

## Diffuse Parenchymal Lung Disease-Diagnostic Approach by Radiology and Histopathology

Aastha Gupta<sup>1</sup>, Shaista M Vasenwala<sup>1</sup>, Kafil Akhtar<sup>1\*</sup>, Rakesh Bhargava<sup>2</sup>, Ibne Ahmad<sup>3</sup> and Veena Maheshwari<sup>1</sup>

<sup>1</sup>Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

<sup>2</sup>T.B Chest & Respiratory Disorder, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

<sup>3</sup>Radio-diagnosis, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

### Abstract

**Aims and objective:** This study aims at evaluating the patients of diffuse parenchymal lung disease (DPLD), by comparing radiological and cyto-histopathological findings to determine the importance of histopathology in the diagnosis of DPLD.

**Materials and methods:** Seventy patients with chief complaints of dyspnoea & cough and bilateral diffuse shadows on chest radiography were selected. High resolution computed tomography (HRCT) and bronchoscopy was done for further assessment.

**Results:** Out of 70 patients, 44 were finally diagnosed on the basis of bronchoscopic findings, as usual interstitial pneumonia (UIP) 24 cases (54.5%) and as non UIP in 20 cases (45.5%). Two cases of UIP additionally suffered from bronchogenic carcinoma.

**Conclusion:** A combination of clinical, radiological, cytological and histological findings is necessary to evaluate the cases of DPLD and transbronchial needle biopsy (TBNB) gives a definitive edge over other diagnostic measures.

**Keywords:** Diffuse parenchymal lung disease; High resolution computed tomography; Transbronchial needle biopsy

**Abbreviations:** DPLD: Diffuse Parenchymal Lung Disease; HRCT: High Resolution Computed Tomography; TBNB: Transbronchial Needle Biopsy

### Introduction

DPLD is a term given to a heterogenous group of clinical entities that share the common features of dyspnoea, hypoxemia, restrictive ventilatory defect and the presence of reticular, nodular, reticulonodular or ground glass infiltrates on chest radiographs [1,2].

Many disease processes of varying etiology present with diffuse lung infiltrates on chest X-ray. These include infections, neoplasms, pulmonary oedema, pulmonary haemorrhage, aspiration pneumonia, bronchiectasis, cystic fibrosis and others. A thorough clinical, occupational and family history with detailed physical, radiological and histopathological examination is required to arrive at a definite diagnosis.

The present study was undertaken to diagnose and evaluate the cases of DPLD by using radiological and histopathological investigations.

### Materials and Methods

Seventy patients with complaints of dyspnoea and cough showing bilateral diffuse shadows on chest X-ray were selected. The relevant clinical history included age, occupation, smoking status, history of anti-tubercular therapy (ATT) and connective tissue diseases. After clinical examination, routine investigations, pulmonary function test (PFT), sputum for acid fast bacilli stain and culture, and high resolution computed tomography (HRCT) were done. The bronchoscopic evaluation included bronchial aspiration (BA), trans-bronchial needle aspiration (TBNA) and trans-bronchial needle biopsy (TBNB). Pleural fluid examination was also carried out. The smears and paraffin embedded tissue sections were stained with Papanicolaou (PAP) and

Haematoxylin & Eosin (H&E) stains respectively. Van Gieson (VG) and Periodic acid Schiff's (PAS) stains were applied as required.

### Results

On clinicoradiological basis, 70 patients were divided into two broad categories of UIP 42 cases (60%) and non UIP 28 cases (40%). (Table 1) In non UIP group, out of 18 cases (64.3%) of bronchiectasis, only 8 cases could be sampled. The rest 10 cases were treated as bronchiectasis on the basis of clinical findings and HRCT.

On bronchoscopic findings 44 out of 70 patients could be sampled adequately and categorized into two groups, as usual interstitial pneumonia group (UIP) 24 cases (54.5%) and non UIP group 20 cases (45.5%) (Table 2). Two cases of UIP additionally suffered from bronchogenic carcinoma. The non UIP group included cases from the other categories of diffuse parenchymal lung diseases.

