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Original Research Article

Clinico-radiological and pathological correlation of interstitial lung diseases: a prospective single centre study

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ABSTRACT

Background: Current investigation was done to study the role of HRCT chest in the diagnosis and characterization of interstitial lung diseases, yield of transbronchial lung biopsy and role of multidisciplinary approach of diagnosis.

Methods: We prospectively analyzed clinical features and radiological findings in 38 patients of ILD. Radiological diagnosis on HRCT was made in every case depending on type of predominant abnormality and pattern of involvement. Following this, TBLB was done in every case.

Results: ILD was diagnosed in all cases on HRCT. Most common ILD type was UIP (31.5%) followed by sarcoidosis (21%) and NSIP (15.7%). Other ILD subtypes encountered were, RB-ILD, AIP and acute silicosis. In 68.4% cases, there was definitive diagnosis on TBLB. Out of which in 15.7% cases, HRCT and TBLB diagnosis were different. In 15.3% cases, TBLB gave diagnosis of only non- specific ILD.

Conclusions: HRCT can detect ILD in 100% cases & can characterize ILD into various patterns. But, HRCT alone without clinical correlation and pathology can cause diagnostic confusion in many cases. However, multidisciplinary approach by engaging clinician, radiologist and pathologist can lead to accurate diagnosis in many cases of ILD. TBLB is a safe, minimally invasive procedure which can establish correct diagnosis in many cases especially in broncho-centric diseases.

Keywords: High resolution computed tomography, Interstitial lung disease, Transbronchial lung biopsy, Multidisciplinary approach

INTRODUCTION

Interstitial lung diseases (ILDs) are a heterogeneous group of disorders which share clinical, radiographic and pathologic features. HRCT of the chest is significantly more sensitive than chest radiograph for detecting abnormalities in ILD and the pattern-based approach can lead to correct diagnosis in many cases.[1] Moreover, it can quantify the disease extent, severity and thus can be used for prognostication.[2] A collaborative multi-disciplinary approach by engaging the clinician, radiologist, and pathologist helps in making accurate diagnosis because individually there are many similarities between these conditions in terms of clinical presentation and radiological/histological findings.[3] Transbronchial lung biopsy (TBLB) being minimally invasive procedure, is gaining wider acceptance in diagnosis of ILD especially in diseases with broncho-centric involvement. This study evaluated pattern-based approach of ILD, yield of transbronchial lung biopsy and role of multidisciplinary approach of diagnosis.

METHODS

A prospective study was conducted over a period of one year (July 2016 to June 2017) involving 38 patients in the department of radio-diagnosis and pulmonary medicine, Indira Gandhi medical college and hospital, Shimla (Himachal Pradesh). The study was conducted after approval by the Institutional review board and ethics

committee. Written informed consent was taken in every case.

Inclusion and exclusion criteria

All patients visiting the hospital from July 2016 to June 2017 with clinical features/pulmonary function tests suggestive of interstitial lung disease were included in our study. Patients who were physically unfit for performing bronchoscopy, pregnant patients, patients with uncorrected coagulopathy and sputum/BAL positive patients for AFB were excluded from the study.

Table 1: Key radiological findings in the various ILDs.

Definite UIP	**Subpleural basal reticular pattern with honeycombing**
Possible UIP	Subpleural basal reticular pattern without honeycombing
NSIP	Bilateral ground glass opacities with reticulation, subpleural sparing
Sarcoidosis	Peribronchovascular thickening, bronchocentric ,subpleural nodules, hilar and mediastinal lymph node enlargement
Classic silicosis	Upper lobe predominant soft and calcified nodules, egg shell calcification of mediastinal lymph nodes
Acute silicosis	Ground glass opacity, interlobular septal thickening, consolidation
Progressive Massive fibrosis	Large mass like conglomerates predominantly in upper lobes associated with radiating strands
RB-ILD	Bronchial wall thickening, ground glass opacity, centrilobular nodules

