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ORIGINAL RESEARCH

DILEMMA OF UNDIAGNOSED PLEURAL EFFUSION UNRAVELED THROUGH THORACOSCOPY: A SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

[1]Dr. Shumail Bashir, [2]Dr Syed Mehvish, [3]Dr. Faisal R Guru, [4]Dr. Naveed Nazir Shah, [5]Dr Haider Guru, [6]Dr Jibran Bashir, [7]Dr Khurshid Ahmad Dar

[1]Assistant Professor, Department of TB and Chest Medicine, Government Medical College, Baramulla, India
[2]Senior Resident, Government Medical College, Srinagar, Jammu and Kashmir, India
[3]Assistant Professor, Department Of Paediatric Oncology, Sher I Kashmir Institute Of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India
[4]Prof. & Head, [7]Associate Professor, Department of TB and Chest Medicine, Chest Disease Hospital, Srinagar, Jammu and Kashmir, India
[5]DM Cardiology, [6]Senior Resident, Sher I Kashmir Institute Of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

Correspondence:
Dr. Faisal R Guru
Assistant Professor, Department Of Paediatric Oncology, Sher I Kashmir Institute Of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

Abstract

Background: Recurrent and persistent pleural exudates are common in clinical practice, and in a large number of patients, thoracocentesis and blind pleural biopsy procedures do not provide a definitive diagnosis. In the Western world, the majority of these exudates are malignant. Thoracoscopy today remains the gold standard technique in providing diagnosis and management in these cases.

Objectives: Diagnostic yield of medical thoracoscopy was evaluated in cases of undiagnosed pleural effusion

Materials and methods: Rigid medical thoracoscopy was performed in 40 patients having undiagnosed pleural effusion at the Chest Disease Hospital, Srinagar, J&K India .

Results: Medical thoracoscopy gave a definitive diagnosis in 38 out of 40 patients with diagnostic yield 95%. Malignancy was diagnosed in 28 patients (70%), one patient was diagnosed as empyema (2.5%), tuberculosis was found in 9 patients (22.5%), and it was non diagnostic in 2 patients (5%). The post-thoracoscopic complications in the studied group have occurred only in 4 patients (10%).

Conclusion: Medical thoracoscopy is a valuable tool in the diagnosis of undiagnosed exudative pleural effusion. It is a simple and safe method with high diagnostic yield and with low complication

Keywords: Pleural effusion, Thoracoscopy, malignancy

Introduction

The use of thoracoscopy for the diagnosis of pleural effusions was first described in 1910 by an internist from Stockholm called Hans-Christian Jacobaeus.[1] In 1925 Jacobaeus then reported the use of rigid urology forceps to diagnose pleural tumour[2] since then little has changed with the techniques applied. Undiagnosed pleural effusions remain a diagnostic

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challenge for pulmonologists. In a patient with an undiagnosed pleural effusion, the first question to answer is whether the fluid is an exudate or a transudate .[3] Investigation of a pleural effusion evident on chest radiographs should follow a stepwise approach to diagnosis. Diagnosis begins with the clinical history, physical examination, and chest radiography and is followed by thoracentesis when appropriate.[4] 'Medical' thoracoscopy can be performed by physicians under conscious sedation with local anesthetic in an endoscopy suite, and as a result is less invasive and less expensive.[5]

Recurrent and persistent pleural exudates are common in clinical practice, and in a large number of patients, thoracocentesis and blind pleural biopsy procedures do not provide a definitive diagnosis. In the Western world, the majority of these exudates are malignant. Thoracoscopy today remains the gold standard technique in providing diagnosis and management in these cases.[6] Thoracoscopy is a minimally invasive procedure that allows visualization of the pleural space and intrathoracic structures. It enables the taking of pleural biopsies under direct vision, therapeutic drainage of effusions and pleurodesis in one sitting.[7] Pleural effusion of unknown origin remains the commonest indication of pleuroscopy and is considered to be one of the techniques with the highest diagnostic yield in ''aspiration cytology negative exudative effusions'' from the recent British Guidelines, with an efficacy almost comparable to video assisted thoracoscopic surgery (VATS).[8] Medical thoracoscopy should be considered in patients with undiagnosed pleural effusions, particularly those lymphocytic exudative effusions where TB and malignant pleural effusion are clinical possibilities and initial pleural fluid analysis is inconclusive.[9]