Our study on 44 cases of DPLD, showed majority of UIP cases, 18/24 (75.0%) in the age group of 51-70 years, and only 3 cases (8.3%) each in the age group of 31-50 years and above 70 years. The 20 cases in the non UIP group were almost evenly distributed between 10-70 years of age. The M:F ratio in UIP group was 3.4:1 whereas in the non UIP group, it was 1.3:1.

**\*Corresponding author:** Kafil Akhtar, Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, E-mail: drkafilakhtar@gmail.com

**Received** August 16, 2011; **Accepted** February 07, 2012; **Published** February 10, 2012

**Citation:** Gupta A, Vasenwala SM, Akhtar K, Bhargava R, Ahmad I, et al. (2012) Diffuse Parenchymal Lung Disease-Diagnostic Approach by Radiology and Histopathology. J Cytol Histol 3:132. doi:10.4172/2157-7099.1000132

**Copyright:** © 2012 Gupta A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Duration of symptoms was more than 6 months in all the 24 cases (100.0%) in UIP group and in 18/20(90%) cases in the non UIP group. Two cases (10.0%) of non UIP group had a short duration of < 3 months.

The most common presenting feature in UIP group was dyspnoea, 20 cases (83.3%), followed by dry or productive cough, 19 cases (79.2%). In the non UIP group, 13 cases (65.0%) complained of dyspnoea, with dry or productive cough in 6 cases (30.0%), chest pain in 2 cases (10.0%) and hemoptysis in a single case (5.0%). Thirteen cases (54.2%) in the UIP and 4 cases (20.0%) in the non UIP group were smokers. The distribution of patients according to their duration and frequency in pack years was also ascertained. The pack year is defined as smoking a pack of 20 cigarette or bidi per day for one year. The mean pack year was found to be  $n10.8 \pm 5.3$  in UIP and  $8.8 \pm 2.3$  in non UIP group.

The history of ATT intake could be obtained in 3/24 cases (12.5%) in UIP group and 13/20 cases (65.0%) in non UIP group. Only 50% of the patients had completed the full course of treatment.

Results of PFT showed that 20/24 cases (83.3%) of UIP had restrictive ventilator defect while 4/24(16.7%) had obstructive defect. In the non UIP group, 6/20 cases (30.0%) had obstructive defect, 4/20 (20.0%) cases had restrictive defect and another 4/20 cases (20.0%) had mixed restrictive and obstructive defects. 6/20 cases (30.0%) showed normal PFT results.

Chest radiography in all the 44 cases of both UIP and non UIP groups showed bilateral diffuse sub pleural shadows in the lower lobes of the lungs while HRCT in all the 24(100%) cases of UIP showed sub pleural honeycombing in the lower zones of the lung. On X-ray and

S No	Diagnosis	Male	Female	Total
1	UIP	33(47.1%)	9(12.9%)	42(60%)
2	Cryptogenic Organizing Pneumonia (COP)	2(2.9%)	1(1.4%)	3(4.3%)
3	Pneumoconiosis	-	1(1.4%)	1(1.4%)
4	Sarcoidosis	-	1(1.4%)	1(1.4%)
5	Hypersensitivity pneumonitis(HP)	2(2.9%)	1(1.4%)	3(4.3%)
6	Bronchiectasis	6(8.6%)	12(17.1%)	18(25.7%)
7	Bronchiolitis	2(2.9%)	-	2(2.9%)
	<b>Total</b>	<b>45(64.3%)</b>	<b>25(35.7%)</b>	<b>70(100%)</b>

Table 1: Clinical diagnosis of patients on clinicoradiological basis(N=70).