Procedure

The study participants were selected randomly in terms of age and sex attributes. Detailed clinical history including age, smoking history, environmental, occupational history, duration and severity of breathlessness and extra-pulmonary features (rashes, arthritis, Raynaud's phenomenon, dysphagia, oral ulcers) were assessed. Pulmonary function tests and chest X-ray was done in all cases. HRCT thorax (full helical scan) was done on 64 slice MDCT GE (general electronics) Light speed VCT Xte machine. Supine scanning was done covering whole lung i.e. from apex to base. Tube voltage was 120 kVp, and tube current was 750 mA. Contrast was given in cases where chest x-ray showed bulky hilum with clinical suspicion of sarcoidosis. HRCT images were reviewed using appropriate lung window settings i.e. window width, window level of 1000, -700 HU and 1500, -600 HU respectively. HRCT scans were interpreted by three radiologists and final diagnosis was made after consensus. On HRCT scan, disease distribution and pattern, predominant abnormality was studied.[4] The diagnosis of various ILDs was made according to the radiological features as described in (Table 1).[5-8] Following HRCT, bronchoscopy was performed under local anesthesia and conscious sedation in every case. Flexible bronchoscope "Pentax" was used. The selection of lobe/segment for biopsy was done on basis of disease pattern on chest CT. Minimum 6 tissue cores were taken in each patient. Only one lung was sampled to avoid a possibility of bilateral pneumothorax. Chest X-ray was done in every patient one hour after the procedure to rule out pneumothorax. The radiological (HRCT) diagnosis was correlated with the histopathological diagnosis. IBM SPSS version 25 software was used for statistical analysis.

RESULTS

The present study comprised of 38 patients out of which 52.6% (N=20) were males and 47.4% (N=18) were females. The age ranged from 16-76 years and mean age of presentation was 52 years. Majority of patients were non-smokers (68.42%, N=26). Shortness of breath was the most common symptom observed in 78.9% (N=30) patients followed by dry cough in 42% (N=16) patients. Duration of symptoms varied over a wide range (from months to years) with mean duration of 11.2 months. Chest x-ray was abnormal in 92.1% (N=35) patients and normal in 7.8% (N=3) patients. Majority of patients had reticular pattern (47.3%, N=18) on chest X-ray. Various chest X-ray findings are as shown in (Table 2).

On HRCT, honeycombing was present in total 12 cases which were radiologically labelled as UIP. However, on histopathological correlation, one of them was diagnosed as NSIP thereby meaning that rarely honeycombing can be present in NSIP as well. Sub-pleural sparing with ground glass opacity was seen in 9 (23.6%) cases which were radiologically categorized as NSIP. Out of which on TBLB, 5(55.5%) patients had NSIP, one each had acute silicosis, sarcoidosis, hypersensitivity pneumonitis and diffuse alveolar hemorrhage. Thereby, meaning that sub-pleural sparing with ground glass opacity is not specific for NSIP, it can be seen in other diseases as well. Various ILD groups diagnosed after HRCT and TBLB are as shown in (Table 3). The TBLB diagnosis was divided into matched diagnosis, different diagnosis, non-specific ILD, inconclusive report. In (Table 4), HRCT diagnosis has been compared with TBLB diagnosis. 26.3% (N=10) cases were categorized as non-specific ILD on TBLB i.e., there was interstitial fibrosis only and couldn't be categorized under particular subtype. One unique case was diagnosed as possible UIP on HRCT, came out to be foreign body granulomatous ILD on TBLB. There was only one case in definite UIP group which had alternate diagnosis on TBLB. Thereby meaning, lower lobe predominant subpleural septal thickening with honeycombing on HRCT should be considered as UIP, until proven otherwise. Yield of TBLB was 68.4%

(including the matched diagnosis and different diagnosis) with highest yield in sarcoidosis (85.7%).

Table 2: Chest X-ray findings.

Chest X-ray	Reticular opacities	Reticulo-nodular opacities	Nodular opacities	Bilateral bulky hilar lymphadenopathy	Bilateral parenchymal haziness	Inhomogenous radioopacity
N	18	3	2	7	4	4
%	47.3	7.8	5.2	18.4	10.5	10.5

Table 3: ILD groups obtained after HRCT and TBLB.

