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Investigating Causes of Undiagnosed Exudative Pleural Effusion Using Medical Pleuroscopy and Closed Biopsy

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ABSTRACT

Introduction: Pleural effusion may develop during various acute or chronic medical conditions. Despite different diagnostic workups, some cases of pleural effusion may remain undiagnosed. Pleuroscopy and closed biopsy are common diagnostic approaches used for the diagnosis of undiagnosed cases. The present research aimed to evaluate the diagnostic yield of medical pleuroscopy and closed biopsy in Iran.

Materials and Methods: The present cross-sectional study was performed within 2016-2018, in the North-East of Iran. Patients who had undiagnosed lymphocytic predominance exudative pleural effusion were included in the present research. Every patient underwent medical pleuroscopy or closed pleural biopsy by an Abrams needle. The collected data were analyzed in SPSS software (version 12).Ap-valuelessthan0.05 was considered statistically significant.

Results: A total of 108 patients with the mean age of 58.73±18.13 years enrolled in the present study. Around 50 patients underwent needle biopsy, while the other 58 patients went through medical pleuroscopy. Chronic pleuritis, malignant pleural effusion, negative results, and tuberculosis were the common results. When pleuritis is regarded as negative results and malignant and tuberculosis pleural effusion as positive results, medical thoracoscopy provides more significant positive results and fewer negative results (P=0.024). No patient developed complications after the procedures.

Conclusion: In contrast to other studies, both of these techniques had low diagnostic yield for the diagnosis of undiagnosed pleural effusion. Therefore, performing other diagnostic workups (e.g., imaging techniques) may decrease the rate of undiagnosed pleural effusion.

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Introduction

Pleural effusion is recognized as the accumulation of pleural fluidin the pleural space. Pleural cavity accounts for approximately 0.26 ml/kg of human body weight and various diseases can disrupt the production or clearance of pleural fluid (1). As there is a long list of the differential diagnosis for pleural effusion, performing a detailed diagnostic workup for each patient is mandatory for achieving the most probable diagnosis as the possible etiology vary from benign to malignant causes (1). One of the earliest approaches in diagnosing

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possible causes of pleural effusion is the evaluation ofthe biological content of fluid which is mostly performed by thoracentesis(2, 3). Depending on the thoracentesis results, further diagnostic workups can be ordered and patients may undergo various diagnostic workups (2). However, the etiology of pleural effusion may remain unclear despite a wide range of diagnostic processes in some patients (2). Ultra-sonographic or computed tomography-guided percutaneous biopsy, as well as thoracoscopy, are the most reliable choices for patients who have undiagnosed exudative pleural effusion (2).In the late ninetieth, exploring the pleural cavity by pleuroscopy was introduced as medical thoracoscopy. It became a new diagnostic method for investigating pleural disease and now it is used globally as a diagnostic modality of pulmonary diseases (3). Nowadays, thoracoscopy is used as a therapeutic and diagnostic technique and pleural effusion is a common indication for medical thoracoscopy which can be made by local anesthesia (4). It has been demonstrated that medical thoracoscopy can provide approximate sensitivity of 95% for the detection of malignant pleural effusion and the sensitivity can increase when combined with other techniques, including analysis of effusion fluid cytology (5).The sensitivity of thoracoscopy is even reported to be near 100% in detecting tuberculosis pleural effusions (5).

In contrast to aclosed needle biopsy, the main advantages of using medical thoracoscopy are mostly because of its direct visualization and the possibility of taking specimens from the pleura. Nowadays, this technique isturning into a good diagnostic modality for the evaluation of pleural disease which has not been diagnosed by other diagnostic modalities (3). The present study aimed to compare the diagnostic results of medical thoracoscopy to needle biopsy in patients with undiagnosed pleural effusion.

Materials and Methods

The present cross-sectional study was conducted in Imam Reza and Ghaem hospitals in Mashhad, Iran, within 2016-2018.

It was approved by the Ethical Committee of Mashhad University of Medical Sciences, Mashhad, Iran (IR.MUMS.fm.REC.1396.41). Patientswho were older than 15 years of age and were diagnosed to have undiagnosed lymphocytic exudative effusion (lymphocytic predominance defined as>50% lymphocytes of total pleural fluid cells) who required pleural needle biopsy were included in the present research. These patients were considered to have undiagnosed pleural effusion as their primary tests, including biochemical and serologic tests of their pleural effusion fluid were unremarkable. After filling the informed consent forms, every patient with a normal platelet count who did not have a coagulating disorder was assumed to be a candidate for pleural biopsy by medical pleuroscopyorclosed biopsy using Abrams needle. All the procedures were performed in a bronchoscopy ward and those patients with unstable hemodynamics were not included in the current study. During the needle biopsy procedure performed by Abrams needle, a pleural biopsy was taken after providing local anesthesia while the patient sitting in an upright position. During pleuroscopy, the patients received general anesthesia and the specimens were taken under direct visualization of pleura.