S.No	Diagnosis	Males	Females	Total
1	UIP	17(42.5%)	5(12.5%)	22(55%)
2	UIP+Malignancy	2(5%)	-	2(5%)
3	Non Specific Interstitial Pneumonia (NSIP)	-	1(2.5%)	1(2.5%)
4	Cryptogenic Organizing Pneumonia (COP)	2(5%)	1(2.5%)	3(7.5%)
5	Pneumoconiosis	-	1(2.5%)	1(2.5%)
6	Sarcoidosis	-	1(2.5%)	1(2.5%)
7	Hypersensitivity Pneumonia (HP)	2(5%)	1(2.5%)	3(7.5%)
8	Chronic Eosinophilic Pneumonia (CEP)	1(2.5%)	-	1(2.5%)
9	Bronchiectasis	4(10%)	4(10%)	8(20%)
10	Bronchiolitis	2(5%)	-	2(5%)
	<b>Total</b>	<b>30(68.2%)</b>	<b>14(31.8%)</b>	<b>44(100%)</b>

Table 2: Diagnosis of cases based on cytohistological analysis of bronchial aspirate, transbronchial needle aspirate, pleural fluid and tranbronchial needle biopsy.

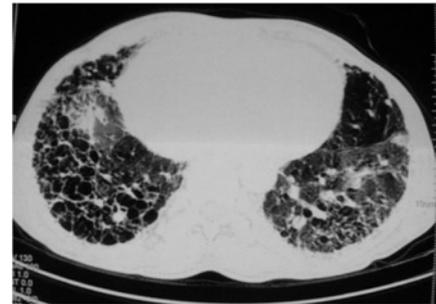


Figure 1: HRCT image shows reticular changes in bilateral basal subpleural lung fields with honeycombing more in right lung and evidence of tractional bronchiectasis in left lower lung field.

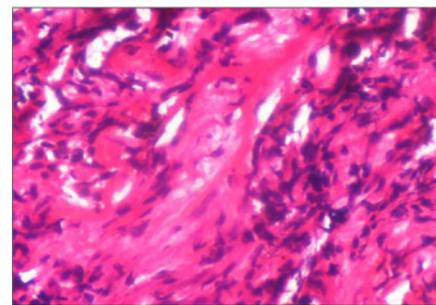


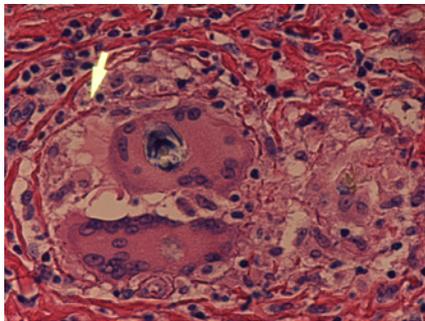
Figure 2: UIP: Fibrosis of alveolar septa and smooth muscle hyperplasia in terminal bronchiole wall. H & E x500.

HRCT, a single case of non specific interstitial pneumonia (NSIP) presented with reticular shadows in the middle and lower zones of both lungs (Figure 1). Three cases of cryptogenic organizing pneumonia (COP) showed foci of peripheral consolidation and all the cases of pneumoconiosis presented with bilateral diffuse/reticular shadows. A single case of sarcoidosis was seen as mediastinal widening with peribronchial multinodular shadows in both lungs and 3 cases of hypersensitivity pneumonitis (HP) showed ground glass opacities. Bilateral reticular shadows were seen mainly in the upper lobes in a single case of chronic eosinophilic pneumonia (CEP). Eight cases of bronchiectasis presented as dilated bronchioles reaching the periphery of the lungs and 2 cases of bronchiolitis showed diffuse reticular shadows in both lungs.

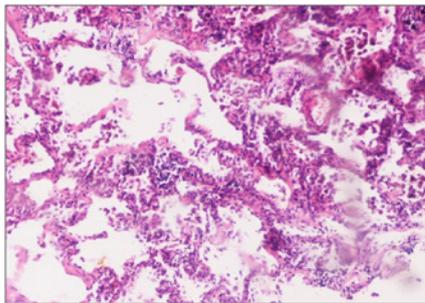
We finalized the diagnosis of 44 cases on cytohistopathological analysis of BA, TBNA, TBNB and pleural fluid. Inflammatory smears were seen in all the cases of UIP (24 cases) and non UIP group (20 cases). Two cases (8.3%) of UIP showed associated carcinoma, as keratinizing squamous cell carcinoma and well differentiated adenocarcinoma, one case each. The single case of sarcoidosis showed numerous lymphocytes and histiocytes while CEP showed eosinophils, lymphocytes and histiocytes on TBNA.

