Al-Azhar Med. J.(Medicine). *Vol. 50(2), April, 2021, 1489 - 1496*
DOI: 10.12816/amj.2021.158639
https://amj.journals.ekb.eg/article_158639.html

ROLE OF TRANSBRONCHIAL LUNG BIOPSY AND BRONCHOALVEOLAR LAVAGE IN DIAGNOSIS OF DIFFUSE PARENCHYMAL LUNG DISEASE

By

Ahmed Rady Abd El-Azeem Erfan, Hamdy Mohamed Zoair, Ibraheem Hassan Mohamed and Khalid Mohamed Halima

Department of Chest, Faculty of medicine, Al-Azhar University, Cairo, Egypt

Corresponding author: Ahmed Rady Abd El-Azeem Erfan,

Mobile: (+20) 01003335637, **E-mail:** kedomedo8@gmail.com

ABSTRACT

Background: Diffuse parenchymal lung diseases (DPLD) constitute a group of over 200 diverse etiologic entities which present with respiratory symptoms and diffuse lung infiltrates and account for 15% of patients seen by a pulmonary physician.

Objective: To evaluate the role of transbronchial lung biopsy and bronchoalveolar lavage in diagnosis of diffuse parenchymal lung disease.

Patients and Methods: This prospective cross-sectional study was carried out at the Department of Chest, Al-Hussein University Hospital, during the period from October 2019 to October 2020, and included sixty patients admitted in the inpatient wards with undiagnosed DPLD, after detailed history taking, physical examinations, routine labs, chest X-ray PA view, HRCT chest, pulmonary function tests (PFTs) as simple spirometry, ECG, echocardiography and Arterial blood gases evaluation. All of them were subjected to fibrooptic bronchoscope, transbronchial lung biopsy and bronchoalveolar lavage.

Results: As regard comparison between bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) diagnostic yield there was a statistical significant difference between TBLB positive and negative patients, as regard BAL predominant cells and BAL microbiology. the comparison of histopathology as regard TBLB diagnostic yield showed a statistical significant difference between TBLB positive and TBLB negative patients.

Conclusion: Bronchoalveolar lavage was a minimally invasive procedure performed during flexible bronchoscopy. BAL cellular analysis alone was insufficient to diagnose the specific type of DPLD, except in malignancies and some rare interstitial lung diseases (ILDs), and the yield of bronchoscopic lung biopsy was high in diseases where the lesions were peri bronchial in distribution such as in sarcoidosis, hypersensitivity pneumonitis and organizing pneumonias.

Key words: Diffuse Parenchymal Lung Disease; Bronchoalveolar Lavage; Transbronchial Lung Biopsy.

INTRODUCTION

Diffuse parenchymal lung diseases (DPLD) constitute a group of over 200 diverse etiologic entities which present with respiratory symptoms and diffuse lung infiltrates and account for 15% of patients seen by a pulmonary physician *(Leslie et al., 2017).*

Bronchoscope is an important tool in the practice of pulmonary medicine in the era of evidence based medicine; Flexible bronchoscopy gives easy access to respiratory samples for cytological studies

and lung tissue for histopathology in DPLD. Lung biopsy studies have unraveled the complex cellular and molecular events in pathogenesis of various types of interstitial lung diseases, and have led to development of novel therapeutic agents for idiopathic pulmonary fibrosis *(Wollin et al., 2015).*

Over the last five decades, greater awareness and easy availability of CT thorax and fibrooptic bronchoscopy has led to diagnosis of diseases such as Sarcoidosis, which were earlier considered to be rare in our country, while dealing with DPLD, the aim is to make early diagnosis for institution of definitive treatment and improvement in long term outcomes *(Jindal et al., 2010).*

The present work aimed to diagnose DPLD via BAL and TBLB

PATIENTS AND METHODS

This prospective cross-sectional study was carried out at the department of Chest, Al Hussein University Hospital Cairo, Egypt, during the period from October 2019 to October 2020, and included sixty patients admitted in the inpatient wards with undiagnosed DPLD.

Exclusion Criteria:

Contraindications for bronchoscopic lung biopsy (BLB)as in advanced interstitial lung disease with respiratory failure and /or pulmonary hypertension, cardiovascular diseases: unstable angina, acute myocardial infarction (< 6 weeks), heart failure, recent or ongoing exacerbation of DPLD or recent pneumonia (<6 weeks),severe hypoxemia: PaO2< 75 mmHg on oxygen (Venturi mask FiO2=0.5), coagulopathy (INR 1.5, PTT> 1.5 times control), thrombocytopenia (platelet count< 1lakh/uL),renal failure (Serum creatinine >3.5 mg/dl) and patients with chronic lung congestion.