Diagnosis	N	%
UIP	6	15.7
NSIP	4	10.5
Foreign body granulomatous ILD	1	2.6
Non-specific ILD	10	26.3
Granulomatous ILD	1	2.6
Diffuse alveolar hemorrhage	1	2.6
Sarcoidosis	1	2.6
RB-ILD	1	2.6
Silicosis	3	5.2
Hypersensitivity pneumonitis	1	2.6
Chronic interstitial pneumonia	7	18.4
Inconclusive report	2	5.2
Total	38	100

The different diagnosis in 15.7% cases implies that HRCT can be incorrect in diagnosing specific ILD type in some cases and multidisciplinary approach plays an important role in reaching the correct diagnosis.

DISCUSSION

The main aim of the study was to demonstrate that multidisciplinary approach using clinical features, radiology and pathology helps in accurate diagnosis of ILD. Similar to study by Epler et al we too found that chest X-ray can be normal in some cases. Thereby meaning, if there is clinical suspicion of ILD, HRCT thorax should be done even if X-ray is normal.[9] On HRCT, predominant disease pattern was basal and peripheral which can be attributed to UIP as dominant ILD pattern. Disease distribution pattern on HRCT has been shown in (Figure1-2) and dominant HRCT pattern shown in (Figure 3). Most common ILD was UIP (31.5%) followed by sarcoidosis (21%) and NSIP (15.7%) respectively (Figure 5). This pattern differed from the data by Indian ILD registry which could be due to different topographical and geographical factors in sub-Himalayan region.[10]

Out of 12 cases of UIP diagnosed on HRCT, one case came out to be NSIP on TBLB. This is contradictory to study by Tafti et al which concluded that the honeycombing is characteristically absent in NSIP.[11] In 15.7% cases, radiological diagnosis was incorrect and TBLB helped establish the correct diagnosis. Also, some unique case scenarios were found such as sub pleural sparing in sarcoidosis, hypersensitivity pneumonitis which has not been described in current literature. We also documented a case of sarcoidosis which had typical imaging features of NSIP i.e., ground glass opacity with fine reticulations and subpleural sparing but was proved to be sarcoidosis on TBLB (Figure 6). Thereby meaning that sarcoidosis can have atypical imaging features and can mimic NSIP on imaging.

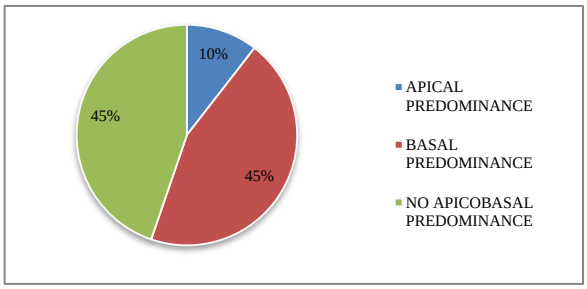

Figure 1: Apico-basal disease distribution patterns on HRCT thorax.

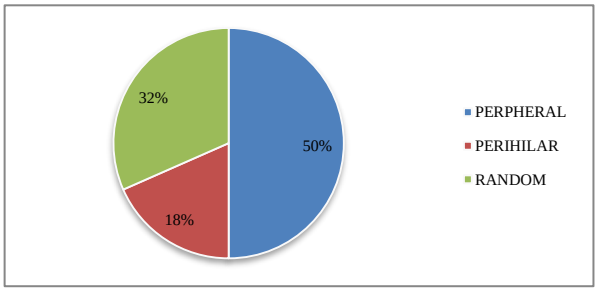

Figure 2: Central peripheral disease distribution patterns on HRCT thorax.

