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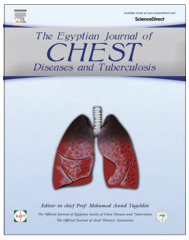

ORIGINAL ARTICLE

Spectrum of diffuse parenchymal lung diseases using medical thoracoscopic lung biopsy: An experience with 55 patients during 2013–2015

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KEYWORDS

Medical thoracoscopic lung biopsy;
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Abstract *Background:* Diffuse parenchymal lung diseases (DPLD) constitute a heterogeneous group of lung diseases characterized by varying degrees of inflammation and fibrosis. In some DPLD, significant morbidity and unfavorable evolution, comparable to those of neoplastic diseases, are seen. Therefore, an efficient and safe method for the diagnostic confirmation of DPLD is needed. Currently, thoracoscopic lung biopsy is widely used for this purpose.

Aim of work: The objective of the present study was to analyze the role of medical thoracoscopic lung biopsy, in the diagnosis of different types of diffuse parenchymal lung diseases.

Patients and methods: This study included 55 patients with undiagnosed DPLD who were selected from Chest Department inpatients, Kasr Alaini Hospital during the period from June 2013 to August 2015. All patients were subjected to written informed consent, full medical history, detailed clinical examination, coagulation profile, echocardiography, immune and collagen profile, arterial blood gases analysis, spirometry, high resolution computed tomography (HRCT) of the chest and medical thoracoscopic lung biopsy.

Results: Out of the 55 patients included in the study, 32 (58.2%) were females, 23 (41.8%) were males, 14 (25.5%) were smokers, 12 (21.8%) had history of raising birds and 12 (21.8%) had positive collagen profile. The mean age was 39.96 years (range, 10–67). HRCT showed different patterns of parenchymal affection in addition to mediastinal lymph node enlargement in 8 (14.5%) patients, and pleural effusion in 11 (20%) patients. Definitive diagnosis was made in 54 patients (98.18%) and idiopathic interstitial pneumonia was the predominant diagnosis (43.64%) followed by DPLD of known cause (36.36%) then granulomatous DPLD (12.7%) and lastly other rare forms of DPLD (5.45%). The most common diagnoses were the usual interstitial pneumonia in 9 (16.4%), metastatic adenocarcinoma in 8 (14.8%), desquamative interstitial pneumonia in 7 (12.7%), hypersensitivity pneumonitis in 5 (9.1%), non specific interstitial pneumonia, sarcoidosis and pneumoconiosis each in 4 (7.3%) cases. The mean duration of intercostal tube insertion was 3.4 days. No reported mortality and complications included prolonged air leak in 4 patients, residual pneumothorax after removal of intercostal tube in 1 patient, and subcutaneous emphysema in 2 patients.

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Conclusions: Lung biopsy through medical thoracoscopy is a safe, effective and viable procedure for the diagnosis of diffuse parenchymal lung diseases.

Introduction

Diffuse parenchymal lung diseases constitute a heterogeneous group of lung diseases, including more than two hundred different interstitial diseases and characterized by varying degrees of inflammation and fibrosis. These non-neoplastic disorders primarily affect the lung interstitium, although the alveolar space, bronchioles and pulmonary vessels can also be affected [1].

The process of diagnosing a DPLD is dynamic. The diagnostic reasoning is based on the joint analysis of clinical, radiological and pathological aspects [1]. Frequently, the definitive diagnosis of DPLD can be established only through pathological examination of the material obtained by lung biopsy. In addition to diagnostic confirmation, this procedure provides information regarding disease activity, disease progression and response to therapy [2].

The options for lung biopsy include bronchoscopy with transbronchial biopsy, open lung biopsy and lung biopsy through video-assisted thoracoscopy. Bronchoscopy with transbronchial biopsy is useful in cases in which the disease presents peribronchial or peribronchiolar distribution. One limitation of this procedure is the small quantity of lung tissue obtained in the biopsy, which is why it is not recommended for the investigation of idiopathic interstitial pneumonia. In addition, its accuracy in the diagnosis of DPLD in immunocompetent patients is only 7–37% [3].

