Original Article

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Surgery Section

Role of Video Assisted Thoracoscopic Surgery in Pleural Effusion

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ABSTRACT

Introduction: Many cases of pleural effusions remain undiagnosed even after investigations including Computed tomography (CT) chest, pleural fluid analysis. Role of Video Assisted Thoracoscopic Surgery (VATS) in undiagnosed pleural effusion is still controversial. VATS has the advantage of taking biopsy under direct vision and therapeutic procedures can be done in the same sitting.

Aim: To evaluate the role of VATS in the diagnosis and management of pleural effusions.

Materials and Methods: The study was conducted in the Department of Surgery, Dayanand Medical College and Hospital, Ludhiana, Punjab, India for a period of one and half year from January 2017 to May 2018. Efficacy of VATS as a diagnostic and therapeutic procedure was evaluated in patients with undiagnosed pleural effusion.

Results: A total of 54 patients were included in the study. Diagnostic yield of VATS in present study was 100%. The most common diagnosis was parapneumonic effusion in 31.5% of the patients followed by chronic non-specific inflammation and tuberculosis in 25.9% patients each. Malignancy was final diagnosis in four patients. Some sort of therapeutic procedure was done in all patients and effective therapeutic yield of VATS in present study was 96.3%.

Conclusion: This study adds to substantial data about the high diagnostic yield and high therapeutic efficacy of VATS in pleural effusions. The diagnostic yield of VATS for undiagnosed effusion is better than repeat thoracocentesis with the added advantage of therapeutic intervention if needed with a high success rate.

Keywords: Diagnosis, Empyema, Exudative, Parapneumonic effusion, Therapeutic, Thoracic surgery, Tuberculosis

INTRODUCTION

Pleural effusion is an abnormal collection of fluid in the pleural space. Pleural effusion can be a presentation of many different underlying diseases. An aetiological diagnosis can be established with the help of pleural fluid cytology and other biochemical parameters in most cases. About 20% cases remain undiagnosed despite diagnostic workup [1,2].

An undiagnosed pleural effusion is often a difficult diagnostic dilemma that needs further invasive procedures for definitive aetiological diagnosis.

The main objective of evaluation in an undiagnosed pleural effusion is to establish an early diagnosis and facilitate treatment with minimal invasive intervention. A common presentation of various causes of pleural effusion, each with different management results in a clinical conundrum for the treating physician. About 30 to 40% of the patients remain undiagnosed even after biochemical, bacteriological and cytological examination of pleural fluid and closed needle biopsy of the pleura [3]. A malignant pleural effusion provided the basis of the first diagnosis of cancer in 46% of the patients in a study conducted by Chernow B and Sahn SA [4].

Pleural fluid cytology achieves a mean diagnostic value of 60% [5] although taking a second sample can further increase the yield up to 27%; this has limited application [6].

Primary pleural effusions are treated by conservative therapy in the form of thoracentesis, intercostal tube drainage and adequate antibiotics and fibrinolytic agents which is adequate to achieve clinical improvement and a small number who were refractory to the aforementioned treatments needed surgical methods like decortication and thoracoplasty [7,8].

VATS is often considered as gold standard investigation for an unexplained pleural effusion with high diagnostic yield [9]. VATS plays a bridging role between medical and aggressive surgical management [10,11]. For many decades this procedure was mainly used by pulmonologists for the diagnostic purpose only, but now it plays important diagnostic as well as therapeutic role. It allows precise exploration of the pleural cavity, biopsy for histopathological examinations and various possible therapeutic procedures like removal of (septated) pleural effusions, pleurodesis, pulmonary decortications, drain positioning under visual control etc.

VATS has various implied advantages over the open thoracotomy procedure such as a minimal surgical scar, sufficient access, quicker recovery of the patient to pre-operative status, lesser pain and analgesic requirement, shorter duration of hospitalisation, fewer intra-operative and post-operative complications, decreased overall morbidity and mortality. The major complications of the procedure include prolonged post-operative air leak, bleeding, infections, post-operative pain and recurrence at port site in case of malignant lesions [12]. The affordability of VATS has been a matter of discussion. It was shown that despite the use of specialised instruments, VATS is cheaper than open procedure as the hospital stay is significantly reduced [13].

Unfortunately, to date, the role of VATS is still controversial and lacks enough study to prove its diagnostic and therapeutic value in unexplained exudative pleural effusions. The present study aimed to evaluate the role of VATS in the diagnosis and treatment of undiagnosed pleural effusion.

