ORIGINAL ARTICLE

EVALUATION OF RADIO-PATHOLOGIC CORRELATION IN INTERSTITIAL PULMONARY DISEASE PATIENTS

Payam Mehrian, Saeid Fallah Tafti, Ali Cheraghvandi, Parham Montazeri, Firouzeh Talischi

Masih Daneshvari Hospital, Shahid Bahonar Blvd., DarAbad, Islamic Republic of Iran.

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ABSTRACT

BACKGROUND: The definition of ILD (interstitial lung disease) is diffuse parenchymal lung involvement due to various etiologies. ILD constitutes 15% of lung diseases. The first step in diagnosis is history, physical exam and focus on information about work exposure, environment, medications and history of symptoms related to collagen vascular diseases. Open lung biopsy or video-assisted thoracoscopic biopsy is performed when clinical information and HRCT are not diagnostic. The purpose of this study was to evaluate radio-pathologic correlation in interstitial lung diseases including sarcoidosis. **MATERIALS AND METHODS:** This was a cross-sectional observational study with chart review of patients with ILD attending our center since HRCT has been used here (since 1999). HRCT of all patients with ILD who had open lung biopsy was reviewed by radiologist in three steps. First was the clinico-radiologic report at the time of diagnosis. Second, after reviewing patient history, important clinical and paraclinical information (pertinent positives), HRCT was reviewed by single radiologist who was blinded to the initial readings. Third pathology of the patient was reviewed, giving three diagnoses which were compared with each other. Predicted diagnoses included UIP/IPF, NSIP, HP, BOOP pattern, and sarcoidosis. Demographic information was also obtained. **RESULTS:** In near 70%, clinicoradiologic diagnosis conferred with pathologic diagnosis and in the remaining 30%, open lung biopsy did not help with specific diagnosis. **DISCUSSION:** In our series of 15 patients, it seems that OLB had small place in reaching final diagnosis in ILD patients.

Key words: Lung Diseases, Interstitial; Radiology; Pathology; Association

Introduction

The definition of interstitial lung disease (ILD) is diffuse involvement of lung parenchyma due to various etiologies. ILD constitutes 15% of pulmonary diseases. Hundred and fifty illnesses exist with possibility of lung involvement under the term ILD. Some diseases were ILD can be found include idiopathic pulmonary fibrosis (IPF), sarcoidosis and collagen vascular diseases.[1-5]

The pathology in interstitial lung disease is often inflammatory and there is need for clinical and radiologic findings to reach a diagnosis that is of use. In ILD, pathologic finding is a result of diffuse parenchymal injury, inflammation and repair. It is the method of injury, acuity, severity and duration that form the final pathologic findings. Many patients can be managed based on clinical and radiologic patterns of disease and pathology may not be needed. Patients may present with acute, subacute or chronic disease. In the acute condition, it is important to consider infections and the immune status of the patient. Next is subacute (weeks to several months) like hypersensitivity pneumonitis. Finally, chronic (many months to years) such as rheumatic diseases. Because of limitation of clinical

Correspondence : Dr. Payam Mehrian
Masih Daneshvari Hospital,
Shahid Bahonar Blvd., DarAbad,
Islamic Republic of Iran.
Tel: 98 (21) 26105050
Email: payaman2000@yahoo.com

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information, radiology can be helpful. HRCT also provides gross pathology information. Major radiologic findings are: 1) ground glass opacity and consolidation (increased attenuation) such as seen in edema and infections; 2) reticulation and distortion of parenchyma (fibrosis) such as seen in Usual Interstitial Pneumonia; 3) nodules such as seen in carcinomas and sarcomas; 4) mosaic patterns and cysts such as in small-airways disease with constrictive bronchiolitis. Radiology helps with interpretation of lung biopsy. Main histopathologic patterns are acute injury (e.g. infection, drug reaction), fibrosis (e.g. pneumoconiosis), cellular infiltrates (e.g. hypersensitivity pneumonitis), airspace filling (e.g. pulmonary edema, acute bronchopneumonia), nodules (e.g. neoplasms) and minimal changes (e.g. pulmonary edema, subtle interstitial infiltrate, pulmonary emboli). Most ILD cases are given a descriptive diagnosis with a list of differential diagnoses. Histopathology also provides useful information regarding etiology, activity, age, reversibility and prognosis of an ILD. Sometimes, we can have overlying pathologies.[6]