Ethical clearance was granted by Al-Azhar Faculty of Medicine Ethics and Research Committee. Informed consents were obtained from all participants.

All subjects were submitted to full history taking, thorough clinical examination, routine laboratory investigations (complete blood count, random blood sugar, liver function tests, kidney function tests and coagulation profile), plain chest X-ray (postero-anterior view), high Resolution CT chest, Pulmonary function tests (PFTs): while the patients are sitting and at rest, the highest values of forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), FEV1/FVC and forced expiratory flow in small airways (FEF 25-75%) after at least three trials are obtained, ECG and echocardiography, arterial blood gases (ABG) and fibrooptic bronchoscope, transbronchial lung biopsy and bronchoalveolar lavage.

Fibrooptic bronchoscope:

The flexible bronchoscope used was Pentax EB-1830T3 video bronchoscope] 5.0 mm insertion tube, 2.2 mm working channel, 60 cm working length[and]3.7 mm insertion tube, 1.2 mm working channel, 60 cm working length].

With the patient in the supine position, the flexible bronchoscope was inserted transnasally or transorally and through the nasopharynx or oropharynx, the visualized vocal cords were sprayed under direct vision with 2% lidocaine, after passing the

cords, anesthesia of the carina and bronchi was achieved using 2% boluses of lidocaine sprayed via the bronchoscope, secondly biopsy was taken and sent for histopathological examination.

Statistical analysis:

Data were collected; coded, revised, package and computerized, statistical analysis of data was performed using Statistical Program for the Social Science (SPSS) version 24. Quantitative data were expressed as mean± standard deviation (SD), and Qualitative data were expressed as frequency and percentage.

Fisher exact test was used when comparing between non-parametric data.

RESULTS

Sixty patients were included in this study, the mean age of all studied patients was 43.9± 14.9 years with minimum age of 15 years and maximum age of 76 years, there were 35 male (58.3%) and 25 females (41.7%),34patients (56.7%) from urban and 26 patients (43.3%) rural,27patients (45%) smokers and 33patients (55%) non-smokers. Dry cough was present in 29 patients (48.3%), dyspnea in 46 patients (76.7%), cyanosis in 6 patients (10%), clubbing in 4 patients (6.7%) and wheeze in 6 patients (10%).

The description of chest CT revealed that Ground glass opacities were present in 23 patients (38.3%), consolidation in 4 patients (6.7%), and nodular infiltration was present in 18 patients (30%).Other CT findings were present as mild plural effusion in 5 patients (8.3%), nodules in 1 patient (1.7%), heterogeneous opacities in 2 patients (3.3%), apical cavities in 1 patient (1.7%) and Hilar mass in 2 patients (3.3%).

Bronchoscopic findings of all studied patients was normal in 52 patients (86.7%), wide carina in 1 patient (1.7%), sub-mucosal infiltration 3 patients (5%) and mucosal hyperemia in 4 patients (6.7%). As regards to BAL predominant cells, it was lymphocytic in 21 patients (35%), Neutrophilic in 5 patient (8.3%), high Eosinophilic in 6 patients (10%) and mixed cellular in 28 patients (46.7%).BAL microbiology was negative in 47 patients (78.3%), positive for TB in 5 patients (8.3%), positive for bacterial growth in 5 patients (8.3%) and positive for fungal growth in 3 patients (5%).

The Comparison of BAL as regard TBLB diagnostic yield shows highly statistical significant difference (p-value < 0.001) between TBLB positive patients & TBLB negative patients as regard BAL predominant cells and BAL microbiology, **(Table 1)**.

Table (1): Comparison of BAL as regard TBLB diagnostic yield

TBLB diagnostic yield		Negative(n = 7)		Positive(n = 53)		P-value
BAL predominant cells	Lymphocytic	1	14.3%	20	37.7%	< 0.001
	Neutrophilic	5	71.4%	0	0%	
	Eosinophilic	0	0%	6	11.3%	
	Mixed cellular	1	14.3%	27	50.9%	
BAL Microbiology	Negative	2	28.6%	45	84.9%	< 0.001
	Positive for TB	0	0%	5	9.4%	
	Bacterial growth	5	71.4%	0	0%	
	Fungal growth	0	0%	3	5.7%	

X2: Chi-square test.

The comparison of histopathology as regard TBLB diagnostic yield shows highly statistical significant difference (p-value < 0.001) between TBLB positive patients & TBLB negative patients as regard histopathology **(Table 2)**.