MATERIALS AND METHODS

This prospective study was conducted between January 1 2017 and May 31 2018, by random sampling of 54 patients with age

above 16 years, who were admitted at Dayanand Medical College and Hospital, Ludhiana, Punjab, India with undiagnosed exudative pleural effusion despite complete clinical examination, routine haematological investigation, radiological examination, sputum smear examination and pleural fluid analysis after thoracocentesis. Approval was obtained from the Institutional Ethics Committee (DMCH/P/2016/1487-94).

Exudative pleural effusion was defined as per the Light's criteria [14].

Light's Criteria

Pleural fluid is exudative if one of the following criteria is present, otherwise, it is transudative.

- Effusion protein/serum protein ratio is greater than 0.5.
- Effusion Lactate Dehydrogenase (LDH)/serum LDH ratio greater than 0.6.
- Effusion LDH level is greater than two thirds the upper limit of the laboratory's reference range of serum LDH.

Patients of age 16 and above with undiagnosed pleural effusion were included in the study.

All the haemodynamically unstable patients, patients with gross cardiovascular insufficiency, history of previous thoracic surgery and/or bleeding disorders were excluded from the study.

After obtaining written informed consent, particulars of the patient were duly noted and a detailed history including symptoms, coexisting comorbid conditions, personal habits like smoking or alcohol consumption, past treatment history was taken. All patients underwent a comprehensive evaluation including all the routine investigations and computed tomography of the chest. The various socio-demographic characteristics and clinical parameters were noted. All patients underwent sputum smears examinations for the presence of Acid-Fast Bacilli (AFB) on two successive days. Also, thoracocentesis was done and the aspirated pleural fluid was sent for a chemical, bacteriological and cytological examination that include proteins, sugar and LDH levels, pH, total and differential leukocyte count, gram staining and culture, AFB smear, malignant cytology and Adenosine Deaminase (ADA) levels.

All the undiagnosed cases after complete evaluation were considered and given the option for diagnostic and therapeutic VATS. After a detailed preanaesthetic checkup and written informed consent, patients were taken up for VATS surgery.

Surgical Technique of VATS [2,15]

The patients received general anaesthesia with double-lumen endotracheal intubation which was confirmed by fibre-optic bronchoscopy in the contralateral decubitus position. Sixth or seventh intercostal space in mid-axillary line was routinely relied upon for trocar protected thoracoscopic access to the pleural cavity. Subsequent intercostal access at 2-4 sites was achieved under the direct thoracoscopic vision to avoid injury to the underlying lung parenchyma. The entire hemithorax was carefully examined. Any free fluid, pus was aspirated and sent for microbiology examination. A thorough assessment of the pleural and lung surface was done and biopsies were taken from suspected areas of pleura or lung tissue accordingly and were sent for histopathological examination. Also, if required, then VATS assisted decortications, wedge resection or lobectomy was done. Chemical pleurodesis with 3-5 grams of talc was done according to intra-operative findings. Once VATS intervention was complete and complete hemostasis achieved, one or two chest tubes were placed through one or more of the intercostal access sites under the vision to facilitate proper drainage. The thoracic cavity was then closed in layers and the aseptic dressing was done.

Intra-operative and post-operative data were collected for all the patients. The data was analysed and the diagnostic and therapeutic yield of VATS in undiagnosed pleural effusion was measured. Serial chest X-rays were done over six months of follow-up period to look for any disease recurrence, relapse or any long term complication.

STATISTICAL ANALYSIS

The data was described in terms of range; mean±standard deviation (±SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Data analysis was done using Statistical Package for the Social Sciences (SPSS) 21 version statistical program for Microsoft Windows.

RESULTS

Total 54 patients with undiagnosed pleural effusion who underwent VATS as the diagnostic as well as therapeutic procedure were included in the study. The patient's distribution according to their age and prevalent symptoms has been well reported in [Table/Fig-1,2].

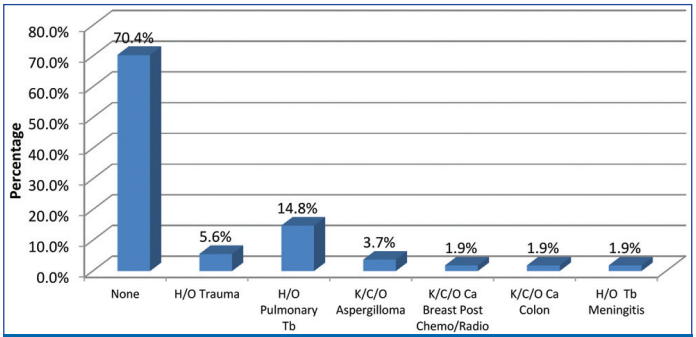
Age group (years)	No. of cases	Percentage
<40	27	50.0%
41-60	15	27.8%
>60	12	22.2%
Total	54	100.0%

[Table/Fig-1]: Age distribution of the patients under study (n=54).