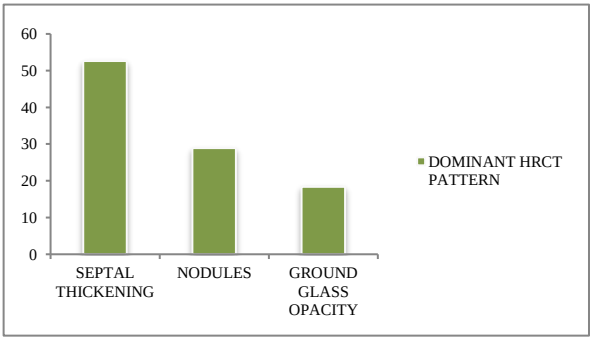

Figure 3: Dominant HRCT pattern.

Many cases of NSIP diagnosed on HRCT turned out of be some other subtype of ILD on TBLB, which can be explained by the fact that NSIP usually presents with a characteristic pattern of ground glass opacity in bilateral lung fields on HRCT which could be the dominant HRCT pattern in many other diseases as well (Figure 7).

Table 4: Correlation of HRCT and TBLB.

Disease groups	Total cases in each group	Matched diagnosis	Non-specific ILD	Different diagnosis	Inconclusive report
Definite UIP	12	5	4	1	2
Possible UIP	2	1	0	1	0
NSIP	9	3	2	4	0
Sarcoidosis	7	6	1	0	0
Silicosis	3	2	1	0	0
Acute silicosis	1	1	0	0	0
Unclassified CIP	1	1	0	0	0
RB-ILD	1	1	0	0	0
PMF	2	0	2	0	0
Total N (%)	38	20 (52.6)	10 (26.3)	6 (15.7)	2 (5.2)

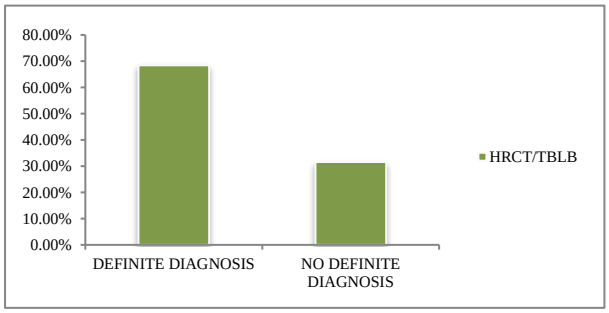

Figure 4: HRCT and TBLB correlation.

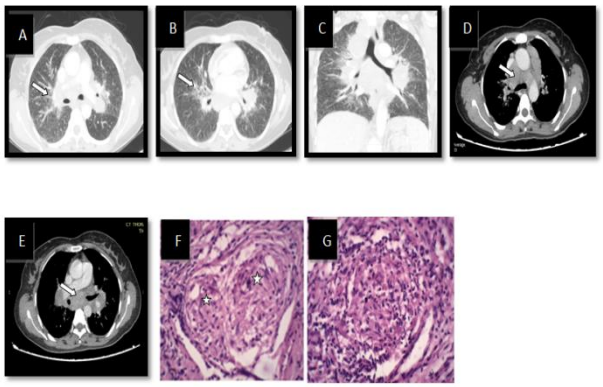

Figure 5: 56 years old female who presented with shortness of breath and dry cough. A-C) CT thorax (lung window) shows multiple small soft tissue nodules and interstitial thickening in the peri bronchovascular distribution, D-E) mediastinal window showing bulky homogenously enhancing mediastinal lymphadenopathy in prevascular, AP window, precarinal, subcarinal and b/l hilar regions. HRCT diagnosis of Sarcoidosis was made, F-G) are HPE images acquired through TBLB showing epitheloid granulomas surrounded by fibrous tissue without any obvious necrosis. histopathological diagnosis of sarcoidosis was made.

