Outcomes and complications of medical thoracoscopy in undiagnosed exudative pleural effusion

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Background Thoracoscopy has long been established as the procedure of choice for various chest diseases, among which is undiagnosed pleural effusions. Thoracoscopy does not only visualizes the extent of the disease but allows adequate tissue biopsy sampling.

Objective The aim of the present study was to detect outcomes and complications of medical thoracoscopy in undiagnosed pleural effusion.

Patients and methods This study was conducted on 50 patients with unexplained exudative pleural effusion referred for medical thoracoscopy at Abbassia Chest Hospital.

Results Medical thoracoscopy is a safe and valuable tool for the diagnosis of pleural effusion, particularly for patients with suspected malignancy. Overall cost-effectiveness of thoracoscopy is better due to its better yield and lesser duration of hospital stay. Medical thoracoscopy gave a definitive diagnosis with a diagnostic yield of 96%. Histopathological results of thoracoscopic pleural biopsy revealed that the most common diagnosis was malignancy (92%), followed by tuberculous pleurisy (2%), and fibrotic pleurisy (2%); only 4% of the patients remained undiagnosed. The most common malignant pathological type was malignant pleural mesothelioma (60%), followed by metastatic adenocarcinoma (12%). According to the residence of studied patients, we found that environmental exposure to asbestos has a relationship with mesothelioma in patients living in Shoubra El-Kheima and Helwan. Medical thoracoscopy is a safe tool for diagnosing pleural effusion; although no major complications were found in the present study, minor complications occurred only in 10% of the patients.

Conclusion Medical thoracoscopy is a valuable tool in the diagnosis of undiagnosed pleural effusion. It is a simple and safe method with a high diagnostic yield and low complication rates.
Egypt J Bronchol 2016 10:93–99
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Introduction

Pleural effusion is an accumulation of fluid in the pleural space, as a result of excessive transudation or exudation from the pleural surface [1]. The differential diagnosis of pleural diseases is often a lengthy process fraught with pitfalls. When a pleural effusion is diagnosed in a patient, the need for a timely and systematic evaluation is indicated [2]. Thoracoscopy has been the procedure of choice in various chest diseases such as undiagnosed pleural effusions; and recurrent, post-traumatic, or complicated spontaneous pneumothorax; it is also especially indicated for accurate staging of lung cancer with pleural spread and for primary pleural malignancies [3]. Thoracoscopy allows visualization of the pleural cavity, including the diaphragmatic, visceral pleura, and the lung. The procedure not only gives information on the extent of the disease itself but also allows adequate tissue biopsy sampling, which helps in distinguishing between viable tumors and other lesions such as fibrotic reaction [4]. The aim of this study was to detect outcomes and complications of medical thoracoscopy in undiagnosed exudative pleural effusion at Abbassia Chest Hospital.

Patients and methods

The present prospective study included 50 patients with undiagnosed exudative pleural effusion who presented to Abbassia Chest Hospital in the period from October 2013 to May 2014. The study was conducted in the Endoscopy Unit of the Respiratory Critical Care Unit in Abbassia Chest Hospital. The study was approved by the Institutional Review Board of the chest department, Ain Shams University.

Study design
Inclusion criteria
Patients were eligible when they presented with a pleural effusion and/or thickening and had at least one nonconclusive diagnostic procedure (e.g. thoracocentesis, closed pleural biopsy).

Exclusion criteria
General contraindications to thoracoscopy – for example, unstable angina, left ventricular failure, uncontrolled hypertension, bleeding tendency, etc.

(1) Lack of fitness for general anesthesia for any possibility of shift from local to general anesthesia due to any cause (fitness for general anesthesia was decided by the anesthesiologist).
(2) All patients were subjected to the following.

Full medical history-taking and clinical examination; laboratory investigations including complete blood picture, liver and kidney functions, and bleeding profile (prothrombin time and concentration); radiological examination including plain chest radiography posteroanterior view, chest ultrasound (lateral view), and computed tomography (CT) scan of the chest; in addition, thoracocentesis was carried for all patients, and the aspirated pleural fluid was sent for full chemical and cytological examination; thoracoscopic examination of the pleural space was carried out using the Richard-Wolf rigid thoracoscopy.