Symptom	No. of cases	Percentage
Fever	44	81.5%
Cough	51	94.4%
Breathlessness	34	63.0%
Weight Loss	21	38.9%

[Table/Fig-2]: Distribution of patients according to symptoms.

In the present study, most of the patients did not have any previous treatment history to a conclusive diagnosis. Nine patients (16.7%) had received antitubercular therapy. Out of these nine patients, eight had a history of pulmonary tuberculosis whereas one case was of tuberculous meningitis. Final histopathology revealed tuberculosis in three patients (33.3%) while no tuberculosis was detected in six patients (66.7%) [Table/Fig-3].

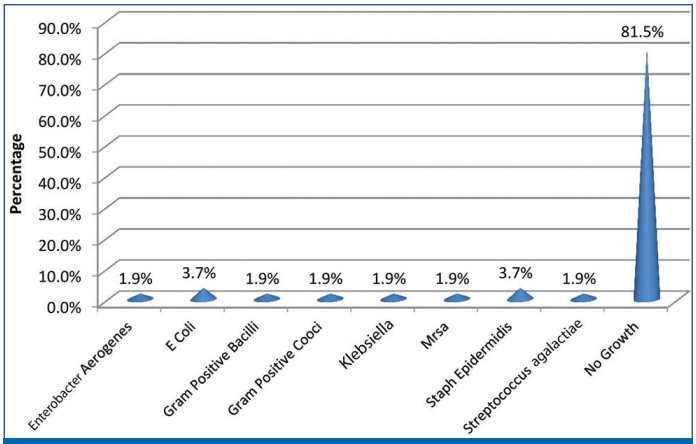


[Table/Fig-3]: Distribution of patients according to previous treatment/relevant finding.
H/O- History of; k/C/O- Known case of

As shown in [Table/Fig-4], majority of the patients remained undiagnosed after the pleura fluid culture sensitivity as it yielded no growth in 44 patients (81.5%).

[Table/Fig-5] shows maximum patients were executed with VATS drainage with decortication and only single patient went through VATS drainage with open pneumonectomy.

Out of 54 patients in present study 50 (92.6%) patients were those in which definitive diagnosis was made, appropriate therapeutic procedure was done, and post-operative antibiotics either broad-spectrum according to aetiology, specific according

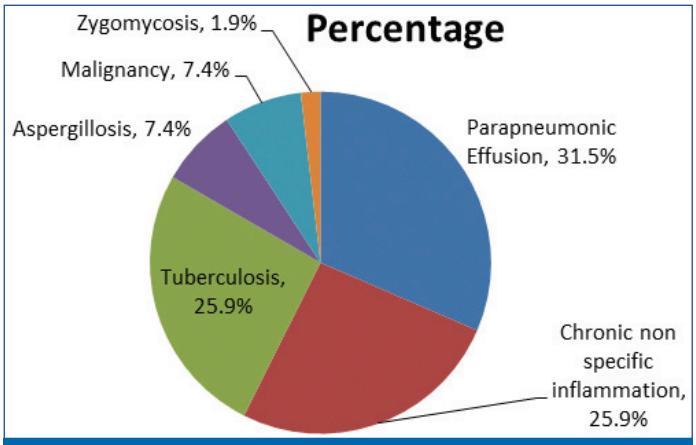


[Table/Fig-4]: Distribution of patients according to culture sensitivity of pleural fluid on pleural tap.