Cases of UIP on TBNB showed non uniform inflammation of the lung parenchyma with fibrosis and smooth muscle proliferation (Figure 2). In non UIP group (20 cases), a single case (10.0%) of NSIP showed diffuse mild inflammation of lung parenchyma and fibrosis. Three cases (15.0%) of COP presented with dense aggregates of fibroblasts with lymphocytes, plasma cells, histiocytes in the interstitium and fibrosed alveoli. A single case (10.0%) of pneumoconiosis showed

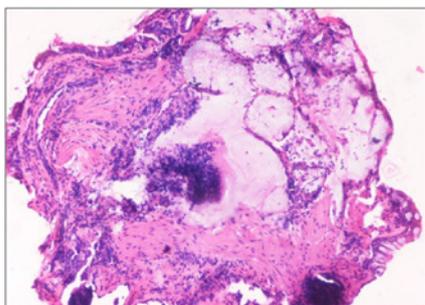
inflammation, extensive fibrosis, pigment deposition and desquamated epithelium. Small submucosal non caseating granulomas consisting of tightly packed epithelioid cells and multinucleated giant cells with Schaumann's body were seen in the single case (10.0%) of sarcoidosis (Figure 3). Three cases (15.0%) of hypersensitivity pneumonitis (HP) showed chronic inflammation of the bronchi and peribronchiolar tissue with giant cells in the interstitium or alveoli. One case (10.0%) of CEP showed alveoli filled with eosinophils and eosinophilic macrophages with type II alveolar cell hyperplasia (Figure 4). Bronchiectasis was diagnosed in 8 cases (40.0%) where dilated bronchiole showed ulcerated mucosa, hypertrophic mucus glands, and loss of elastic tissue, disorganised smooth muscle, inflammatory infiltrate and fibrosis (Figure 5).



**Figure 3:** Sarcoidosis: Small submucosal non caseating granulomas consisting of tightly packed epithelioid cells and multinucleated giant cells with Schaumann's body. H & E x500.



**Figure 4:** Chronic eosinophilic pneumonia (CEP): Alveoli filled with eosinophils and eosinophilic macrophages with type II alveolar cell hyperplasia. H & E x125.



**Figure 5:** Bronchiectasis: Dilated bronchiole shows ulcerated mucosa, hypertrophic mucus glands, loss of elastic tissue, disorganised smooth muscle, inflammatory infiltrate and fibrosis. H & E x125.

Clinicoradiology	Cytohistopathology		
Diseases	No of Cases	Concordant	Non Concordant
UIP	26	UIP=22	UIP+Malignancy=2
NSIP=1			
CEP=1			
COP	3	COP=3	
Pneumoconiosis	1	Pneumoconiosis=1	
Sarcoidosis	1	Sarcoidosis=1	
Hypersensitivity Pneumonia(HP)	3	1HP=3	
Bronchiectasis	8	Bronchiectasis=7	Bronchiectasis+
Pneumoconiosis=1			
Bronchiolitis	2	Bronchiolitis=2	
<b>Total</b>	<b>44(100%)</b>	<b>39(88.6%)</b>	<b>5(11.4%)</b>

**Table 3:** Comparative analysis of clinicoradiological and cytohistological diagnoses (n=44).

A correlation of clinicoradiological and cytohistological findings in 44 patients revealed that in 5 cases (11.4%) cytohistopathology was most valuable in diagnosing the missed entities, i.e., UIP with malignancy in 2 cases and NSIP, CEP and bronchiectasis with pneumoconiosis in 1 case each (Table 3). A positive predictive value of 83.5% and sensitivity of 100% was found on clinicoradiological and cytohistological correlation in our study.

