was seen that 28 of these patients were consulted to Chest Diseases. The demographic characteristics of the patients, their diuretic use histories and their symptoms at presentation are given in **Table 1**. The mean age of the study group was 71.23±2.36 years. There was no significant difference between the patients in terms of having or not smoking history. In cases with pleural effusion, patients using diuretic therapy were statistically significantly higher than patients not using it. ($p<0.05$). There was also a significant difference in the comparison of the patients in terms of hemodialysis application ($p<0.05$). In patients with chronic renal failure (CRF) with pleural effusion, the number of patients undergoing hemodialysis was less ($p<0.05$). There were no patients on peritoneal dialysis. **Table 2** shows the underlying diseases in transudative PE cases.

Although there were patients with more than one etiological cause of pleural effusion, the most common etiological cause was CHF. According to **Table 3**, hypertension (HT) was the most common comorbidity. The least common chronic lung diseases; asthma and chronic obstructive pulmonary disease (COPD). There were also cases with more than one comorbid disease among the patients.

Table 1. General features

Characteristics	Patients , n (%)	p value
Gender		
Female	36 (60)	P<0.05
Male	24 (40)	
Smoking history		
Yes	31 (51.7)	P=0.79
No	29 (48.3)	
Diuretic use		
Yes	39 (65)	P<0.05
No	21 (35)	
Hemodialysis		
Applied	8 (13.3)	P<0.05
Not applied	52 (86.7)	
Presenting symptoms		
Asymtomatic	1 (1.7)	
Dyspnea	46 (76.7)	
Cough	2 (3.3)	P<0.05
Fever	2 (3.3)	
Cough and dyspnea	8 (13.3)	
Chest pain	1 (1.7)	

One-way Chi-Square test used and $p<0.05$ level was considered statistically significant.

Table 2. Underlying diseases		
Characteristics	**Patients , n (%)**	**p value**
Congestive heart failure		P<0.05
Yes	39 (65)	
No	21 (35)	
Chronic renal failure		P<0.05
Yes	14 (23.3)	
No	46 (76.7)	
Chronic liver failure		P<0.05
Yes	4 (6.7)	
No	56 (93.3)	
Malignancy		P<0.05
Yes	14 (23.3)	
No	46 (76.7)	

One-way Chi-Square test used and p<0.05 level was considered statistically significant.

Table 3. Concominant diseases	
Characteristics	**Patients , n (%)**
Chronic obstructive pulmonary disease	
Yes	12 (20)
No	48 (80)
Asthma	
Yes	4 (6.7)
No	56 (93.3)
Atrial fibrillation	
Yes	19 (31.7)
No	41 (68.3)
Hypertension	
Yes	39 (65)
No	21 (35)
Diabetes mellitus	
Yes	23 (38.3)
No	37 (61.7)

As for pleural fluid localization, 50 (83.3%) cases were unilateral and 10 (16.7%) cases were bilateral (p<0.05). 39 (65%) of 50 unilateral pleural effusion cases were right-sided (p<0.05). Pleural effusion was detected in 98.3% of the patients by taking posteroanterior (PA) X-ray. Statistically significant moderate amount of pleural effusion was more common in the patients.

It was observed that 36.7% of the patients had repeated thoracentesis during the two-month follow-up. A minimum of 150 ml and a maximum of 3500 ml of fluid were drained in the thoracentesis procedures performed once or more in patients. It was observed that a maximum of 1500 ml of fluid was drained during a single thoracentesis procedure performed under USG guidance by interventional radiology in all patients. After the thoracentesis procedure, 59 (98.3%) of the patients had a control PA chest X-ray. Complications were seen in only 1 (1.7%) patient. This complication was minimal pneumothorax, which did not require a chest tube in the treatment.

Biochemical measurement results in all pleural fluids were transudate according to the Light Criteria. A total of 57 patients pleural fluid was sent to microbiology and no growth was observed in any of them. The fluid of the remaining 3 cases was not evaluated microbiologically. Pleural fluids were sent for cytological evaluation in 44 of 60 patients, and cytological examination was not performed in 16. As a result of the 44 pleural fluid cytology sent, mesothelial cells and inflammatory cells were detected in 21 (51.2%) of the cases. Malignant cells were detected in the pleural fluid cytology of 2 cases (3.3%).