Operation	No. of cases	Percentage
VATS* drainage with decortication	31	57.4%
VATS drainage and decortication with lobectomy	8	14.8%
VATS drainage with decortication with wedge resection	4	7.4%
VATS drainage with tissue biopsy with pleurodesis	4	7.4%
VATS drainage and biopsy	3	5.6%
VATS drainage and decortication with BPF# repair	3	5.6%
VATS drainage with open pneumonectomy	1	1.9%
Total	54	100.0%

[Table/Fig-5]: Distribution of patients according to operative procedure executed.
*Video-assisted thoracoscopic surgery
#Bronchopleural fistula

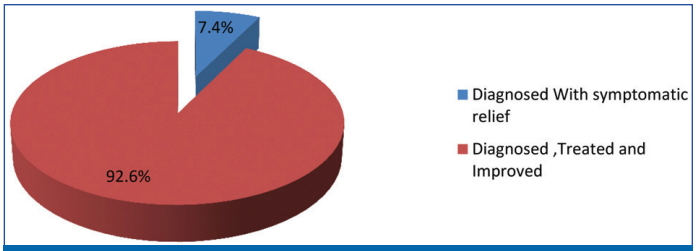
to culture sensitivity results, antifungals in cases of aspergillosis or Antitubercular Treatment (ATT) in cases of Tuberculosis were started, these patients improved and were discharged in satisfactory conditions. Four patients (7.4%) in present study included those in which histopathology came out to be a malignancy, these patients had resolution of symptoms as talc pleurodesis was done and were discharged, But these patients required further workup, definitive treatment and close follow-up. Two patients out of these two had metastatic effusion on histopathology, so talc pleurodesis was palliative treatment in these patients [Table/Fig-6-8].



[Table/Fig-6]: Distribution of patients according to final diagnosis.

>40 Adenosine Deaminase levels	No. of cases	Percentage
Paraneumonic effusions	6	16.0%
Aspergillosis	1	4.0%
Chronic inflammation	5	16.0%
Malignancy	2	8.0%
Tuberculosis	11	44.0%
Total	25	100.0%

[Table/Fig-7]: Distribution of patients with adenosine deaminase levels >40 based on final diagnosis.



[Table/Fig-8]: Distribution of patients based on final outcome.

DISCUSSION

Pleural effusion is one of the most challenging areas of respiratory medicine and surgery because of varied symptoms at presentation and a variety of underlying pathologies ranging from a simple inflammatory reaction to tuberculosis and malignancy.

In present study, 54 patients with clinically detected pleural effusion and who met the inclusion and exclusion criteria were included to ascertain the diagnostic and therapeutic yield of VATS.

Dhital KR et al., in their study of 100 patients with diagnosed pleural effusion found that the predominant age group was 21-30 years [16]. Concurring with the study by Dhital KR et al., the present study had a predominance of patients between the 2nd-4th decade of life as this working-age group is more exposed to environmental pathogens and carcinogens contact [16].

There was a predominance of male subjects in the present study (72.2%) reflecting the working population in this country as reported by Gupta R et al., by predominance of male subjects (75%) in their study of 1000 patients [17].

The cough was the most common presentation in present study (94.4%) followed by fever (81.5%). Breathlessness occurred in 63% and weight loss occurred in 38.9% of patients. In the study by Karkhanis VS and Joshi JM the most common presenting symptom among the study population was breathlessness and dry cough [18].

In present study, 27.8% of patients had diabetes mellitus, 18.5% had a history of ischemic heart disease, 9.3% had a history of chronic obstructive pulmonary disease and 7.4% were hypertensive. Chertow BS et al., in their study noted that pleural effusion is more common in case of long-standing diabetes mellitus patients than non-diabetic patients [19]. Meveychuck A et al., in their study concluded that pleural effusion is more common among the patients with Chronic Obstructive Pulmonary Disease (COPD) and the exacerbation of COPD was more common and frequent in patients with pleural effusion [20].

In present study, right hemithorax was predominantly affected by pleural effusion. Similar findings were noted in the study by Beheshtirouy S et al., in which right hemithorax was predominantly affected by pleural effusion (61.5%) [21].

In present study, out of total nine patients with prior history of having received anti-tubercular treatment for tuberculosis, final histopathology revealed tuberculosis in only three cases while in six cases there was no evidence of tuberculosis on final histopathology report. This might be attributed to the fact that having completed the course of ATT, resulted in the successful treatment of TB.

Light LW stated that if the pleural fluid ADA level is more than 40 U/L with lymphocyte to the neutrophil ratio of >0.75, a presumptive diagnosis of tubercular pleural effusion can be made [22]. Wang H et al., found out that ADA or IFN-γ levels in combination with Dipeptidyl Peptidase-4 (DPP4) or IP-10 can aid in differentiation between tubercular and non-tubercular pleural effusion with improved specificity and diagnostic efficiency [23]. ADA activity in pleural fluid >250 U/L is highly suggestive of empyema or lymphoma rather than TB [24]. There were 25 patients in present study with

pleural fluid adenosine deaminase level >40 U/L. Among these 25 cases, 11 cases (44%) were finally diagnosed with tuberculosis. Six cases (16%) diagnosed as parapneumonic effusion, 5 (16%) as chronic non-specific inflammation.