Statistical analysis

Descriptive data analysis was presented as mean and standard deviation (SD) for continuous variables and frequency and percentage for categorical variables. The chi-square or Fisher exact test was used to compare the distribution of categorical variables, including symptoms. Independent t-tests and Mann-Whitney tests were performed to compare the continuous variables between groups.

In comparison using the chi-square test with the degree of freedom was larger than one, the pairwise comparison was only made if the result of the overall chi-square test was statistically significant. A p-value less than0.05 was considered statistically significant and the collected data were analyzed using SPSS software (version 12).

Results

Among the total number of 108 patients with a mean age of 58.73±18.13 years, 50 and 58 patients underwent needle biopsy and medical pleuroscopy, respectively. The demographic data of all the participants are summarized in Table 1. There was no significant difference in the presence of symptomsbetween the study groups (P=0.986; Figure 1).Thirty-three (30%) patients had chronic pleuritis and 32 (29.62%) patients suffered from malignant pleural effusion, while 28 (25.92%) patients had no pathologic finding and 15(13.88%) patients had tuberculosis (Table 2).

When pleuritis is regarded as negative results and malignant and tuberculosis pleural effusion as positive results, medical thoracoscopy provides more significant positive results and fewer negative results (P=0.024).

Among the study participants, 12(11.11%) patients had a history of cancer, while only 8 (7.4%) and 5 (4.62%) patients had a history of hypertension and diabetes mellitus, respectively. The distribution of these underlying illnesses is illustrated infigure 1. The underlying cause of pleural effusion was not significantly related to these underlying diseases (P=0.865). None of the patients developed any complica tions after the procedures.

Table 1. Demographic data of study participants

		Study groups		P-value
		Needle biopsy (%)	Pleuroscopy (%)	
Gender	Male	28(56)	30(51.73)	0.702*
	Female	22(44)	28(48.27)	
Pleural effusion	Right	22(44.89)	32(57.14)	0.243*
	Left	27(55.11)	24(42.86)	
Effusion volume	Massive	34(69.38)	35(64.81)	0.138*
	Moderate	9(18.36)	17(31.48)	
	Mild	6(12.25)	2(3.71)	
Pleural fluid lactate dehydrogenase (LDH)		881.97±117	801±69	0.670**
Pleural fluid protein		4.68±1.31	4.48±0.91	0.377**
Lymphocyte (%)		76.35±14.89	80.12±20.3	0.298**
serum lactate dehydrogenase (LDH)		432.73±224	516.64±486	0.290**
Serum protein		7.38±6.4	6.53±4	0.5**
Erythrocyte sedimentation rate		58.65±31.48	51.27±4.72	0.707**
C-reactive protein		25.52±3.67	43.14±8.63	0.051**

* Chi squire test
** T-test

		Study groups		P- value
		Needle biopsy (%)	Pleuroscopy (%)	
Pathology results	Negative	13(26)	15(25.87)	0.077*
	Malignancy	11(22)	21(36.20)	
	Chronic Pleuritis	21(42)	12(20.69)	
	Tuberculosis	5(10)	10(17.24)	

*Fisher exact test

Discussion

The present study demonstrated that chronic pleuritis and malignant pleural effusion constituted the most common causes of undiagnosed pleural effusions diagnosed either by pleuroscopy or biopsy. Diagnosis of pleural effusion requires a systematic approach to reduce costs and save time for the management of serious medical conditions (6). Similar to any other diseases, history, and physical examination provide the most reliable clues for diagnosing almost every medical condition and especially the pleural effusion. Although most common symptoms of pleural effusion are considered to be dyspnea, cough, and pleuritic chest pain, most of the patients