## Discussion

The term DPLD, often used synonymously with interstitial lung disease (ILD), refers to diseases that cause inflammation of the pulmonary interstitium. There are about 200 disorders that are implicated in the causation of DPLD [1]. Approximately two-third cases of DPLD are idiopathic, whereas one-third result from known endogenous and exogenous causes, including occupational factors, infections, drugs and radiation. Many other diseases mimic the clinical presentation or radiological features of ILD and hence extensive investigations are required to differentiate ILD from other diseases, which is seldom possible. Hence ILD often remains a diagnosis of exclusion.

We found majority of the cases, 18/24 (75.5%) of UIP group in late stages (IPF), in the age group of 51-70 years and all the 20 cases in the non UIP group were evenly distributed between 10-70 years of age. Hamid et al. [3] have stated that interstitial pulmonary fibrosis (IPF) or late stage of UIP is commonly seen in the middle aged and there is increase in incidence with advancing age while Jindal et al. [4] have reported 26.8% cases of IPF above 60 years of age.

Our study showed all the cases except 2 (10%) cases of non UIP with symptoms for more than 6 months. Nagai et al. [5] on 234 histologically proven Japanese patients with IPF have reported that symptoms were present for more than 6 months. In our study, dyspnoea was the major presenting feature in 20/24 cases (83.3%) in the UIP and 13/20 cases (65.0%) in the non UIP group. Smith et al. [6] have reported dyspnoea in 100% of their cases.

Regarding relationship between smoking and DPLD, in our study 13 cases (54.2%) of UIP and 4 cases (20.0%) of non UIP presented with a history of smoking. Hanley et al. [7] reported that, 75.0% cases of IPF had a history of smoking, which was associated with acceleration of disease process.

On PFT, a restrictive ventilatory defect is the most frequent finding in patients of DPLD, especially in IPF [8]. Jindal et al. [4] have reported a restrictive defect in 81.2% cases of IPF, similar to our study which showed 20 cases (83.3%) of UIP with restrictive defects.

Thirteen cases (54.3%) diagnosed as late stage of UIP (IPF), presented with bilateral diffuse shadows on chest X-ray in our study. Quite similarly, Lynch et al. [9] observed that pulmonary fibrosis preferentially involved the basilar regions with a proclivity for the sub-pleural regions. However Sharma et al. [10] and Subhash et al. [11] have reported 28.6% and 45% cases of IPF respectively with bilateral diffuse shadows on chest X-ray, in their study on patients of DPLD.

In our study, HRCT showed honeycombing in the sub-pleural region of the lower lung zones in all the cases in the UIP group, a finding supported by Sumikawa et al. [12] We found patchy consolidation in 2/3rd cases of COP in the non UIP group on HRCT similar to findings of Cordier et al. [13]. In our study 3 cases of HP presented with ground glass nodules on HRCT and one case each of pneumoconiosis, sarcoidosis and bronchiolitis presented with centrilobular nodules, findings consistent with Collins [14].

Cytological analysis of the bronchial aspirate and TBNA smears of UIP lesions in our study showed predominantly inflammatory smears, findings concordant with cytologic impressions of Koss [15]. In bronchiectasis, hyperplastic vacuolated cells were seen in the background of mucus. The bronchiolitic aspirates showed necrosis, columnar and squamous cells, lymphohistiocytic infiltrates and spiral mucus threads, findings supported by Koss [15].

We observed patchy/non uniform involvement of the lung parenchyma with inflammation, fibroblastic and smooth muscle proliferation in 10/26 cases (38.5%) of UIP on TBNB, similar to findings of Katzenstein et al. [16]. A single case diagnosed as UIP on HRCT turned out to be NSIP on biopsy. There was extensive fibrosis, inflammation, pigment deposition and desquamated epithelium seen in the 2 cases of pneumoconiosis, findings consistent with the reports of Wall et al. [17]. Majority of our cases in the non UIP group i.e., 64.3% were diagnosed as bronchiectasis, based on the findings of dilated bronchi with ulcerated mucosa, hypertrophic mucus glands, inflammation and fibrosis, as reported by Travis et al. [18].