Table (2): Comparison of histopathology as regard TBLB diagnostic yield

	TBLB diagnostic yield				P-value
	Diagnosis	Negative(n = 7)		Positive(n = 53)	
Histopathology	Non-specific inflammation	7	100%	0	0.0%	< 0.001
	IPF	0	0%	11	20.8%	
	Bronchogenic carcinoma	0	0%	3	5.7%	
	TB	0	0%	5	9.4%	
	Metastasis	0	0%	6	11.3%	
	NSIP	0	0%	1	1.9%	
	Fungal	0	0%	3	5.7%	
	Wegener Granulomatosis	0	0%	2	3.8%	
	HP	0	0%	14	26.4%	
	Amyloidosis	0	0%	1	1.9%	
	Sarcoidosis	0	0%	3	5.7%	
	Silicosis	0	0%	1	1.9%	
	OP	0	0%	2	3.8%	
	Alveolar proteniosis	0	0%	1	1.9%	

X2: Chi-square test.

DISCUSSION

This study was performed between October 2019 and October 2020 in chest departments, Al-Hussein University Hospitals, aiming for evaluation of the role of TBLB and BAL in diagnosis of DPLD, and the results revealed that. The mean age of all studied patients was 43.9±14.9 years with minimum age of 15 years and maximum age of 76 years. There were 35 males (58.3%) and 25

females (41.7%), 34 patients (56.7%) from urban and 26 patients (43.3%) from rural, 27 patients (45%) smokers and 33 patients (55%) non-smokers. As regard the description of extra-pulmonary manifestation of all studied patients. Loin pain was present in 1.7%, breast cancer in 3.3%, uterine carcinoma in 1.7%, uterine fibroid in 1.7%, arthritis in 5%, weight loss in 15%, saddle nose in 1.7%, tight skin in 1.7%, generalized lymphadenopathy in 1.7%, Potts disease in 1.7% and goiter was present in 1.7%.

As regards to BAL predominant cells, it was lymphocytic in 35%, neutrophilic in 8.3%, high esinophilic in 10% and mixed cellular in 46.7%. Changes in the relative and absolute numbers of cells in BAL fluid have been described in a variety of interstitial lung diseases (ILD). Usually, these changes are nonspecific but occasionally they are sufficiently characteristic to narrow the differential diagnosis, on the other hand 801 patients with lung infiltrates who performed cytologic studies of lavage fluid of 491 patients who also underwent bronchoalveolar lavage (BAL). A specific histopathological diagnosis was made in (29%) by *Poletti and his colleagues (2014).*

The histopathology of biopsy revealed that non-specific inflammation in 11.7%, idiopathic pulmonary fibrosis (IPF) in 18.3%, bronchogenic carcinoma in 5%, TB in 8.3%. Metastasis in 10%, nonspecific interstitial pneumonia (NSIP) in 1.7%, fungal in 5%, Wegener Granulomatosis in 3.3%, hypersensitivity pneumonitis (HP) in 23.3%, Amyloidosis in 1.7%, Sarcoidosis in 5%, Silicosis in 1.7%, OP in 3.3% and alveolar proteinosis in 1.7%.

Poletti and his colleagues (2014) revealed that histopathological changes consistent with the clinical pattern were present in 37% .

Qian Han and his colleagues (2014) revealed that TBLB failed to obtain lung parenchyma in 23.3%. TBLB was considered clinically helpful in 30.4%. The majority were diagnosed as pulmonary alveolar proteinosis (PAP) (33.2%), connective tissue disease-related ILDs (CTD-ILDs) (32.2%) and idiopathic pulmonary fibrosis (IPF) (16.3%). Although TBLB could provide definitive histopathological diagnoses in all cases diagnosed as PAP, only few cases of IPF (21.2% of IPF diagnoses) and CTD-ILDs (13.8% of CTD-ILD diagnoses) could be identified by TBLBs.

As regard to TBLB diagnostic yield of all studied patients, there was negative yield in 11.7% and positive yield in 88.3%.In study done by *Kebbe and Tony (2017)*, the overall diagnostic yield of TBLB is around 25–75%, but it varies largely depending on the underlying ILD. It can be as low as 20–30% for IPF, and as high as 80–90% for non-fibrotic ILDs.

The Comparison of BAL as regard TBLB diagnostic yield showed statistical significant difference between TBLB positive patients and TBLB negative patients as regard BAL predominant cells and BAL microbiology. The Comparison of histopathology as regard TBLB diagnostic yield showed statistical significant difference between TBLB positive patients and TBLB negative patients as regard histopathology, while another study by *Fend and his colleagues*

(2012) showed no evidence of interstitial lung disease during the course of follow-up. Sufficient lung parenchyma was present in 81 of 91 biopsy specimens (including four repeat biopsies), and 79 of 91 BAL samples were considered adequate.