In the present study, pre-operative culture was positive in 18.5% of patients pleural fluid culture positivity varies with the stage of pleural infection between 30% and 75% with higher yields in the empyema stage [25].

In present study of 54 patients, VATS had a diagnostic yield of 100% while the therapeutic yield was 96.3%. In the study by Shadmehr MB et al., VATS had a diagnostic yield of 77.7% (21 out of 27 cases) [26]. Three out of six had diagnostic failures in VATS was due to pleural adhesions, two patients were those whose pathology report showed benign pleural disease but on follow-up pleural malignancy was detected. Das B and Dey I in their study on 60 patients with undiagnosed pleural effusion were able to reach a diagnosis in 52 out of 60 patients giving a diagnostic yield of 86.67% [9]. They also stated that the diagnosis of pleural effusion was much easy with VATS because of better visualisation and the ease to take a large sample of representative tissue because of proper instrumentation. In the case of multiloculated pleural effusion, the loculi were broken down during the procedure thereby, facilitating the drainage of fluid through the ICD placed.

VATS had 100% diagnostic yield in present study. The study observed that maximum patients were diagnosed with parapneumonic effusion (31.5%), followed by tuberculosis and chronic non-specific inflammation (25.9% each). Aspergillosis and malignancy were diagnosed in 4 patients each (7.4%). In the study by Das B and Dey I tuberculosis was diagnosed in 43.3% of the patients, chronic non-specific inflammation was found in 13.33% of the patients, pleural malignancy was found in 10% and parapneumonic effusion was found in 10% [8]. The difference in the statistics can be due to the geographical distribution of certain diseases in specific areas, early detection through screening programs and treatment of tuberculosis patients. High incidence of parapneumonic effusions in present study can be attributed to various causes including under treatment of these conditions, late presentation of patients to the hospital or late referral to higher centre.

In the present study, therapeutic procedure was done in all patients. VATS drainage with decortication was most performed therapeutic procedure in 31 (57.4%), which is incongruous of our diagnostic yield as parapneumonic effusion was most common diagnosis (31.5%) and these conditions generally require drainage and decortication only. VATS drainage with decortication with lobectomy was done in 8 patients (14.8%). Lobectomy was required in patients having lung necrosis, fungal ball or large Bronchopleural Fistula (BPF). VATS drainage with decortication with wedge resection was done in 4 patients (7.4%). VATS drainage with decortication with BPF repair was done in 3 patients. VATS drainage with open pneumonectomy was done in a patient with extensive aspergillosis.

In the remaining 4 patients, VATS drainage with tissue biopsy with pleurodesis was done, these patients were suspected cases of malignancy and after taking biopsies pleurodesis was done to prevent recurrence of effusion. In these four cases, the biopsy report was malignancy and therefore further workup and other modalities of treatment were required, So although talc pleurodesis was done VATS was not the definitive therapeutic procedure in these patients but acted as a palliative procedure in two patients in which biopsy was suggestive of secondary metastasis. So, overall therapeutic yield in the study was 96.3%.

Limitation(s)

Studies with larger sample size are required to assess the efficacy of VATS as a diagnostic and therapeutic procedure to attain more reliable results.

CONCLUSION(S)

This study adds to the substantial data the high efficacy of VATS as a diagnostic procedure in undiagnosed pleural effusions or pleural effusion with doubtful diagnosis, and also as an optimal therapeutic procedure in the management of parapneumonic and other inflammatory and granulomatous effusion in benign conditions, and effective pleurodesis in cases of malignant effusions.

A multidisciplinary team should be employed in such patients to provide the optimal treatment for undiagnosed pleural effusion by avoiding unnecessary repeat inconclusive investigations and offering diagnostic VATS, resulting in more therapeutically successful outcomes.