Medical thoracoscopy
Prethoracoscopic assessment
Patients were assessed for fitness to the procedure (it was done under local anesthesia for all patients). The procedure was explained to each patient and an informed written consent was obtained from all patients.

Thoracoscopy procedure
Pleural tapping was carried out 1 day before the thoracoscopic procedure to improve lung function. Local infiltration anesthesia, using 15 ml of 2% lidocaine, was administered to all 50 patients. The patient was placed in lateral decubitus position with the affected side upwards. Skin was sterilized, followed by blunt dissection to enter the pleural space, usually between the fourth and the fifth intercostal space along the midaxillary line. The trocar of the thoracoscope was then inserted along the skin incision and then into the pleural space (the single entry technique was used). A catheter connected to a suction apparatus was used for draining the fluid present in the pleural space, with special attention not to touch the pleural surfaces to avoid trauma. This was followed by induction of an ipsilateral pneumothorax. The pleural space (parietal, visceral, and diaphragmatic) was inspected by white light using rigid thoracoscope with a xenon light source, which satisfied high-quality visual exposure; suspicious lesions were identified and located. Abnormal (suspicious) areas seen were biopsied. All biopsies were taken under direct visual control and

tissues were collected in 4% formalin solution for staining with hematoxylin and eosin for histopathological examination. Finally, at the end of the procedure, an intercostal tube under-water seal was then inserted before wound closure to evacuate air and residual fluid.

Post-thoracoscopy assessment
Chest radiography was obtained after the procedure and then daily until total lung inflation and fluid drainage. When daily fluid drainage reached a level less than or equal to 150 ml, chemical pleurodesis using sclerosing agents was carried out for proven malignant cases, and then finally the chest tube was removed.

Data analysis
All analysis was carried out using the statistical package for the social science software, version 15 for Windows (SPSS Inc., Chicago, Illinois, USA); data were described as frequency and percentage for qualitative data, and as mean±SD for quantitative data. The χ^2-test was also used. A P value less than or equal to 0.05 was considered significant.

Results
The study included 50 patients (32 men and 18 women); their mean age was 54.22±9.84 years; at the time of the study, 23 out of the 50 (46%) patients were living in Shoubra El-Kheima and 11 (22%) were living in Helwan, whereas eight (16%) were living in Cairo and the remaining eight (16%) in other areas. As regards the occupation, 16 (32%) patients were housewives and 11 (22%) patients were factory workers. Regarding special habits, 25 (50%) patients were active smokers; 15 (30%) patients had other comorbidities such as diabetes mellitus, hypertension, and ischemic heart disease (Table 1).

As regards the radiographic diagnostic studies, the site of the pathology, the amount of effusion, the ultrasonographic and CT findings were variable and some patients were expected to have more than one finding such as pleural thickening and lymphadenopathy (Table 2).

Analysis of aspirated pleural effusion fluids revealed that the mean pleural protein was 4.38±0.85, the mean pleural glucose was 75.2±59.06, and the mean pleural lactate dehydrogenases was 733.08±306.68 (Table 3). The most common cytology finding was atypical mesothelial cells in 31 (62%) patients, followed by lymphocytes in seven (14%) patients (Table 4).

Table 1 Descriptive data of the studied patients

	Number of cases (%)
Occupation	
Housewife	16 (32)
Factory worker	11 (22)
Others	9 (18)
Employee	8 (16)
Office work	4 (8)
Driver	2 (4)
Special habits	
Smoking	25 (50)
Cigarette	14 (28)
Cigarette and shisha	10 (20)
Shisha	1 (2)
Comorbidities	15 (30)

Table 2 Radiographic findings

	N=50 [n (%)]
Site	
Right	36 (72)
Left	14 (28)
Amount	
Massive	42 (84)
Moderate	8 (16)
US findings	
Pleural thickening	15 (30)
CT findings	
Pleural thickening	7 (14)
Lymphadenopathy	13 (26)
Pleural thickening and lymphadenopathy	5 (10)

CT, computed tomography; US, ultrasound.