Table 4. Biochemical results for transudate criteria				
Characteristics	**minimum**	**maximum**	**mean**	**Standart deviasion**
Pleura protein (gr/dl)	0.8	6.3	2.12	0.14
Serum protein (gr/dl)	0.19	8.2	6.05	0.19
Pleura / serum protein	0.06	0.6	0.32	0.01
Pleura LDH (U/L)	48	204	102.6	5.95
Serum LDH (U/L)	140	688	282.5	17.82
Pleura / serum LDH	0.14	1.2	0.38	0.02
Pleura albumin (gr/dl)	0.04	2.7	1.14	0.07
Serum albumin (gr/dl)	2	4.3	3.11	0.07
Albumin gradiyent	0.31	3.06	1.92	0.07

DISCUSSION

In our study, we evaluated 60 cases who underwent therapeutic thoracentesis under USG guidance by the interventional radiology clinic of our hospital between 01.01.2012 and 30.11.2012 and whose pleural fluid result was determined as transudate according to light criteria. We found the complication rate after the procedure to be significantly low (1.7%) in these cases, and we found that pleural effusion did not develop again in any of them with thorax USG control performed after 2 months of clinical follow-up.

The mean age of the patients included in our study was 71.2±2.3. Transudative pleural effusions are usually the problems of the older age group, as in our cases. When other demographic characteristics were examined, our findings were in line with the literature in terms of gender distribution in 36 female cases (60%) (10).

According to the data of "Global Adult Tobacco Survey 2016"; 19.2 million people (31.6%) in Turkey still use tobacco products. The prevalence of tobacco use is higher in men (44.1%) than in women (19.2%) (11). In our study, we found the rate of smoking to be 51.7% higher in our patient group with intertwined comorbidities. Smoking rates in hospitalized patients are generally reported at higher rates in parallel with our findings (12,13). Smoking is among the important risk factors in the etiology of the underlying diseases of our patients.

65% of our cases with transudative pleural effusion were receiving diuretic therapy. This suggested that pleural fluid may occur despite the use of diuretic therapy in

CHF. Consistent with the literature, CHF was the most common cause of transudative pleural effusion in our cases (14). While peripheral edema is resolved in a shorter time with diuretic treatment, fluids in third body cavities such as pleura and peritoneum may persist. In this case, an unloading process is required for palliation. Our study also supports this observation.

In our daily practice, we may also encounter "difficult transudates" that acquire the character of exudate despite having a transudate, that we have difficulty in treating or that we cannot explain (15). Under diuretic therapy, the pleural fluid feature may shift to exudate. The fluid in these cases is interpreted as "awaited transudate". In their study investigating the effect of diuretics on protein concentrations in the transudative pleural fluids of patients with CHF, Romero et al. (16) concluded that the use of protein and albumin serum-fluid gradient is more beneficial in the separation of pleural fluid transudate-exudate. Since all of our cases were indisputably transudate, there was no need to evaluate these parameters in our study.

Hemodialysis was applied to 8 of 14 patients with CRF diagnosis. Dialysis indication has not yet been established in other CRF patients. Although our hospital is a reference center in solid organ transplantation, CRF was ranked second in our series in the etiology of transudate. The low rate of this can be explained by the effective fluid withdrawal in patients' dialysis programs. An effective hemodialysis program in CRF can significantly reduce the volume load in the body and the likelihood of developing pleural effusion.

One of the most common symptoms in pleural effusion is dyspnea (17). Cough and chest pain are also common symptoms. Dyspnea was the most common presenting symptom in 76.7% of our cases. Dyspnea is often the main reason for the need for therapeutic thoracentesis. Therapeutic thoracentesis is recommended for symptom palliation even if the amount of pleural fluid is small. Our study also supports this view.

There was a diagnosis of malignant disease in 23.3% of our cases. However, in such cases, there is usually more than one underlying cause of pleural effusion, and it should not be attributed to malignant disease alone. There are many transudate causes such as malnutrition and hypoalbuminemia, hypervolemia and heart failure, immobility and atelectasis secondary to malignancy (18). This can also be explained by our detection of malignancy as the cause of transudative pleural effusion in approximately one fourth of our cases.

One of the most important findings of our study was that approximately half of the cases who underwent thoracentesis were referred to the radiology department without evaluation by our department. The fact that patients were consulted to our department at a lower rate (47%) before the thoracentesis procedure can be explained by the fact that the diagnoses of COPD and asthma, which are the accompanying chronic lung diseases, are quite low (26.7% in total). When the pleural effusion problem is attributed to extrapulmonary causes according to the clinical findings of the patient, it is usually managed by the relevant departments. We think that the number of recurrent thoracentesis can be reduced by applying a multidisciplinary approach, including chest diseases from the beginning. It is an important result of our study that 36.7% of the cases are performed more than once in thoracentesis.