The gold standard for the diagnosis of DPLD is surgical lung biopsy, which should be used whenever it is not possible to establish a definitive diagnosis based on the available clinical and radiological data [4]. It can be performed as an open procedure or through video-assisted thoracoscopy. Open lung biopsy has a high diagnostic yield (92%), as well as low rates of morbidity and mortality (2.5% and 0.3%, respectively) [5]. Video-assisted thoracoscopy is considered a minimally invasive technique. It provides excellent visualization of the intra-thoracic structures and allows the collection of a greater number of lung samples, when necessary. Since it is a less invasive procedure, video-assisted thoracoscopy has come to be used as the principal mean of diagnosing DPLD. However, its use must be evaluated in terms of safety and diagnostic resolution [5].

While thoracoscopic surgery is rapidly replacing standard thoracotomy in the evaluation and management of many pleuropulmonary diseases, thoracoscopic lung biopsy is becoming the procedure of first choice for the diagnosis of many localized and diffuse lung diseases and an adjunct to conventional bronchoscopic evaluation [6,7].

Forceps lung biopsy during thoracoscopy under local anesthesia has been used for many years by pulmonologists and has been frequently described as an integral technique of the method defined today as medical thoracoscopy [8]. Therefore, the objective of the present study was to analyze the role of this currently widely used method, which is medical thoracoscopic lung biopsy, in the diagnosis of different types of diffuse parenchymal lung diseases.

Patients and methods

The present study was conducted on 55 patients with diffuse parenchymal lung disease admitted in Chest Department, Kasr El-Aini Hospital, Cairo University during the period from June 2013 to August 2015. All patients of DPLD on HRCT chest with unproved diagnosis and of different ages, regardless the gender, were included in the study. Patients with severe hypoxia, Type II respiratory failure, severe pulmonary hypertension, coagulopathy (prothrombin concentration $\leqslant$ 50% or platelet count $\leqslant$ 7000/ml), cardiac disorders (arrhythmia, MI, unstable angina) or end stage systemic disease were excluded from the study.

All patients were subjected to written informed consent, full medical history, including smoking and occupational history, history of raising birds, detailed clinical examination, coagulation profile (prothrombin concentration and platelet count), echocardiography, immune and collagen profile, arterial blood gas analysis, spirometry, high resolution computed tomography of the chest and medical thoracoscopic lung biopsy.

Medical thoracoscopic lung biopsy

Equipment

Rigid thoracoscope with a cold light source was used using KARL-STORZ rigid thoracoscope, coagulation diathermy forceps and diathermy apparatus.

Technique

The patients were fasting for at least 6 h before the procedure with the explanation of the procedure to each patient. The procedure was performed in the endoscopy suit. Pre-medications in the form of atropine 1 mg IM injection to control vasovagal tone and Pethidine 100 mg (50 mg IM, 50 mg IV injection) to ensure proper control of pain and good analgesia were given. The vital signs of the patients were monitored (blood pressure, heart rate respiratory rate) during the procedure; also oxygen saturation was measured by pulse oximetry with spontaneous ventilation during the procedure. Supplementary oxygen was provided to the patient to maintain oxygen saturation above 90%.

The patient was placed in the lateral decubitus position with side that will be operated upon up and the arms above the head. The lateral chest wall at the side of entry (4th or 5th intercostals space, midaxillary line) was sterilized with iodo-povidone antiseptic solution. The skin, subcutaneous tissues, periosteum of the ribs and parietal pleura at site of entry were infiltrated by lidocaine 2% as local anesthesia.

Skin incision about 1 cm was made at the planned thoracoscopic insertion point. Blunt dissection with round ended

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scissors was carefully performed through the chest wall. Plastic trocar (8 mm) was gently advanced thorough the chest wall until the pleural cavity was reached then the inner part of the trocar was removed to allow the induction of pneumothorax with lung collapse. The rigid thoracoscope (Karl-storz Endoscopy, Germany®) was passed through the trocar port. The parietal, visceral pleurae and lung were examined. The electro-coagulation biopsy forceps connected to diathermy coagulation (Olympus DSD 20) was passed through the working channel of the rigid thoracoscopy then the forceps was dipped in the lung surface in an open position then closed and lung biopsies were taken while applying short pulses of diathermy (adjusted at 60 W coagulation). Usually 2–3 biopsies were obtained from different lobes.