have an underlying medical illness which massages tthe presence of pleural effusion(6).The previoushistory of cardiac, hepatic, or renal disease maybe suggestive of transudate effusion, while the presence of malignancies or infections may be suggestive of malignant or para-pneumonic pleural effusion(6).According to such diagnostic clues, special diagnostic workups, including diagnostic thoracentesis and fluid analysis should be performed (6). However, the main cause of the pleural effusion may not be determined in some patients and these cases are regarded as undiagnosed pleural effusions and should be referred to asrespirologists(7). Besides, the management of such undiagnosed effusions is controversial. Most of the patients with undiagnosed pleural effusion undergo pleural biopsy or medical thoracoscopy (7). The overall superiority of these two techniques is not established as there are no large scale studies performed in this regard (8).Moreover, both of these techniques can be performed in different ways. For instance, medical thoracoscopy can be performed in two main ways, either by rigid or fiber opticthoracoscopy. Shaheen et al. compared the efficacy of using fiber optic and rigid thoracoscopy for the diagnosis of undiagnosed pleural effusion (9). While both techniques were safelyperformed without any complications, they demonstrated that rigid thoracoscopy provides a better diagnostic yield (9). They demonstrated that most cases had malignant and tuberculosis pleural effusion (9).

Taking a pleural biopsy can be performed in different ways and image-guided cutting needle biopsies have a high diagnostic yield in undiagnosed pleural effusion (10). However, other types of closed biopsies can be performed in such undiagnosed cases. In the present research, the Abrams needle was used. It has been demonstrated that closed biopsy by Abrams needle can provide high diagnostic yield in cases who are more likely to have tuberculosis as their underlying cause of effusion (10). Tuberculosis is a chronic respiratory infection that is endemic in some regions of Iran (11). Tuberculous pleural effusion is a common cause of pleural effusion in endemic areas and patients with immunodeficiency are more prone to develop tuberculous pleural effusion (12). The prevalence of tuberculous pleural effusion diagnosed by medical thoracoscopy is varied across different countries, ranging from a high ratio of more than 80% to lower than 2% in European countries and United States (13-15). It has been shownthat medical thoracoscopy is a safe method for organized tuberculous pleural effusion (16). Our study demonstrated that approximately 14% of patients have tuberculous pleural effusion and 66% of patients were diagnosed by medical thoracoscopy. Consequently, even in endemic countries for tuberculosis, performing thoracoscopy for diagnosing undiagnosed pleural effusion may be superior to closed biopsy by Abrams needle. Moreover, in contrast to a needle biopsy, thoracoscopy provides visualization of pleuropericardial space and facilitates the diagnostic workup of pleural lesions. In vein with the findings of the current research, Mahmoodlou et al. indicated that dyspnea is the most common primary symptom ofpleural effusions with unknown origin (17). Although the study conducted by Mahmoodlou et al. consisted of only 31 participants in Iran, their findings were similar to the results of the present study as malignant pathologies account for the most common causes of undiagnosed pleural effusion (17). Although the results of these diagnostic techniques may not always be informative, the positive results may guide respirologists to plan their further workups for similar patients. The main causes of the most undiagnosed pleural effusions are malignancies, pneumonia, tuberculosis, and pulmonary embolisms (18). Based on the findings of the present research, either using biopsy or medical thoracoscopy, 43.5% of the undiagnosed cases may either be due to malignancy or tuberculosis and in only 24% of patients of these workups were still unremarkable. The diagnostic rate of undiagnosed pleural effusion varies among different studies. Patil et al. evaluated a group of undiagnosed pleural effusion by thoracoscopy pleural biopsy and demonstrated that the diagnostic yield of this diagnostic approach at 85.2 %(19). While their study population was

approximately similar to our study, the most common findings in their patients' workups weremalignancy which was reported to be three times (66.4%) and tuberculosis was reported two times (28.2%) more prevalent in contrast to the present study(19). In astudycarried out by Ahmed et al., it was reported that medical thoracoscopy gave a definitive diagnosis in 96% of undiagnosed pleural effusion (20). They showed that 92% of their patients had malignant effusion and only 2% of patients had tuberculosis (20). Helala et al. provided similar diagnostic results for medical thoracoscopy on 40 patients (21). They also demonstrated that 70% of their patients had malignant effusion and 22.5% had tuberculosis (21).

Limitations

The current research evaluated a considerable population of patients with undiagnosed pleural effusion; however, there were some limitations present. One of the main limitations of the present study was using Abrams closed needle biopsy. This technique is mostly preferred in centers that are not well-equipped or are endemic for tuberculosis. Another limitation could be the lack of further imaging workups (e.g., computed tomography of the lungs). Some possible causes of the undiagnosed pleural effusion may be revealed using such imaging techniques or even performing closed pleural biopsies under the imaging guide.