Thoracoscopy is the gold standard for the diagnosis and treatment of pleural diseases. Its diagnostic yield is 95% in patients with malignant pleural disease, with approximately 90% successful pleurodesis for malignant pleural effusion and 95% for pneumothorax.[10] In patients with suspected tuberculous pleurisy, thoracoscopic pleural biopsy under local anesthesia should be actively performed, because the technique has a high diagnostic rate, and can be easily and safely performed.[11] The semirigid thoracoscope achieves a diagnostic yield similar to that of the conventional rigid instrument despite the smaller biopsy size. Both instruments remain valuable in the evaluation and management of pleural disease.[12] The aim of this study was to detect the diagnostic yield of medical thoracoscopy in the diagnosis of cases of exudative pleural effusions of unidentified etiology.

Materials & Methods

This is a hospital-based observational study conducted from January 2015 to January 2016 at the department of Chest medicine at Chest Disease Hospital,Srinagar. Jammu and Kashmir. Forty patients with undiagnosed exudative pleural effusion after being evaluated by thoracocentesis were selected from those attending the department of Chest medicine at our hospital. However the patients with transudative pleural effusion, according to Light's criteria, patients whose initial pleural fluid examination through thoracocentesis could reach a definitive histopathological diagnosis, patients who are not fit for performing thoracoscopy as in the following cases like severe uncorrected hypoxemia despite continuous oxygen administration, unstable cardiovascular or haemodynamic status,coagulation defects were excluded.

Also patients with absolute contraindications as in the following conditions:

Patients in whom the pleural space was judged to be inaccessible easily, those who had their pleural space obliterated by fibrous tissue or those who were suspected of having multiloculated effusions, patients with very thickened pleural as demonstrated by CT scanning as it would impair the expansion of the underlying lung following the procedure, patients with honey comb lung, pulmonary arteriovenous aneurysms, suspected hydatid cysts and highly vascularized pulmonary lesions were also excluded.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

A thorough history and clinical examination was done all the patients.The following investigations were were done in all the patients. Full routine laboratory investigations: Complete blood picture, liver and kidney functions and bleeding profile. (Prothrombin time and concentration). Sputum smears examinations for the presence of Acid-Fast Bacilli (AFB) on two successive days. Tuberculin skin testing using five tuberculin units (TU) injected intradermally and interpreted after 48–72 h. Radiological examination, through plain chest Xray postero-anterior and lateral views, as well as CT scanning of the chest.

Thoracocentesis: Pleural fluid aspirated from the patient was sent for full chemical, bacteriological and cytological examination. Thoracoscopic examination of the pleural space using a rigid thoracoscopy. Technique: one punctures technique was the method used in the present study. A 2 cm stab incision was made, digital palpation determined the presence of adhesions and bleeders from the wound were checked. If none was present an 11 mm trocar was inserted through which a 10 mm Karl Storz rigid telescope was inserted avoiding uncontrolled deep penetration. Then evacuation of the entire fluid collection and ipsilateral pneumothorax was induced. Introduction of the telescope was done to explore the entire pleural cavity, rigid telescope allows visualization of remote or concealed lesions. Examination of the pleural cavity was done systematically starting at the apex and then the costal pleura, diaphragm and finally the mediastinal pleura, ending back at the apex. After that, biopsies were taken from suspicious areas over costal and diaphragmatic parietal pleura and this was typically performed under direct vision. Biopsies were be placed in formalin for histopathology. Pleurodesis was done in the same sitting with talc poudrage for cases where nodular lesions were seen and suspicion of malignancy was very high. At the end of the procedure, a chest tube was introduced and connected to underwater seal drainage. A plain CXR was done to confirm the tube position and correct drain function.