Of our cases, 83.3% of pleural effusions were unilateral, of which 76% were on the right side. In the reviews published by Light and Sahn (19), who are important authors in pleural diseases in the world, it is argued that if the fluid is bilateral and/or in small amounts in a patient with CHF, the treatment response for failure should be followed without trying torecentesis. However, although the majority of our cases were CHF patients, the pleural fluid was highly unilateral (83.3%). This situation has led to the widening of thoracentesis indication.

98.3% of our patients had a PA chest X-ray and therapeutic thoracentesis was performed in all of our patients with thoracic USG in interventional radiology. USG guidance increases the success rate of pleural aspirations. Many studies have shown that in 88% of patients in whom clinical and plain radiography-guided interventions fail, fluid can be successfully removed using USG (20). The very low incidence of complications detected after thoracentesis in our cases was also associated with performing the procedure under USG guidance.

98.3% of our patients, whose thoracentesis procedures were all performed under USG, had a control PA chest X-ray after the procedure. Complications were seen only at a rate of 1.7% (in 1 patient). This showed that it is safe to perform the procedure with USG and that it is necessary to take a PA chest X-ray after the procedure. Barnes et al. (21) analyzed the records of 450 patients who underwent diagnostic thoracentesis for the first time in their centers. They found a decrease in pneumothorax and tube thoracostomy rates with the routine use of USG during diagnostic thoracentesis. Grogan et al. (22) also showed that the complication rate was independent of the amount of effusion in their study by randomized 52 patients. USG can also be a preliminary idea in the evaluation of pleural fluid in terms of transudate and exudate. The presence of septations brings the clinician closer to the exudate, while the appearance of free and

homogeneous fluid suggests the possibility of transudate. Since the diagnostic and therapeutic procedures were applied simultaneously in our cases, such a preliminary evaluation could not be made.

Considering the amount of pleural effusion in our patients, only 15% were massive. Massive pleural effusions are most commonly associated with malignancy (23). In our cases, the diagnosis of malignancy was 23.3%. Kıral et al. (24). retrospectively analyzed 159 cases with effusion on PA chest X-ray. They found the etiology as malignancy in 46.9% of massive effusions. The low number of our cases prevents us from obtaining sufficient data in the evaluation of this relationship.

In 57 of our cases, pleural fluid samples were sent to culture and there was no growth observed in any of them. Growth in culture in transudate fluids is not an expected result. Microbiological processes increase the cost unnecessarily. Another self-criticism of this study is that we found that almost all of the pleural fluids resulting from transudate were sent to the microbiology laboratory.

Fluid samples were sent to cytology in 44 (73.3%) of our patients. When we look at the cell contents according to the cytology results, the majority of them were mesothelial cells. This was an expected result for transudative fluids. The incidence of malignant cells at a rate of 3.3% suggested that cytological examination would be significant in this group. This situation reveals the necessity of sending the fluid to cytology in all patients.

Gonlugür et al. (25) retrospectively reviewed all cases diagnosed as malignant or paramalignant pleural effusion in a tertiary hospital over a 10-year period. 67 patients with malignant mesothelioma, 45 patients with metastatic disease and 36 patients with paramalignant effusion were included in the study. 1.5% of malignant mesotheliomas, 6.8% of metastatic diseases and 11.1% of paramalignant effusions were classified as transudate. In conclusion, they thought that the examination of pleural fluid in patients with unexplained transudative effusion was essential in excluding malignant processes.

Our limitations in this article can be considered as; being a single center and having relatively low number of patients.

CONCLUSION

We checked our cases for effusion with thoracic USG 2 months after the pleural effusion was drained and observed that the transudative fluids did not reoccur. All patients were also receiving treatment for their effective primary disease after therapeutic thoracentesis. Until recently, it was accepted that there was no need for additional examination and treatment effort in transudate fluids. We determined that there is a need for detailed evaluation regarding the necessity of therapeutic thoracentesis procedure in transudative fluids. We are of the opinion that there is a need for series consisting of more cases with longer follow-ups on the course of transudative fluids.

ETHICAL DECLARATIONS

Ethics Committee Approval: This retrospective study was approved by the Baskent University Clinical Researches institional review board (Date: 28.02.2012, Decision No:12/32,).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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