ILD's have been divided into 4 major groups: known etiology (medications, collagen vascular disease, etc.), with unknown etiology, granulomatosis (like sarcoidosis) and other forms (such as LAM, lymphangiolyomyomatosis, and Histiocytosis X). Interstitial lung disease due to unknown etiology itself is grouped into 7 conditions: Usual Interstitial Pneumonia, Desquamative Interstitial Pneumonia, Acute IP, Nonspecific IP, Respiratory bronchiolitis ILD, Cryptogenic Organizing Pneumonia and Lymphocytic IP.[7]

The radiologic characteristics of UIP are reticular opacities in the bases and peripheral areas of the lung with honeycombing and traction bronchiectasis. In NSIP, ground glass opacities are found at the bases and are more pronounced than reticulonodular opacities and in advanced disease, traction bronchiectasis is seen. In RB-ILD and DIP, centrilobular nodules and ground glass opacities are found. In LIP, ground glass opacities and cystic lesions can be found. In AIP, diffuse involvement and ground glass opacities are found and usually end in fibrosis. At the end, diagnosis of ILD is by histology, but this histology can have its own radiologic appearance.[8]

The purpose of this study was a radio-pathologic correlation in interstitial lung diseases including sarcoidosis. Researchers of our study, planned to radiologically evaluate cases of ILD at Masih Daneshvari Hospital and compare results with pathologic and final clinicopathologic diagnosis. The latter may shed light into new information regarding radiologic diagnosis of DILD (Diffuse Interstitial Lung Disease) when HRCT is used.

Materials and Methods

This was a cross-sectional observational study with chart review of patients with ILD attending our center since HRCT has been used here (since 1999-2012). HRCT of all patients with ILD who had open lung biopsy was reviewed by radiologist in three steps. First was the clinico-radiologic report at time of diagnosis. The radiologist who read the HRCT for remainder of this study was blinded to the first report. Second, by reviewing patient history, important clinical and paraclinical information (pertinent positives), HRCT was reviewed by single radiologist. Third pathology of the patient was reviewed, giving three diagnoses which were compared with each other. In the last column of the results table, final diagnosis which was reached by clinician at time of diagnosis is recorded. Predicted diagnoses included UIP/IPF, NSIP, HP, OP pattern, and sarcoidosis. Demographic information was also obtained and reported as distribution.

All ILD patients based on computer data base were included who were in one of the following groups: precise diagnosis such as NSIP, HP and DIP, overlap diagnosis such as NSIP/UIP and HP/NSIP, patterns such as OP and NSIP pattern, had characteristics of ILD with CXR and CT in the chart. Patients were evaluated for information including medication, rheumatologic diseases, skin and joint findings, mucosal findings, for collagen vascular diseases and serologies were included based on clinical findings such as ACE, RF, ANA, C-ANCA, PANCA. Patients were excluded if they had diagnosis of ILD before coming to this center, had immune compromise status, were hemodynamically unstable and did not have pathology specimen.

All patients had HRCT without contrast. CT was

performed using spiral CT scanner (Somatom: Emotion, Siemens). Imaging parameters were 110 KVp, 120 mAs, slice thickness and collimation were 1mm. Imaging was from lung apices to bases. Images were viewed in standard lung windows settings (-600 HU, 1500HU).

The study was perfomed via chart review and patient personal information was held confident. Study was approved by hospital ethics committee.

Results

Clinical, radiologic, pathologic and final diagnoses are summarized in (Tab. 1).

No	Age and Gender	Clinico-Radilogic Diagnosis	Radiologic Diagnosis	Pathologic Diagnosis	Final Diagnosis
1	42 Year old Female	IPF/UIP Heart Failure	Fibrotic NSIP / UIP	Honey comb associated with chronic granulomatous inflamation	Honey combing/UIP Heart Failure
2	50 year old Female	HP / BOOP	NSIP / HP	HP / BOOP	HP
3	45 year old Female	Fibrotic NSIP	UIP	UIP	Fibrotic NSIP / UIP
4	30 year old Male	UIP / Fibrotic NSIP	Sarcoidosis	UIP	Fibrotic NSIP / UIP
5	81 year old Male	HP / sarcoidosis	Chronic TB/pulmonary fibrosis	Interstitial fibrosis and inflammation	Chronic HP / chronic sarcoidosis
6	23 year old Female	Chronic sarcoidosis	Chronic granulomatosis	Pulmonary veno-occlusive disease	Chronic sarcoidosis
7	30 year old Male	NSIP	NSIP	NSIP	NSIP
8	41 year old Male	NSIP	UIP	NSIP	NSIP
9	63 year old Male	BOOP / peripheral fibrotic changes	BOOP	ILD with marked interstitial fibrosis/ unclassified	BOOP / peripheral fibrosis nonspecific
10	33 year old Female	Chronic eosinopholic pneumonia / BOOP	Labular multiple scattered subpleural changes	Chronic eosinophilic pneumonia	Mild chronic eosinophilic pneumonia / BOOP
11	70 year old Female	ILD	ILD	ILD	ILD
12	45 year old Male	Early NSIP	Bilateral symmetric ground glass opacity with mild increased reticulation in RLL and LLL	Constrictive bronchiolotis obliterans	Early NSIP
13	66 year old Female	BOOP	BOOP	BOOP	BOOP
14	25 year old Male	Chronic sarcoidosis	Chronic sarcoidosis	Chronic HP	Chronic sarcoidosis
15	53 year old Male	ILD / HP	NSIP / HP	Suggestive HP	HP