Results

The study was conducted on 40 patients with undiagnosed pleural effusion after not being diagnosed by aspiration. The study included 28 males and 12 females with mean age of 51.3 ± 16.3 years. (Table 1)

Table 1: Socio-demographic distribution of the studied group.

Age	**Range 20–72**	**Mean ± SD 51.3 ± 16.3**
	Number	**%**
Sex		
Male	28	70
Females	12	30
Occupation		
Shop Keepers	20	50
Driver	2	5
Employee	2	5
Engineer	1	2.5
Housewife	11	27.5
Office work	2	5
Student	1	2.5

Pleural fluid examination for malignant cells yielded positive results in only 3 patients (7.5%). (Table 2)

Table 2: Pleural fluid examination for malignant cells in the studied group.

	Number	**%**
Malignant cells		

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

Positive	3	Positive 3(7.5%)
Negative	37	Negative 37(92.5%)

Medical thoracoscopy gave the final histopathological diagnosis in 38 patients from total 40 patients with diagnostic yield 95%. There was only 2 patients undiagnosed (5%). (Table 3)

Table 3: Diagnostic yield of the medical thoracoscopy in the studied group.

	Number	%
Diagnosed	38	95%
Undiagnosed	2	5%

The findings on gross observations were nodule in twenty eight (70%) patients,sago grain nodule in five (12.5%), pus, mass were found in one patient each (2.5%) and there were no specific findings in only one patient (2.5%).(Table 4)

Table 4: Gross thoracoscopic findings in the studied group.

Thoracoscopic Finding	Number	%
Non Specific	1	2.5
Nodule	28	70
Sago-Grain nodule	5	12.5
Adhesion	3	7.5
Collection of pus	1	2.5
Mass	1	2.5
Violaceous lesion	1	2.5

Twenty-eight patients (70%) were malignant, 9 patients (22.5%) were tuberculous, 1 patient (2.5%) was diagnosed as empyema and there were 2 patients (5%) who were not diagnosed.(Table 5)

Table 5: The histopathological results obtained by thoracoscopic pleural biopsy in the studied group.

	Number	%
Histopathology		
Empyema	1	2.5
Malignancy	28	70
Tuberculosis	9	22.5
No definite lesion	2	5

The most common type of malignancy obtained by thoracoscopic pleural biopsy in the studied group was malignant mesothelioma which was found in 15 patients (53.6%). (Table 6)

Table 6: Histopathological types of malignancy in the studied group.

	Number	%
Histopathology type(n=28)		
Malignant mesothelioma	15	53.6
Metastatic adenocarcinoma	10	35.6
Muco-epidermoid carcinoma	2	7.2
Non Hodgkin lymphoma	1	3.6

92.9% of patients with nodules were malignant, while only 3.6% were non-malignant and this difference was statistically highly significant. 100% of patients with sago grain nodules were non-malignant (all diagnosed as tuberculous pleural effusion), it was of high statistical

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significance. Also 100% of patients with adhesions were non-malignant. It was statistically significant (Table 7).

Table 7: Distribution of the diagnosed patients in the studied group in relation to the thoracoscopic findings.

	Malignant (n = 28)	Non malignant (n = 10)	P
Nodule(s)	26(92.9%)	1(3.6%)	0.001
Sago Grain Nodule	0	5(100%)	0.005
Adhesions	0	3(100%)	0.001
Collection of pus	0	1(100%)	0.5
Mass	1(100%)	0	0.5
Violaceus lesion	1(100%)	0	0.5

The post thoracoscopic complications in the studied group occurred in only 4 patients (10%). The complications were surgical emphysema in one patient (2.5%), while the remaining 3 patients (7.5%) experienced pain which was shortly controlled by analgesia (Table 8).

Table 8: Post-thoracoscopic complications in the studied group.