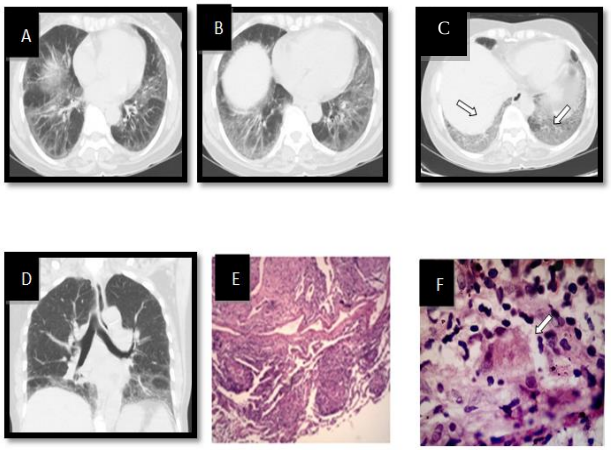

Figure 6: A-D) HRCT lung images of 60 years female showing symmetrical lower lobe predominant inter-intralobular septal thickening with ground glass haze with sub pleural sparing. HRCT findings suggests NSIP, E-F) HPE images acquired through TBLB showing multiple epitheloid cell granulomas with giant cell aggregates and showing asteroid body in the center of image characteristic of sarcoidosis.

So, HRCT alone can be wrong in diagnosing the specific ILD. In such cases, comes the role of clinical history and pathological correlation. In two cases of progressive massive fibrosis, TBLB revealed non-specific interstitial fibrosis. But combining the clinical history and radiological findings, diagnosis of PMF was made. Again, meaning that multidisciplinary approach can guide us toward the final diagnosis. TBLB was diagnostic in 85.7% of sarcoidosis patients in our study. The yield was higher compared to the study by Ocakali et al who reported the diagnostic yield of TBLB of 45% among 63 patients of pulmonary sarcoidosis.[12] Our study emphasized on importance of TBLB in sarcoidosis patients. TBLB is a minimally invasive diagnostic procedure. It can establish correct diagnosis in many

cases, especially in diseases with broncho-centric involvement such as sarcoidosis (Figure 4) depicting HRCT TBLB correlation). In our study the yield of TBLB was 68.4% with highest yield in patients of sarcoidosis (85.7%) pertaining to its perihilar distribution. This suggests that TBLB definitely has a role in diagnosis of ILD.

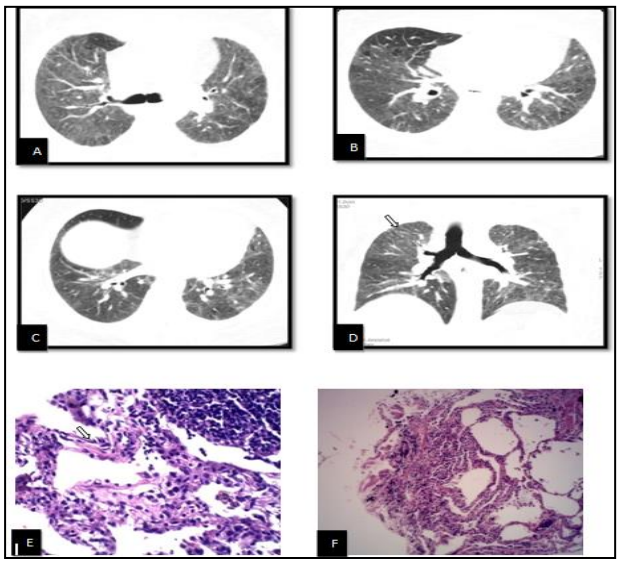

Figure 7: 52-Year-old male presenting with Shortness of breath and dry cough. A-D) HRCT lung images showing multiple areas of Ground glass Haze in b/l lung fields with no apico-basal gradient. Coronal reformatted image showing subpleural sparing along right upper lobe, E-F) HPE images acquired through TBLB showing dense lymphocytic infiltrate uniformly involving alveolar septae characteristic of NSIP. Note made of adjacent emphysematous changes.

Limitations

Limitations of current study were; small sample size of the study. Samples obtained through TBLB are usually small in size. TBLB could not adequately sample the desired areas because of the more peripheral distribution of most of the ILDs leading to lesser yield of TBLB in current study.

CONCLUSION

Thus, to conclude HRCT and TBLB alone do not have a high diagnostic value in diagnosing specific ILD subtype. But multidisciplinary approach helps in accurate diagnosis of ILD in many cases.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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