The same study revealed that combination of BAL and TBLB was more efficient (efficiency 80.3% vs. 67.9% in TBLB and 64.6% in BAL) than either method alone. With Sensitivity showed a similar increase from 58.8% in TBLB and 73.9% in BAL to 79.5% for both combined and Specificity for BAL was a low 60.7% due to contamination by inflammatory cells from upper airways, whereas specificity for TBLB was 100% *(Fend et al., 2012).*

CONCLUSION

BAL cellular analysis may be a useful in the diagnostic evaluation of individuals who lack a confident usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) chest, Bronchoscopic lung biopsy has a high yield in DPLD with peri-bronchial in distribution such as Sarcoidosis, hypersensitivity pneumonitis, organizing pneumonias.

REFERENCES

1. **Andersen HA and Fontana RS. (2012):** Transbronchoscopic lung biopsy for diffuse pulmonary diseases: technique and results in 450 cases. Chest., 62:125-8.
2. **Cantrell ET, Martin RR, Warr GA, Busbee DL. (2013):** Induction of aryl hydrocarbon hydroxylase in human pulmonary alveolar macrophages by cigarette smoking. Trans Assoc Am Physicians., 86:121-30.
3. **F Fend, G Mikuz, G Ott and J Rothmund. (2012):** Combined transbronchial lung biopsy and bronchoalveolar lavage in diffuse parenchymal lung disease,Pathol Res Pract. Mar; 184(3):312-7.
4. **Jindal SK, Gupta D and Aggarwal AN. (2010):** Sarcoidosis in developing countries. Current Opinion in Pulmonary Medicine, 6:448–454.
5. **Kebbe J and Tony A. (2017):** the diagnostic role of bronchoscope in interstitial lung disease, 10:2103-37.
6. **Leslie KO. (2016):** My approach to interstitial lung disease using clinical, radiological and histopathological patterns. J Clin Pathol 62:387-401.
7. **Meyer KC, Raghu G, Baughman RP and Brown K (2012):** An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. Am J Respir Crit Care Med., 185: 1004-14. 10.1164/rccm.201202-0320ST.
8. **Poletti V, Chilosi M and Olivieri D. (2014):** Diagnostic invasive procedures in diffuse infiltrative lung diseases. Respiration., 71:107-19.
9. **Quin H, Qun Lo, Xiaobo C, Jiaxing X, Lulu Wu and Rongchang Chen (2017):** Transbronchial lung biopsy and bronchoalveolar lavage in diffuse parenchymal lung disease Clin Respir J,; 11(2):168-175.
10. **Reynolds HY. (2017):** Bronchoalveolar Lavage 1, 2. American Review of Respiratory Disease. Am Thoracic Soc., 135:250-63.
11. **Wollin L, Wex E, Pautsch A and Schnapp G. (2015):** Mode of action of Nintedanib in the treatment of idiopathic pulmonary fibrosis. Eur Respir J., 45:1434–1445.

دور المنظار الشعبي في تشخيص أمراض أنسجة الرئة الخلالية المنتشرة عن طريق أخذ عينة رئوية والغسيل القصبي الشعبي

أحمد راضي عبد العظيم عرفان، حمدي محمد زعير، إبراهيم حسن محمد، خالد محمد حليمه

قسم الأمراض الصدرية، كلية الطب، جامعة الأزهر، القاهرة

E-mail: kedomedo8@gmail.com

خلفيـــة البحـــث: تعتبـــر أمـــراض أنســـجة الرئـــة الخلاليـــة المنتشـــرة مجموعـــه مـــن الأمـــراض التـــي تتـــألف مـــن أكثـــر مـــن 20 ســـببا وجميعهـــا تتشـــابه فـــي الأعـــراض التنفســـية التـــي يشخصـــها الأطبـــاء المتخصصـــين فـــي الأمـــراض الصـــدرية ويعـــد المنظـــار الشـــعبي مـــن أهـــم الأدوات المســـتخدمة فـــي مجـــال الصـــدر لتشـــخيص العديـــد مـــن الأمـــراض ومـــنهم أمـــراض أنســـجة الرئـــة الخلاليـــة المنتشـــرة عـــن طريـــق أخـــذ عينـــة رئويـــة و الغسيل القصبي الشعبي.

الهـــدف مـــن البحـــث: توضـــيح دور المنظـــار الشـــعبي فـــي تشـــخيص أمـــراض أنســـجة الرئة الخلالية المنتشرة عن طريق أخذ عينة رئوية و الغسيل القصبي الشعبي.