Table 1: Clinical, radiologic, pathologic and final diagnosis of patients.

Cases were there was agreement between radiology and pathology included UIP, HP, NSIP and BOOP. Cases were the radiology and pathology disagreed included sarcoidosis instead of UIP, sarcoidosis instead of chronic HP and UIP instead of NSIP.

Discussion

Overall, in our observations, the patients formed two groups. In near 70%, clinicoradiologic diagnosis conferred with pathologic diagnosis and in the remaining 30%, open lung biopsy did not help with specific diagnosis.

For the patient who has previously been healthy and attends the clinic with chronic dyspnea and diffuse ground glass opacity in radiology, most common differential diagnosis considered include HP, DIP, RBILD, NSIP, sarcoidosis, OP pattern and finally UIP/IPF. Although rarer conditions such as PAP, bronchoalveolar carcinoma and/or lymphoma can also be considered. History of smoking is specifically and almost exclusively seen in patients with DIP and RB-ILD.[9,10]

Undoubtedly, complete clinical evaluation has a key place in the diagnosis of this group of patients with unknown cause. They include evaluation of patient history, chief complaint, involvement of other organs, detailed evaluation of drug history including OTC (over the counter) medications and naturopathic medications and finally the patient's medical, social, familial, and work history for evaluation of environmental factors is very important in reaching a diagnosis. Careful physical exam has a significant place in narrowing down the broad differential diagnosis.

Other than clinical findings, HRCT with sensitivity of more than 90% can be helpful in diagnoses that are probable with focus on history and clinical findings. HRCT can show pattern of mixed conditions such as emphysema and ILD and is a good tool for showing other abnormal findings in the hilum, pleura and mediastinum. HRCT can even show the different stages of inflammation such as granulomatous changes, fibrosis, advanced parenchymal destruction such as honey combing. It is important that open lung biopsy is utilized when after suitable work up, for which there is no clear

and satisfying definition, diagnosis is not reached. In these 15 patients that were discussed, in no cases has tissue biopsy changed clinico-radiologic diagnosis and has also not been able to change prognosis or care of the patients based on histologic findings. In an overall view of tissue diagnoses, significant correlation exists between tissue diagnosis and clinico-radiologic diagnosis, such that it is specifically consistent with the radiologic findings in the patient.

It seems that in certain specific patients where histologic diagnosis appears necessary, performing TBLB with high diagnostic yield might be helpful such as finding a granulomatous lesion in sarcoidosis or finding cancerous cells for alveolar carcinoma. As a result, tissue biopsy in the form of OLB as a final diagnosis prior to irreversible changes and fibrosis may be able to help with treatment and outcome of some patients but in most cases such as seen in these series of patients, tissue biopsy results have the same diagnostic and clinicopathologic and HRCT findings associated with it. It seems that after the discovery of HRCT, the phrase "the interval between discovery of the lesion and biopsy must be reduced" becomes less pronounced. It is true that when the ILD disease is in it's primary stages and radiologic findings are minimal, performing pulmonary physiologic tests such as the DLCO will show the severity of illness very well. It should not be forgotten that in general for reaching a definitive diagnosis for some forms of ILD such as HP and eosinophilic pneumonia, one can utilize more important diagnostic indices other than tissue diagnosis and that for elder patients or those with extensive honeycombing, OLB can be dangerous without a resulting therapeutic standpoint. As a result, even in conditions such as the presence of a mass in the setting of ILD or possibility of opportunistic infections in patients with immune deficiency, biopsy via fiberoptic bronchoscopy (TBLB) or CT guided biopsy can in most situations provide valuable diagnostic clues. Subsequently, it can be suggested that in more than 90% of patients with IPF/UIP without tissue biopsy, diagnostic clues are available. In the remaining cases also clinical evaluation and patient history, pulmonary physiologic testing and HRCT alongside with BAL, and TBLB tissue sampling can help reach correct diagnosis and OLB has acquired a less pronounced place compared to the past.[11-15]

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