Table 3 Chemical analysis of aspirated pleural effusion

	Range	Mean±SD	Exudative range
Protein	3.1–6.4	4.38±0.85	<3 mg/dl
Glucose	10–300	75.22±59.06	>60 mg/dl
LDH	222–1475	733.08±306.68	<1000 IU/l

LDH, lactate dehydrogenase.

Table 4 Cytology of the pleural fluid

Cytology	Number of cases (%)
Atypical mesothelial cells	31 (62)
Lymphocytes	7 (14)
Mesothelial cells	3 (6)
Atypical cells and lymphocytes	9 (18)

Thoracoscopic findings were different as nodules, adhesions, congestion, and greyish white membrane. The most common finding was pleural nodules in 31 (62%) patients (Table 5).

The most common diagnosis of pleural diseases was malignant mesothelioma (epithelial type) in 30 (60%) patients, followed by metastatic carcinoma in six (12%) patients. As regards other nonmalignant diagnosis, tuberculous pleurisy was found in one patient (2%), fibrotic pleurisy in one patient (2%), and two other cases (4%) remained undiagnosed (Table 6).

Overall, 90% of the patients had no complications with and after medical thoracoscopy; only five patients (10%) had minor complications: two patients (4%) had infection (cellulitis) at the drain site, two patients (4%) had surgical emphysema, and the remaining one patient (2%) had bronchopleural fistula (Table 7).

The range of the total duration of patient hospital stay was 7–39 days, with a mean of 17.56±5.459 days (Table 8).

After thoracoscopy and final diagnosis, 44 (88%) patients had pleurodesis, and were referred to the Oncology Center; three patients (6%) received medical treatment (anti-inflammatory), one patient (2%) received antituberculous treatment, and two patients (4%) died (Table 9).

Discussion

Pleural effusion is defined as an accumulation of fluid in the pleural space in an excess of 15–20 ml. The etiology for the development of a pleural effusion includes changes in the hydrostatic or colloid-osmotic pressure of the pleural and pulmonary capillaries, changes in pleural vascular permeability, and impaired lymphatic drainage [5]. Pleural effusion is a common presentation in clinical practice and can be caused by a large variety of malignant or benign causes [6]. Investigations of a pleural effusion evident on chest radiographs should follow a stepwise approach to diagnosis. Diagnosis begins with the clinical history-taking, physical examination, and chest radiography, and is followed by thoracentesis when appropriate [7]. In the case of a proven exudate with nonconclusive cytology after (repeated) thoracocentesis, an additional procedure to obtain pleural histology tissue should be the next step. This can be carried out with a minimal invasive procedure in four ways: closed pleural biopsy (abrams biopsy), thoracoscopy, ultrasound-guided biopsy, and CT-guided biopsy [8]. Thoracoscopy is a safe and valuable tool for the diagnosis of undiagnosed pleural effusion, particularly for patients with high probability of malignancy. Overall cost-effectiveness of thoracoscopy is better in view of its better yield and lesser duration of hospital stay [5]. In this prospective study, an effort was made to detect outcomes and complications of medical thoracoscopy during the diagnosis of exudative pleural

Table 5 Thoracoscopic findings of the studied cases

	Number of cases (%)
Nodules	31 (62)
Adhesions	1 (2)
Greyish white membrane	1 (2)
Nodules and congested pleura	6 (12)
Nodules and adhesions	7 (14)
Nodules and congested pleura and adhesions	2 (4)

Table 7 Illustration of complicated cases.