Conclusion

The present study evaluated the role of Abrams closed needle biopsy and medical pleuroscopy in patients who had undiagnosed pleural effusion. In contrast to other studies, both of these techniques had low diagnostic yield for the diagnosis of undiagnosed pleural effusion. Therefore, performing other diagnostic workups, including imaging techniques may decrease the rate of undiagnosed pleural effusion. Moreover, in line with the findings of similar studies, malignancies are the common cause of undiagnosed pleural effusions and could be considered even in patients who are not able to undergo diagnostic workups of undiagnosed pleural effusions.

Conflicts of Interest:

The authors declare that there is no conflict of interest.

References

1.Feller-Kopman D, Light R. Pleural disease. N Engl J Med. 2018;378:740-51.
2. Beaudoin S, Gonzalez AV. Evaluation of the patient with pleural effusion. CMAJ. 2018;190:E291-5.
3.Loddenkemper R, Mathur PN, Lee P, Noppen M. History and clinical use of thoracoscopy/pleuroscopy in respiratory medicine. Breathe. 2011;8:144-55.
4.Rodriguez-Panadero F, Janssen JP, Astoul P. Thoracoscopy: general overview and place in the diagnosis and management of pleural effusion. Eur Respir J. 2006;28:409-22.
5.Loddenkemper R. Thoracoscopy--state of the art. Eur Respir J. 1998;11:213-21.
6. McGrath EE, Anderson PB. Diagnosis of pleural effusion: a systematic approach. Am J Crit Care. 2011;20:119-27.
7.Hooper C, Lee YG, Maskell NJ;BTS Pleural Guideline Group.Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010;65:ii4-17.
8.Dixon G, de Fonseka D, Maskell N. Pleural controversies: image guided biopsy vs. thoracoscopy for undiagnosed pleural effusions? J Thorac Dis. 2015;7:1041-51.
9. Shaheen MM, Shaaban AY, Mahmoud MI, Shaaban AA, Sweed RA. The diagnostic role of thoracoscope in undiagnosed pleural effusion: rigid versus flexible. Egyp J Chest Dis Tuberc. 2014;63:635-42.
10.Bibby AC, Maskell NA. Pleural biopsies in undiagnosed pleural effusions; Abrams vs image-guided vs thoracoscopic biopsies. Curr Opin Pulm Med. 2016;22:392-8.
11.Haghdoost AA, Afshari M, Baneshi MR, Gouya MM, Nasehi M, Movahednia M. Estimating the annual risk of tuberculosis infection and disease in southeast of iran using the bayesian mixture method. Iran Red Crescent Med J. 2014;16:e15308.
12.Zhai K, Lu Y, Shi HZ. Tuberculous pleural effusion. J Thorac Dis. 2016;8:E486-94.
13.DePew ZS, Wigle D, Mullon JJ, Nichols FC, Deschamps C, Maldonado F. Feasibility and safety of outpatient medical thoracoscopy at a large tertiary medical center: a collaborative medical-surgical initiative. Chest. 2014;146:398-405.
14.Diacon AH, Van de Wal BW, Wyser C, Smedema JP, Bezuidenhout J, Bolliger CT, et al. Diagnostic tools in tuberculous pleurisy: a

direct comparative study. Eur Respir J. 2003;22:589-91.
15.Hansen M, Faurschou P, Clementsen P. Medical thoracoscopy, results and complications in 146 patients: a retrospective study. Respir Med. 1998;92:228-32.
16.Xiong Y, Gao X, Zhu H, Ding C, Wang J. Role of medical thoracoscopy in the treatment of tuberculous pleural effusion. J Thorac Dis. 2016;8:52-60.
17.Mahmodlou R, Seyed Mokhtari SA, Sarbazzadeh J. The role of thoracoscopy in the diagnosis of pleural effusion of unknown origin. J Babol Univ Med Sci. 2018;20:31-6.
18.Light RW. The undiagnosed pleural effusion. Clin Chest Med.2006;27:309-19.
19.Patil C, Dixit R, Gupta R, Gupta N, Indushekar V. Thoracoscopic evaluation of 129 cases having undiagnosed exudative pleural effusions. Lung India. 2016;33:502-6.
20.Ahmed MM, Halim HA, Aziz ET, El-Shorbagy RM. Outcomes and complications of medical thoracoscopy in undiagnosed exudative pleural effusion. Egyp JBronchol. 2016;10:93.
21.Helala LA, El-Assal GM, Farghally AA, El Rady MM. Diagnostic yield of medical thoracoscopy in cases of undiagnosed pleural effusion in Kobri El-Kobba Military Hospital. Egyp J Chest Dis Tuberc. 2014;63:629-34.