At the end of the procedure, a chest tube connected to under water seal was inserted in place and fixed to the skin of the patient at its exit from the chest wall by a suture after removal of the port cannula.

Post thoracoscopy care and follow up

All patients were followed post procedure for vital signs, oxygen saturation, chest tube drainage including air leak and fluid or blood drainage if present. Patients were given broad spectrum antibiotic and potent analgesics. Also chest X-ray was done for confirmation of full lung expansion. When the lung is fully expanded with the absence of air leak and fluid drainage less than 100 ml/24 h, the tube was removed with or without pleurodesis according to the situation.

Histopathological examination

The biopsy specimens were preserved in formalin containing cups and sent for histopathological examinations were the specimens were stained with hematoxylin and eosin stains and examined under light microscopy. Further immunohistochemical studies sometimes were done if needed (e.g. to differentiate between adenocarcinoma and other epithelial tumors).

Additional tests were done according to the clinical situation e.g.; CT abdomen and pelvis, tumor markers, upper GIT endoscopy or colonoscopy to search for primary neoplasm. Bone scan, CT brain or pelvi-abdominal sonar were done to assess distant metastasis.

Statistical analysis

Quantitative data were presented as minimum, maximum, mean and standard deviation (±SD) values. Qualitative data were presented as frequencies (number of cases) and percentages. Chi square (χ^2) test was used to determine significant association between different qualitative variables. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

Results

This study included 55 patients with DPLD on HRCT chest with unconfirmed diagnosis who were selected from chest department inpatients, Kasr Alaini Hospital during the period from June 2103 to August 2015. Their ages ranged from 10 to 67 years with a mean value of 39.96 and ±SD 13.31. They included 32 (58.2%) females and 23 (41.8%) males. Among the study population, 14 (25.5%) patients were smokers, 12 (21.8%) patients had history of raising birds and also 12 (21.8%) patients had positive collagen profile (Table 1).

Regarding the HRCT chest findings, there were different patterns of parenchymal affection in addition to mediastinal lymph nodes enlargement in 8 (14.5%) patients, pleural effusion in 11 (20%) patients as shown in Table 1. Also other systems affection was present in 8 (14.5%) patients (Table 1). The arterial blood gases and spirometric data are listed in Table 2.

Regarding the lung biopsy side, lung biopsies were obtained from the right lung in 38 (69.09%) patients and from the left lung in 17 (30.91%) patients according to the HRCT predominant pattern and avoiding areas with extensive fibrosis and honeycombing.

The different histopathological types of DPLD based on thoracoscopic lung biopsy results were shown in Table 3. Definitive diagnosis was obtained in 54 patients (98.18%) and idiopathic interstitial pneumonia was the predominant diagnosis (in 24 cases with percent of 43.64) followed by DPLD of known cause (in 20 cases with a percent of 36.36) then granulomatous DPLD (in 7 cases with a percent of 12.7) and lastly other rare forms (Fig. 2) of DPLD (in 3 cases with a percent of 5.45). The most common diagnoses were usual interstitial pneumonia in 9 (16.4%), metastatic adenocarcinoma in 8 (14.8%) (Fig. 1), desquamative interstitial pneumonia in 7 (12.7%), hypersensitivity pneumonitis in 5 (9.1%), non specific interstitial pneumonia, sarcoidosis and pneumoconiosis each in 4 (7.3%) cases.

The duration of intercostals tube insertion post procedure ranged from 2 to 10 days with a mean value of 3.4 days and ±SD 1.63. No reported mortality and complications occurred only in 7 (12.7%) patients including prolonged air leak in 4 patients which stopped spontaneously with no further interference, residual pneumothorax after removal of intercostal tube in 1 patient, and subcutaneous emphysema in 2 patients.