REFERENCES

[1] Collins TR, Sahn SA. Thoracocentesis: Clinical value, complications, technical problems and patient experience. Chest. 1987;91:817-22.
[2] Ali MS, Light RW, Maldonado F. Pleuroscopy or video-assisted thoracoscopic surgery for exudative pleural effusion: A comparative overview. J Thorac Dis. 2019;11(7):3207-16. doi: 10.21037/jtd.2019.03.86.
[3] Daniel TM. Diagnostic thoracoscopy for pleural disease. Ann Thorac Surg. 1993;56:639-40.
[4] Chernow B, Sahn SA. Carcinomatous involvement of the pleura: An analysis of 96 patients. Am J Med. 1977;63:695-702.
[5] Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: Analysis of 414 cases. Mayo Clin Proc. 1985;60:158-64.
[6] Garcia LW, Ducatman BS, Wang HH. The value of multiple fluid specimens in the cytological diagnosis of malignancy. Mod Pathol. 1994;7:665-68.
[7] Colice GL, Curtis A, Deslauriers J, Heffner J, Light R, Littenberg B, et al. Medical and surgical treatment of parapneumonic effusions: An evidence-based guideline. Chest. 2000;118(4):1158-71.
[8] Luh SP, Chou MC, Wang LS, Chen JY, Tsai TP. Video-assisted thoracoscopic surgery in the treatment of complicated parapneumonic effusions or empyemas, outcome of 234 patients. Chest. 2005;127:1427-32.
[9] Das B, Dey I. Role of video assisted thoracic surgery in the diagnosis of pleural effusion- A prospective study in a tertiary hospital of West Bengal. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2016;15:31-35.
[10] Landreneau RJ, Keenan RJ, Hazelrigg SR, Mack MJ, Naunheim KS. Thoracoscopy for empyema and hemothorax. Chest. 1996;109:18-24.
[11] Liu HP, Hsieh MJ, Lu HI, Liu YH, Wu YC, Lin PJ. Thoracoscopic-assisted management of postpneumonic empyema in children refractory to medical response. Surg Endosc. 2002;16(11):1612-14.
[12] Łochowski MP, Kozak J. Video-assisted thoracic surgery complications. Wideochir Inne Tech Maloinwazyjne. 2014;9(4):495-500.
[13] Casali G, Walker WS. Video assisted thoracic surgery lobectomy: Can we afford it? Eur J Cardiothorac Surg. 2009;35:423-28.
[14] Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: The diagnostic separation of transudates and exudates. Ann Intern Med. 1972;77(4):507-13.
[15] Mehrotra M, Arthur ME. Video-Assisted Thoracoscopy (VATS) [Updated 2020 Feb 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532952.
[16] Dhital KR, Acharya R, Bhandari R, Kharel P, Giri KP, Tamrakar R. Clinical profile of patients with pleural effusion admitted to KMCTH. Kathmandu Univ Med J (KUMJ). 2009;7(28):438-44.
[17] Gupta R, Gupta A, Ilyas M. Video assisted rigid thoracoscopy in the diagnosis of unexplained exudative pleural effusion. J Cardiovasc Thorac Res. 2013;5(3):87-90.
[18] Karkhanis VS, Joshi JM. Pleural effusion: Diagnosis, treatment, and management. Open Access Emerg Med. 2012;4:31-52.
[19] Chertow BS, Kadzielawa R, Burger AJ. Benign pleural effusions in long-standing diabetes mellitus. Chest. 1991;99(5):1108-11.
[20] Meveychuck A, Osadchy A, Chen B, Shitrit D. Pleural effusion in chronic obstructive pulmonary medicine (COPD) patients in a medical intensive care unit: Characteristics and clinical implications. Harefuah. 2012;151(4):198-201.
[21] Beheshtirouy S, Kakaei F, Mirzaaghazadeh M. Video assisted rigid thoracoscopy in the diagnosis of unexplained exudative pleural effusion. J Cardiovasc Thorac Res. 2013;5(3):87-90.
[22] Light RW. Update on tuberculous pleural effusion. Respirology. 2010;15(3):451-58.
[23] Wang H, Yue J, Yang J, Gao R, Liu J. Clinical diagnostic utility of adenosine deaminase, interferon-γ, interferon-γ-induced protein of 10 kDa, and dipeptidyl peptidase 4 levels in tuberculous pleural effusions. Heart Lung. 2012;41(1):70-75.
[24] Porcel J, Vázquez P, Vives M, Nogués A, Falguera M, Manonelles A. Pleural space infections: Microbiologic and fluid characteristics in 84 patients. Internet J Pulmon Med. 2002;3(1):01-05.

[25] Porcel JM, Esquerda A, Bielsa S. Diagnostic performance of adenosine deaminase activity in pleural fluid: A single-center experience with over 2100 consecutive patients. Eur J Intern Med. 2010;21:419-23.

[26] Shadmehr MB, Arab M, Dezfouli AA, Keshoofi M, Amjadi MR, Farzanegan R, et al. Role of VATS in pleural effusions with unknown etiology. Tanaffos. 2004;3(12):25-33.

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