## Conclusion

A high positive predictive value and sensitivity on clinico-radiological and cytohistological correlation in our study asserts that a correlation of clinical, radiological, cytological and histological findings is necessary to evaluate the cases of diffuse parenchymal lung diseases and TBNB gives a definitive edge over other diagnostic interventions in the diagnosis and prognosis of DPLD.

## References

1. Carrington CB, Gaensler EA, Couto RE, FitzGerald MX, Gupta RG (1978) Natural history and treated course of usual and desquamative interstitial pneumonia. *N Engl J Med* 298: 801-809.
2. Fletcher C, Peto R (1977) The natural history of chronic airflow obstruction. *Br Med J* 1: 1645-1648.
3. Hamid RJ, Payam T, Mina E, Forozaan M, Mehrdad K, et al. (2006) Clinical pattern of idiopathic pulmonary fibrosis: a retrospective study. *Tanaffos* 5: 27-32.
4. Jindal SK, Malik SK, Deodhar SD, Sharma BK (1979) Fibrosing Alveolitis: A

report of 61 cases seen over the past 5 years. *Indian J Chest Dis Allied Sci* 21: 174-179.

5. Nagai S, Kitaichi M, Itoh H, Nishimura K, Izumi T, et al. (1998) Idiopathic nonspecific interstitial pneumonia/fibrosis: comparison with idiopathic pulmonary fibrosis and BOOP. *Eur Respir J* 12: 1010-1019.
6. Smith C, Feldman C, Levy H, Kallenbach JM, Zwi S (1990) Cryptogenic fibrosing alveolitis. A study of an indigenous African population. *Respiration* 57: 364-371.
7. Hanley ME, King TE, Schwarz MI, Watters LC, Shen AS, et al. (1991) The impact of smoking on mechanical properties of the lungs in idiopathic pulmonary fibrosis and sarcoidosis. *Am Rev Respir Dis* 144: 1102-1106.
8. Jindal SK, Gupta D (1997) Incidence and recognition of interstitial pulmonary fibrosis in developing countries. *Curr Opin Pulm Med* 3: 378-383.
9. Lynch DA, Godwin JD, Safrin S, Starko KM, Hormel P, et al. (2005) High resolution computed tomography in idiopathic pulmonary fibrosis: diagnosis and prognosis. *Am J Respir Crit Care Med* 172: 488-493.
10. Sharma SK, Pande JM, Guleria JS (1984) Diffuse interstitial pulmonary fibrosis. *Indian J Chest Dis Allied Sci* 26: 214-219.
11. Subhash HS, Ashwin I, Solomon SK, David T, Cherian AM, et al. (2004) A comparative study on idiopathic pulmonary fibrosis and secondary diffuse parenchymal lung disease. *Indian J Med Sci* 58: 185-190.
12. Sumikawa H, Johkoh T, Colby TV, Ichikado K, Suga M, et al. (2008) Computed tomography findings in pathological usual interstitial pneumonia: relationship to survival. *Am J Respir Crit Care Med* 177: 433-439.
13. Cordier JF (2000) Organising pneumonia. *Thorax* 55: 318-328.
14. Collins J (2001) CT signs and patterns of lung disease. *Radiol Clin North Am* 39: 1115-1135.
15. Koss LG (2005) *Diagnostic Cytopathology and its histologic basis*. Lippincott Williams & Wilkins.
16. Katzenstein AL, Zisman DA, Litzky LA, Nguyen BT, Kotloff RM (2002) Usual interstitial pneumonia: histologic study of biopsy explants specimens. *Am J Surg Pathol* 26: 1567-1577.
17. Wall CP, Gaensler EA, Carrington CB, Hayes JA (1981) Comparison of transbronchial and open biopsies in chronic infiltrative lung diseases. *Am Rev Respir Dis* 123: 280-285.
18. Travis WD, Matsui K, Moss J, Ferrans VJ (2000) Idiopathic nonspecific interstitial pneumonia: prognostic significance of cellular and fibrosing patterns: survival comparison with usual interstitial pneumonia and desquamative interstitial pneumonia. *Am J Surg Pathol* 24: 19-33.