Table 1 Characteristics of the study patients.

Character	Number (total = 55)	Percent (100%)
Female	32	58.2
Male	23	41.8
Smoking history	14	25.5
History of raising birds	12	21.8
Positive immune and collagen profile	12	21.8
Predominant HRCT pattern		
Consolidation	12	21.8
Cystic lesion	1	1.8
Ground glass opacities	12	21.8
Ground glass and air trapping	3	5.5
Military shadows	3	5.5
Nodular lesion	8	14.5
Reticulonodular shadows and fibrosis	14	25.5
Reticulonodular shadows and air trapping	2	3.6
Mediastinal lymph node enlargement	8	14.5
Pleural effusion	11	20
Other systems affection	8	14.5

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Table 2 Arterial blood gases parameters & spirometric data of the study patients.

Character	Number (%)	Mean ± SD
PaO_2 mm Hg	55 (100)	62.04 ± 7.90
$PaCO_2$ mm Hg	55 (100)	37.95 ± 4.55
SaO_2%	55 (100)	91.38 ± 3.69
FVC%	55 (100)	57.13 ± 21.37
FEV1%	55 (100)	55.82 ± 17.99
FEV1/FVC%	55 (100)	90.11 ± 10.18
FEF25–75%	55 (100)	47.82 ± 13.69

Table 3 Spectrum of diagnoses of DPLD according to histopathology results of thoracoscopic lung biopsy.

Histopathology type	Number	Percent
Idiopathic interstitial pneumonias: 24 (43.64%)		
Cryptogenic organizing pneumonia	3	5.5
Desquamative interstitial pneumonia	7	12.7
Non specific interstitial pneumonia	4	7.3
Usual interstitial pneumonia	9	16.4
Pleuroparenchymal fibroelastosis	1	1.8
Granulomatous DPLD: 7 (12.7%)		
Sarcoidosis	4	7.3
Pulmonary tuberculosis	2	3.6
Weagner's granulmatosis	1	1.8
DPLD of known cause: 20 (36.36%)		
Hypersensitivity pneumonitis	5	9.1
Metastatic adenocarcinoma	8	14.5
Pneumoconiosis	4	7.3
Exogenous lipoid pneumonia	2	3.6
Pneumocystis Carinii Pneumonia	1	1.8
Other forms of DPLD: 3 (5.45%)		
Idiopathic pulmonary hemosiderosis	1	1.8
Alveolar proteinosis	1	1.8
Pulmonary Langerhan's Cell histocytosis	1	1.8
Undiagnosed		
Chronic non specific inflammation	1	1.8
Total	55	100%

Discussion

The DPLDs constitute a heterogeneous group of lung diseases characterized by varying degrees of inflammation and fibrosis. In some DPLDs, significant morbidity and unfavorable evolution, comparable to those of neoplastic diseases, are seen. Therefore, an efficient and safe method for the diagnostic confirmation of DPLD is needed [9].

Lung biopsy is required for diagnosis in about one third of patients with diffuse infiltrative disease. Transbronchial biopsy is less painful, less invasive, and considerably less costly, compared with open or thoracoscopic procedure, and entails a lower incidence of mortality and of morbidity [10]. However, transbronchial biopsy has introduced new diagnostic problems for the pathologist because the specimen has all the features that open biopsy tries to avoid: it is unselected and exceedingly small, the lung tissue is crushed and it comes from regions immediately adjacent to bronchi.