	Number	%
Complications		
Surgical emphysema	1	2.5
Pain	3	7.5
No complications	36	90

The average number of days for which the intercostal tube was in situ was 3 and majority of patients were discharged by day 5.

Discussion

Pleural effusion is a common presentation in clinical practice and can be caused by a large variety of malignant or benign causes .[13] Investigation of a pleural effusion evident on chest radiographs should follow a stepwise approach to diagnosis. Diagnosis begins with the clinical history, physical examination, and chest radiography and is followed by thoracentesis when appropriate. In the case of a proven exudate with inconclusive cytology after (repeated) thoracocentesis, an additional procedure to obtain pleural histology tissue is the next step. This can be done with a minimal invasive procedure in four ways: closed pleural biopsy (CPB; Abrams biopsy), thoracoscopy, ultrasound (US)-guided biopsy, and computed tomography (CT)- guided biopsy.[14] Thoracoscopy is a safe and valuable tool for 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.[15] The aim of this study was to evaluate the diagnostic yield of medical thoracoscopy in cases of undiagnosed exudative pleural effusion. The study included forty patients with undiagnosed exudative pleural effusion after being not diagnosed by thoracocentesis .It included 28 males and 12 females with mean age of 51.3 ± 16.3 years. In the current study medical thoracoscopy gave a definitive diagnosis in 38 out of 40 patients with diagnostic yield 95%. Malignancy was diagnosed in 28 patients (70%), one patient was diagnosed as empyema (2.5%), tuberculosis was found in 9 patients (22.5%), and it was non diagnostic in 2 patients (5%). A compelling support to the present study was given by Prabhu and Narasimhan (2012)[16] who performed pleuroscopy in a total of 68 patients (55 males and 13 females; mean age 49 years), malignancy was diagnosed in 24 patients, 22 patients had non-specific inflammation, tuberculosis was found in 16 patients, empyema was found in 2 patients, one patient had sarcoidosis, one patient had normal pleura and it was non-diagnostic in 2 patients. The diagnostic yield was 97%. Huang et al. (2011)[17], performed flexi rigid thoracoscopy in forty-seven patients with pleural effusion and thickening of unknown

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etiology. Diagnosis was obtained in 44 patients while negative result was found in 3 (6.4%) of the cases. The diagnostic accuracy rate of flexi rigid thoracoscopy reached 93.6%. Also, Ng et al. (2008)[18] could achieve diagnosis with thoracoscopic pleural biopsy in only 45.5% (10/22) patients with undiagnosed pleural effusions. This low diagnostic yield compared with other studies may be due to insufficient pleural biopsy samples.