المرضـــى وطريقـــة البحـــث: أجريـــت هـــذه الدراســـة فـــي قســـم الأمـــراض الصـــدرية بمستشـــفى الحســـين الجـــامعي بجامعـــه الأزهـــر علـــى ســـتين مريضـــا ومريضـــة اشـــتبه فـــي إصـــابتهم بمـــرض أنســـجة الرئـــة الخلاليـــة المنتشـــرة بأخـــذ التـــاريخ المرضـــي والفحـــص الإكلينيكـــي بعـــد اســـتبعاد الحـــالات التـــي لاتتماشـــى مـــع معـــايير هـــذه الدراســـة وذلـــك فـــي الفتـــرة الزمنيـــة مـــن أكتـــوبر 2019حتـــى أكتـــوبر 2020 وبعـــد أخـــذ التـــاريخ المرضـــي كـــاملا لكـــل المرضـــى تـــم اجـــراء فحـــص إكلينيكـــي شـــامل، صـــورة دم، وظـــائف كبـــد وكلـــي ومعامـــل مناعـــة، أشـــعه عاديـــه علـــي الصـــدر خلفـــي و أمـــامي و أشـــعة مقطعيـــة علـــي الصـــدر عاليـــة التبـــاين و وظـــائف تـــنفس و رســـم قلـــب وموجـــات صـــوتية علـــي القلـــب وتحليـــل غـــازات بالـــدم وعمـــل منظـــار شـــعبي وأخـــذ عينـــة رئويـــة و غســـيل قصـــبي شعبي.

نتـــائج البحـــث: أظهـــرت الدراســـة أن نتـــائج المنظـــار القصـــبي كانـــت طبيعيـــة فـــي عـــدد 52 مـــن المرضـــي(86.7٪) بينمـــا مريضـــا واحـــدا فقـــط ذو كارينـــا واســـعه (1.7٪) وعـــدد 3 مرضـــي ذوي ارتشـــاح تحـــت الغشـــاء المخـــاطي (5٪)، وعـــدد 4 مرضـــي ذوي احتقـــان مخـــاطي (6.7٪). وبـــالنظر لنتـــائج خزعـــة الرئـــة عبـــر القصـــبة الهوائيـــة لجميـــع المرضـــى الخاضـــعين للدراســـة نجـــد أنـــه كـــان هنـــاك عائـــدا ســـلبيا فـــي 7 مرضـــى (11.7٪) وعائـــدا إيجابيـــا فـــي 53 مريضـــاً (88.3٪)، ولا توجـــد فـــروق ذات دلالـــة إحصـــائية بـــين المرضـــى ذوي النتـــائج الموجبـــة والمرضـــى ذوي النتـــائج الســـالبة فيمـــا يتعلـــق بـــالجنس والمهنـــة والإقامـــة والتـــدخين، وكـــان هنـــاك فرقـــا معتـــدا بـــه إحصـــائيًا بـــين المرضـــى الإيجـــابيون عـــن طريـــق أخـــذ عينـــة رئويـــة والمرضـــى الســـلبيون عـــن طريـــق أخـــذ عينـــة رئويـــة فيمـــا يتعلـــق بـــالعمر. وبمقارنـــة نتـــائج خلايـــا الغســـيل الشـــعبي ونتـــائج خلايـــا الأنســـجة فيمـــا يتعلـــق بإنتاجيـــة التشـــخيص عـــن طريـــق أخـــذ عينـــة رئويـــة فقـــد وجدت دلالة إحصائية عالية بين المرضى الموجبين والمرضى السلبيين.

الاســـتنتاج: تشـــخيص أمـــراض أنســـجة الرئـــة الخلاليـــة المنتشـــرة متنـــوع وكثيـــر بدايـــة مـــن التشـــخيص الإكلينيكـــي وعمـــل الاشـــعه ووظـــائف التـــنفس والمنظـــار الشـــعبي الليفـــي حيـــث يعـــد مـــع أخـــذ عينـــة مـــن الرئـــة وعمـــل غســـيل شـــعبي مـــن اهـــم الأدوات المســـتخدمة فـــي التشـــخيص، لـــذا يوصـــي باســـتخدامه مـــع الغســـيل القصـــبي الشـــعبي لتشـــخيص أمـــراض أنســـجة الرئـــة الخلاليـــة المنتشـــرة مقترنـــا بتحليـــل شـــامل للغســـيل الشـــعبي لمعرفة نوع وعدد الخلايا الموجودة وخصوصا الخلايا الليمفاوية.

الكلمات الدالة : المرض الرئوى المنتشر – عينة من االرئة والقصبية الهيوائة .