	Number of cases (%)
Complications	5 (10)
Infection (cellulitis) at drain site	2 (4)
Surgical emphysema	2 (4)
Bronchopleural fistula	1 (2)

Table 6 Final diagnosis

	Number of cases (%)
Malignant mesothelioma epithelial type	30 (60)
Malignant mesothelioma biphasic type	5 (10)
Metastatic carcinoma	6 (12)
Malignant mesothelioma epithelial type versus metastatic adenocarcinoma	4 (8)
Atypical lymphoid proliferative angiofollicular hyperplasia (Castleman's disease)	1 (2)
Undiagnosed	2 (4)
Tuberculous pleurisy	1 (2)
Fibrotic pleurisy	1 (2)

effusions of unidentified etiology at Abbassia Chest Hospital. The present study included 50 patients, all of whom had pleural effusion that had not been diagnosed after history-taking, general or local examination, and investigations including thoracocentesis with physical, chemical, bacteriological, and cytological examination of the pleural fluid. In the current study, medical thoracoscopy gave a definitive diagnosis in 50 out of 50 patients with a diagnostic yield of 100%. This is in agreement with a prospective study by Mohamed and Shaban [9], which was conducted on 117 patients with undiagnosed exudative pleural effusions admitted to the Chest Department of the Faculty of Medicine, Cairo University, during the period from January 2012 to December 2012. Medical thoracoscopy gave a definitive diagnosis in 117 out of 117 patients with a diagnostic yield of 100%. In addition, our results were in agreement with a study by Helala et al. [10], which was conducted in Kobri El-Kobba Military Chest Hospital on 40 patients with undiagnosed exudative pleural effusions during the period from March 2010 and October 2012; medical thoracoscopy, in this study, gave a definitive diagnosis in 38 out of 40 patients with a diagnostic yield of 95%. Furthermore, our study was in agreement with a study by Prabhu and Narasimhan [11], who performed thoracoscopy for 68 patients at the Department of Respiratory Medicine, Apollo Hospitals, Chennai, India, which gave a definitive diagnosis in 66 out of 68 patients and was nondiagnostic in two patients, with a diagnostic yield of 97%. In their study, Guo and colleagues obtained similar results; they performed thoracoscopy for 47 patients with pleural effusion and thickening of unknown etiology. The diagnosis was obtained for 44 patients, whereas

negative result was obtained for three (6.4%) cases. The diagnostic accuracy rate reached 93.6% [12]. In contrast to our results, Thangakunam and Christopher in their study, conducted in the Department of Pulmonary Medicine, Christian Medical College and Hospital, Vellore, India, performed thoracoscopy on 21 patients. The thoracoscopic biopsy was positive for 12 out of 18 patients (66.7%) [13]. In addition, a study by Zhang et al. [14], conducted in the Department of Internal Medicine, Kulliyyah of Medicine, International Islamic University Malaysia, achieved diagnosis with thoracoscopic pleural biopsy in only 45.5% (10/22) of the included patients with undiagnosed pleural effusions. In the current study, the histopathological results of thoracoscopic pleural biopsy among the study population revealed that the most common diagnosis was malignancy in 46 patients (92%), followed by chronic nonspecific pleurisy in two patients (4%), then tuberculous pleurisy in one patient (2%) and fibrotic pleurisy in one patient (2%). This is in agreement with a study by Mohamed and Shaban [9], who found that the most common diagnosis was malignancy in 87/117 patients (74.3%), followed by chronic nonspecific pleurisy in 16/117 patients (13.6%), tuberculous pleurisy in five patients (4.27%), septic empyema in six patients (5.13%), sarcoidosis in two patients (1.7%), and systemic lupus erythematosus in one patient (0.85%). In the current study, the most common pathological malignant type was malignant pleural mesothelioma (MPM) (epithelial type) in 30 patients (60%), followed by metastatic adenocarcinoma in six patients (12%). The results were in agreement with a study by Helala et al. [10], which revealed that the most common pathological type was MPM in 15/28 patients (53.6%), followed by metastatic adenocarcinoma in 10/28 patients (in 35.6%). In addition, a study by Mohamed and Shaban [9] revealed that the most common pathological type was MPM in 55/117 patients (47.01%), followed by metastatic adenocarcinoma in 26/117 patients

Table 8 Duration of patient hospital stay

	Range (days)	Mean±SD
Time lag from admission date till thoracoscopy date	2–19	9.24±3.695
Chest tube duration after thoracoscope	5–27	8.6±3.33
Total duration of hospital stay	7–39	17.56±5.459

Data are presented as range and mean±SD.