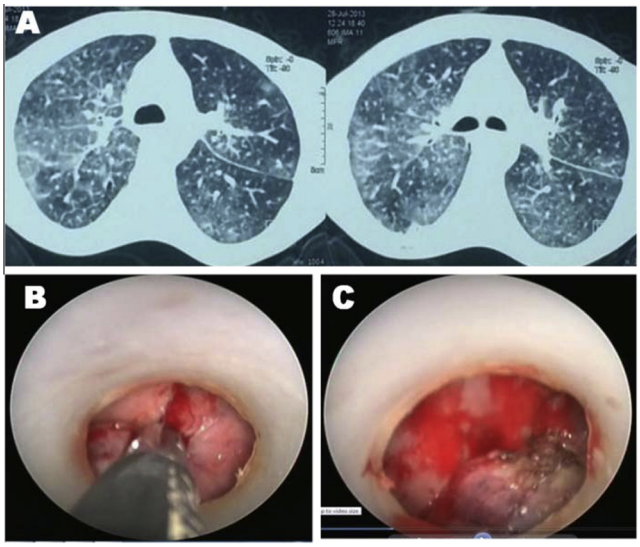

Figure 1 Female patient 24 year old complaining of fever, dry cough and exertional dyspnea, 3 months ago. HRCT chest (picture A) showed widespread nodular infiltration and ground glass opacification with some reticulations. Picture B showing the coagulation biopsy forceps taking punch from lung tissue. Picture C showing area of scar in the lung surface after taking a biopsy. Histopathology result of lung biopsy showed "metastatic signet ring cell carcinoma variant of adenocarcinoma". Upper and lower gastrointestinal endoscopies were done searching for primary and revealed primary gastric signet ring cell carcinoma.

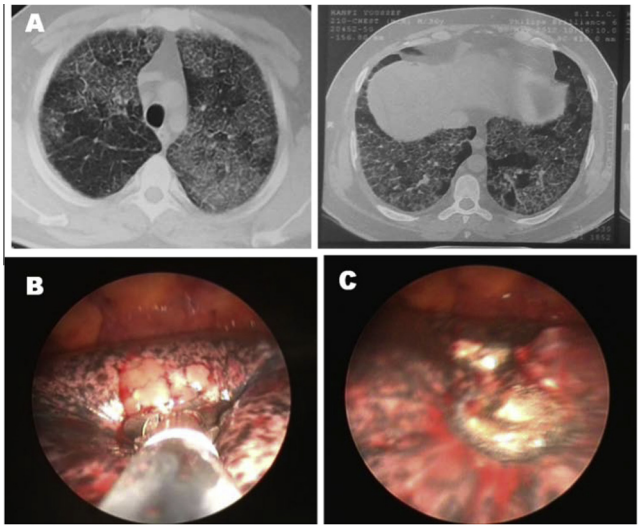

Figure 2 37 year old male patient complaining of gradual progressive exertional dyspnea and dry cough of 7 months duration. HRCT (picture A) showed crazy paving appearance. Picture B showing anthracotic lung surface with the coagulation biopsy forceps taking punch from lung tissue. Picture C showing area of scar in the lung surface after taking biopsy. Histopathology result of lung biopsy showed alveolar proteiniosis.

Lung biopsy under vision has higher diagnostic yield when compared to transbronchial lung biopsy [11]. The British Thoracic Society (BTS) guidelines suggest that it should be

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standard practice to take lung biopsy samples in DPLD when the diagnosis remains uncertain after clinical and radiological assessments, unless there are patient contraindications or when the samples are very unlikely to contribute to management [12].

The aim of the present study was to evaluate the role of medical thoracoscopic lung biopsy as a tool in the diagnosis of different types of diffuse parenchymal lung diseases.

This study included 55 patients with undiagnosed DPLD who were subjected to medical thoracoscopic lung biopsy. The study population showed predominance of females (58.2%) over males (32%). These result matched with those of Abdollah (2012) [13] who performed medical thoracoscopic lung biopsies in 10 patients with DPLD and found that females (60%) were predominant over males (40%). Similarly study of Ishie et al. (2009) [9] showed predominance of females (52.08%) over males (47.92%). However, other authors have found a slight predominance of males [14].

The mean age of DPLD patients in this study was 39.9 years with ±SD 13.3 years. This finding is similar to those reported by Abdollah (2012) [13] who found that the mean age in their study was 42.2 with ±SD 9.5 years. On the other hand Vansteenkiste et al. (1999) [15] found that the mean age was 52.3 ± SD 16.7 years.