The increased diagnostic yield of medical thoracoscopy is explainable by the improved visualization and larger biopsy sample size attained during the procedure. In the current study cytological examination of pleural fluid yielded malignant cells in only three patients (7.5%) out of forty with no definite histopathological diagnosis. Two of them were diagnosed as metastatic adenocarcinoma & the other was malignant pleural mesothelioma (after doing the thoracoscopic pleural biopsy). The diagnostic yield for malignancy of pleural cytology is in the order of 55–60% (Loddenkemper and Boutin, 1993).[19] Cytological examination of pleural fluid is only diagnostic in less than 20% in patients with mesothelioma (Colt, 1999).[20] In the current study malignancy was diagnosed in 28 patients (70%), Malignant pleural mesothelioma was diagnosed in 15 patients (53.6%), while metastatic pleural malignancy was found in 13 patients. Metastatic adenocarcinoma was found in 10 patients (35.6%), Non-Hodgkin lymphoma was found in one patient (3.6%), Mucoepidermoid carcinoma was found in two patients (7.2).This finding is in accordance with Huang et al. (2011)[17], who performed flexi rigid thoracoscopy in Forty-seven patients with pleural effusion and thickening of unknown etiology and found that the most common diagnosis was malignancy. It was confirmed in 21 patients (44.7%), followed by tuberculosis in 17 (36.2%), idiopathic hypereosinophilic syndrome in one patient (2.1%), nocardiosis in one patient (2.1%), constrictive pericarditis in one patient (2.1%), chronic empyema in 2 (4.3%), and uusplenic artery embolization in one patient (2.1%). In the current study the most common pathological type of malignancy was the malignant pleural mesothelioma which was found in 15 patients (53.6%), this finding matches the results of Abdollah et al. (2010)[21], who performed medical thoracoscopy for 30 patients. The most common diagnosis was malignancy which was found in 17 patients (56.67%) and 8 of them (47.06%) were diagnosed as malignant pleural mesothelioma. The results of our study contradict the results of Prabhu and Narasimhan (2012),[16] who performed medical thoracoscopy for 68 patients and among which 24 of them were diagnosed as malignant pleural effusion. In 24 patients who had malignancy, mesothelioma was diagnosed only in three patients. The most common diagnosis was metastatic adenocarcinoma which was found in 15 patients. In the current study Tuberculosis is proved to be the cause of pleural effusion in 9 patients (22.5%) from the totally studied 40 patients. Seven of them were males while the other 2 patients were females. Cytological examination of the pleural fluid revealed predominant lymphocytes but negative for smear examination for AFB. Koegelenberg and Diacon (2007)[22], reported that Microscopy reveals inflammatory cells with lymphocytic predominance. Polymorphonuclear cells may predominate in very early exudates .The presence of >5% mesothelial cells is unusual in TB pleuritis. Microscopy and culture are often negative due to the paucibacillary nature of the disease. Regarding the thoracoscopic findings in the studied group, nodules were found in 28 patients (77%), 5 patients(12.5%) had sago grain nodules, 3 patients (7.5%) had adhesions, one patient had collection of pus, one patient (2.5%) had a mass, one patient (2.5%) had Violaceous lesion, and one patient (2.5%) had normal pleura. When these findings were compared with the final histopathological diagnosis, it was found that 92.9% of patients who had nodules had malignant pleural effusion, 100% of patients who had sago grain nodules had tuberculous pleural effusion, and 100% of patients who had adhesion had non-malignant lesion. A compelling support to the present study was given by Prabhu and Narasimhan (2012)[16] who performed pleuroscopy in a total of 68 patients (55 males and 13 females; mean age 49 years), nodules were found in 33 patients, 26 patients had adhesions, 8 patients had

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sago grain appearance, and one patient had normal pleura. They reported that, the direct visualization of the pleural surfaces had an advantage in arriving diagnosis. When the pleuroscopic findings were compared with the final histopathological examination reports, it was found that >70% of patients who had nodules had malignant lesion, >96% of patients who had adhesion had chronic or sub-acute inflammation (non-malignant lesion) and 100% of patients who had sago grain nodules had tuberculosis. Serious complications following thoracoscopy are rare.[23] The procedure is generally considered to be safe and well-tolerated, especially with semi-rigid instruments with no reported mortality to date.[24,25] Mortality rates with rigid instruments were reported to be between 0.09% and 0.24%, and with reported complication rates from 2% to 6 %.[26,27,28] In the current study the post-thoracoscopic complications in the studied group have occurred only in 4 patients (10%). One patient (2.5%) developed surgical emphysema which was resolved spontaneously 3 days later (the case was diagnosed as malignant pleural mesothelioma), and the other 3 patients (7.5%) developed pain which was transient and controlled by analgesics. Prabhu and Narasimhan (2012)[16], reported that out of 68 patients, there were no major complications, only 4 patients (5.8%) had minor complications like subcutaneous emphysema (3 patients) and prolonged air leak (one patient). This was also comparable with most other studies like in Menzies and Charbonneau (1991)[29], & Munavvar et al[30] Also Mehta et al. (2012)[31], reported that pleuroscopy is a safe & well-tolerated procedure. Overall, the incidence rate of these complications was <1 %.

Conflicts of Interest

Nil

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