(22.2%). Similar results were obtained in a study by Abdollah and collaegues. They carried out medical thoracoscopy for 30 patients. The most common diagnosis was malignancy, which was found in 17 patients (56.67%), eight of whom (47.06%) were diagnosed with MPM [15]. In contrast, in their study, Prabhu and Narasimhan carried out medical thoracoscopy for 68 patients at the Department of Respiratory Medicine, Apollo Hospitals, Chennai, India, and 24/68 (35.2%) of the patients were diagnosed with malignant pleural effusion. In 24 patients who had malignancy, mesothelioma was diagnosed only in 3/24 patients (12.5%). The most common diagnosis was metastatic adenocarcinoma, which was found in 15/24 patients (62.5%) [11]. In the current study, according to the residence of the studied patients, we found the majority of the patients [23/50 (46%)] living in Shoubra El-Kheima and 11/50 (22%) living in Helwan. In total, 27 out of these 34 patients (68%) were diagnosed with malignant mesothelioma, and 2/34 (5.8%) with metastatic adenocarcinoma. It means that environmental exposure to asbestos has a relationship with mesothelioma in patients working or living in the neighborhood with asbestos factories. This is supported by the study conducted by Ibrahim and colleagues in Kasr Al Aini Center of Radiation Oncology and Nuclear Medicine, Kasr Al Aini School of Medicine, Cairo University. It included retrospective cases of malignant mesothelioma presenting to the Palliative Care Unit from January 2009 to December 2011. They were diagnosed in the period between June 2005 and July 2011,which releaved 15 cases (37.5%) of mesothelioma from Shoubra and eight cases (20%) from Helwan [16]. In their study, Mehta and colleagues in 2009 found that these factories affect an area of 5–7 km in radius, which explains the high incidence of mesothelioma in the neighborhood of these factories. Workers employed since 1948 by the Egyptian asbestos company Sigwart at the mills in greater Cairo (El-Maasara and Shubra El-Kheima) had an increased risk for mesothelioma. The ministerial council decided to ban asbestos imports in 2004 and the Sigwart plants were closed in November 2004. Therefore, it has been estimated that the incidence of mesothelioma in Egypt will reach its peak around 2040

Table 9 Patient fate after thoracoscopy and final diagnosis

	Number of cases (%)
Oncology center	44 (88)
Medical treatment (anti-inflammatory)	3 (6)
Antituberculous treatment	1 (2)
Died	2 (4)

[17]. A study by Mahmoud declared that mesothelioma in Egypt is mainly attributed to an environmental origin – that is, exposure to asbestos – with a high incidence in women and young adults. Epidemiological data of 635 patients with malignant mesothelioma over 4 years were collected from the National Cancer Institute, Cairo University, and Abbassia Chest Hospital. This number is more than four times the number of patients that were diagnosed in the previous 11 years at the National Cancer Institute [18]. In the current study, 31/50 (62%) patients showed atypical mesothelial cells, and were proved to be malignant pleural disease with characteristic nodules in pleura, such as thoracoscopic findings. On the other hand, a study by Mohamed and Shaban reported only five patients to be positive for malignant cells in pleural fluid cytological analysis, and then proved by thoracoscopic pleural biopsy to be MPM, and only seven patients showed atypical mesothelial cells, which were then proved to be MPM (six cases) and tuberculous pleurisy (one case). The remaining 105 patients showed exudative effusion with no evidence of malignant cells in the pleural fluid cytological analysis [9]. As regards the non-neoplastic results of this study, two patients were diagnosed with chronic nonspecific pleurisy, one patient with fibrotic pleurisy and only one patient who had the thoracoscopic findings suggestive of tuberculosis. Although tuberculous pleural effusion is common, the small number of patients diagnosed by using this procedure suggests that it is diagnosed in the majority without thoracoscopy [19]. In the current study, we found no post-thoracoscopic complications in 45/50 patients (90%), whereas minor complications occurred only in 5/50 patients (10%); 2/50 patients (4%) developed surgical emphysema (the two patients were diagnosed with MPM, and died after 2 days), 2/50 patients (4%) developed cellulitis (drain site), which was transient and controlled, and 1/50 patient (2%) developed