In the present study, a definitive diagnosis was obtained in 54 (98.18%) out of the 55 studied patients and the idiopathic interstitial pneumonia was the predominant diagnosis (in 24 cases with percent of 43.64) followed by DPLD of known cause (in 20 cases with a percent of 36.36) then granulomatous DPLD (in 7 cases with a percent of 12.7) and lastly other rare forms of DPLD (in 3 cases with a percent of 5.45). The higher prevalence of diseases was belonging to usual interstitial pneumonia (UIP) in 9 (16.4%) cases, metastatic adenocarcinoma in 8 (14.8%) cases, desquamative interstitial pneumonia (DIP) in 7 (12.7%) cases, hypersensitivity pneumonitis in 5 (9.1%) cases, non specific interstitial pneumonia (NSIP), sarcoidosis and pneumoconiosis each in 4 (7.3%) cases.

These results matched with those of Nitin et al. (2011) [16] who reported that UIP (59.3%) was the most frequent histopathological pattern within 63 patients involved in their study. While Abdollah [13] found that out of 10 patients, 3 (30%) of them had metastatic adenocarcinoma, one patient with chronic pulmonary infection and 6 (60%) patients with interstitial lung disease (ILD) divided as 2 patients had UIP, 3 patients had DIP and 1 Patient had NSIP.

Dijkman et al. (1982) [17] study included 63 cases, 57 (90.48%) cases of them were diagnosed with medical thoracoscopy. The most common diagnoses were UIP in 17 cases, sarcoidosis in 7 cases, lymphangitic carcinoma in 5 cases, eosinophilic pneumonia in 3 cases and histocytosis X in 5 cases. Also in Andrew et al. (2002) [18] study which included 62 patients, diagnoses were obtained in 61 (98.39%) patients; the most common diagnoses were neoplasm in 25 patients (40%), interstitial lung disease in 18 patients (29.5%) and granulomatous disease in 7 patients.

In the literature, the prevalence of hypersensitivity pneumonia ranges from 1.5% to 14%. Similarly, the prevalence of pneumoconiosis ranges from 4% to 10.4% [19].

In this study sarcoidosis was found in only 4 cases (7.3%). In contrast, in the literature, sarcoidosis is described as a common DPLD. In a study involving 3152 patients [20], sarcoidosis was the most common disease (in 33.72% of the cases), followed by idiopathic pulmonary fibrosis (in 27.41% of the cases). This is due to the fact that sarcoidosis, due to its characteristic peribronchial or peribronchiolar distribution, is preferably diagnosed by transbronchial biopsy [21]. Therefore, in suspected cases of sarcoidosis, surgical lung biopsy is used only when the diagnosis cannot be made by transbronchial biopsy.

In the present study, medical thoracoscopy provided adequate lung tissue samples with high diagnostic efficacy. The definitive diagnosis was made in 98.18% of the cases. This finding is in agreement with the studies performed by Nitin et al. (2011) [16], Abdollah (2012) [13] and Vansteenkiste et al. (1999) [15] where the diagnostic yield in their studies was 98.3%, 90% and 91%, respectively.

Overall no reported mortality, major complication, or prolonged post-thoracoscopic hospital stay and this agreed with that of Abdollah (2012) [13] who concluded in their study that medical thoracoscopic lung biopsy is safe, feasible and useful technique in the diagnosis of DPLD.

In conclusion, this study illustrated that medical thoracoscopy with lung biopsy is an effective and safe procedure in the hands of well trained interventional pulmonologists. Depending on institutional habits and local expertise, it can be an interesting, and probably less expensive in diagnostic work-up of DPLD. The analysis of the results of our study revealed that, as long as there is an investigation and appropriate pre-planning, as well as careful selection of candidates, medical thoracoscopy is an option with a good success rate when adequate lung biopsy is indicated.

Conflict of interest

No conflict of interest.

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[1] American Thoracic Society, European Respiratory Society, American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001, Am. J. Respir. Crit. Care Med. 165 (2) 277–304. Erratum in: Am. J. Respir. Crit. Care Med. 166 (3) (2002) 426.

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