bronchopleural fistula. The results were in agreement with that of a study by Prabhu and Narasimhan [11], who reported no major complications out of 68 patients; only 4/68 patients (5.8%) had minor complications, like subcutaneous emphysema in 3/68 patients (4.4%) and prolonged air leak in 1/68 (1.4%) patient. In addition, our results were in agreement with those of a study by Mootha and colleagues [20], who, working in the Department of Pulmonary Medicine, the Postgraduate Institute of Medical Education and Research, Chandigarh, India, reported that out of 35 thoracoscopic procedures, only two patients (5.2%) developed empyema; no other complication was recorded in their study. In addition, our results were in agreement with that of a prospective study by Galbis et al. [21], which was conducted on 110 patients undergoing thoracoscopy in General University Hospital of Valencia and reported complications in 15/110 patients (13.6%). In the current study, surgical emphysema as a complication of medical thoracoscopy occurred only in 2/50 cases (4%). This is in agreement with a study by Gao et al. [22], which was conducted the Three Gorges University and Yichang Central People's Hospital, Yichang, China, and included 215 patients with undiagnosed pleural effusions who underwent medical thoracoscopy. They reported that surgical emphysema occurred in 10 cases (4.6%) postoperatively. Our results were also in agreement with that of a retrospective study by Wang and colleagues [23], which was conducted in Capital Medical University, Beijing, China on 50 patients with undiagnosed pleural effusions; 27 of them underwent medical thoracoscopy; surgical emphysema was detected in 1/27 cases (3.7%) and there were two cases of postoperative fever, which was self-limiting. In contrast to our results, Brims et al. [24], who conducted a retrospective study in Portsmouth Hospitals, UK, over a 12-month period on 57 patients undergoing thoracoscopy for unexplained exudative pleural effusion, reported a high percent of complications for 23 patients (40.3%): the most common complications included trapped lung in 10/57 patients (17.5%), cellulitis (drain site) in 4/57 patients (7%), surgical emphysema in 3/57 patients (5.3%), pneumonia in 4/57 patients (7%), and empyema in 2/57(3.5%). In the current study, we found that the time lag from admission date till the date on which thoracoscopy was carried out ranged from 2 to 19 days, with a mean of 9.24±3.96 days; during this time all diagnostic tools performed to patient started with the clinical history, physical examination, and chest radiography and is followed by thoracentesis, and undiagnosed patients underwent medical thoracoscopy. Chest tube duration range was 5–27 days, with a mean of 8.6±3.33 days; the total time of hospital stay was 7–39 days, with a mean of 17.56±5.4 days; patients experiencing complications led to a prolonged hospital stay. This is in agreement with a study done by Brims et al. [24], who had found six cases with a patient stay longer than 2 weeks. Five of them were malignant and three had a trapped lung. Four of the six had hospital acquired infections, two had pneumonia, two empyemas, and the remaining two both had an acute renal failure.

In conclusion, medical thoracoscopy is a valuable tool in the diagnosis of undiagnosed pleural effusion. It is a simple and safe method with a high diagnostic yield and low complication rates. Due to its high diagnostic yield the future of it is very bright.

Recommendations
It is advised to use medical thoracoscopy as early as possible after a failure of initial investigations to diagnose the causes of pleural effusion.

(1) Patients with radiological findings suspicious for pleural malignancy (e.g. nodularity, focal thickening) are preferably evaluated with medical thoracoscopy.
(2) It is highly recommended for pulmonologists to be well trained for using medical thoracoscopy to solve medical problems previously difficult to be solved.
(3) Further prospective multicenter studies on larger population are required to achieve a more objective assessment of the value and feasibility of medical thoracoscopy.
(4) There is a necessity of more strict application of laws prohibiting the use of asbestos and other hazardous materials in the industry.
(5) Factories dealing with hazardous occupational elements should be established very far away from residential areas.

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