Criteria for confident HRCT diagnosis of usual interstitial pneumonia (UIP)

Assem El Essawy (١) & Amr A. Nassef (٢)

Abstract

Identification of interstitial pneumonia (IP) was mainly based on histological criteria but now there is a well established role for high resolution CT (HRCT) where recent researches claims criteria for confident HRCT diagnosis of usual interstitial pneumonia (UIP). Interstitial pneumonia could be idiopathic; UIP or may be secondary to some causes such as collagen vascular disease, drugs or inhalation. Thus careful clinical and laboratory evaluation is required to identify the underlying cause. Our aim is to elaborate the HRCT diagnostic criteria of usual interstitial pneumonia.

Subjects & Methods: Twenty four patients [١٤ females and ١٠ males] with ages ranging from ٣٨ to ٦٢ years (mean age ٤٣.٦years) were included in this study. Patients presented with clinical symptoms suggestive of interstitial lung disease including history of progressive dyspnea and chronic dry cough. HRCT chest examination was done to all patients in Kasr-Al-Aini Radiology Department.

Results: All cases (١٠٠%) showed bilateral fairly symmetrical predominantly basal sub-pleural coarse reticulation, mounting to honey combing in ١٦ cases (٦٧%) . Few cases showed other features; six cases (٢٥%) showed superadded ground glass opacification. Two cases (٨.٣%) had evidence of air trapping and one case (٤.١٧%) had septal thickening. All cases (١٠٠%) showed decrease of lung volume bilaterally and traction bronchiectasis.

Conclusion: The presence of bilateral fairly symmetrical predominantly basal sub-pleural coarse reticulation mounting to honey combing on HRCT scan are diagnostic criteria of UIP.

Key Words: idiopathic interstitial pneumonia, high resolution CT, usual interstitial pneumonia

Contacts: Assem El Essawy: email:aelessawy@hotmail.com. Mobile: ٠١٠١٤١٤٩٤٩

(١) Chest Department faculty of medicine Fayoum University, (٢) Department of Radio diagnosis Faculty of Medicine Cairo University

Introduction

The American Thoracic Society–European Respiratory Society classification of idiopathic interstitial pneumonias (IIPs), published in 2002, defines the morphologic patterns on which clinical-radiologic-

pathologic diagnosis of IIPs is based. IIPs include seven entities: idiopathic pulmonary fibrosis, which is characterized by the morphologic pattern of usual interstitial pneumonia (UIP); nonspecific interstitial pneumonia (NSIP); cryptogenic organizing pneumonia (COP); respiratory bronchiolitis–associated interstitial lung disease (RB-ILD); desquamative interstitial pneumonia (DIP); lymphoid interstitial pneumonia (LIP); and acute interstitial pneumonia (AIP). The characteristic high resolution computed tomography findings in UIP are predominantly basal and peripheral reticular opacities with honeycombing and traction bronchiectasis. In NSIP, basal ground-glass opacities tend to predominate over reticular opacities, with traction bronchiectasis only in advanced disease. COP is characterized by patchy peripheral or peribronchovascular consolidation. RB-ILD and DIP are smoking-related diseases characterized by centrilobular nodules and ground-glass opacities. LIP is characterized by ground-glass opacities, often in combination with cystic lesions. AIP manifests as diffuse lung consolidation with ground-glass opacities, which usually progress to fibrosis in patients who survive the acute phase of the disease. Correct diagnosis of IIPs can be achieved only by means of interdisciplinary consensus and stringent correlation of clinical, imaging, and pathologic findings[١]..

Accordingly the clinician, radiologist and pathologist have complementary role in diagnosing type of IIP [٢].

Usual interstitial pneumonia (UIP) is the most common type of IP, while Cryptogenic organizing pneumonia (COP) is relatively common and desquamative interstitial pneumonia (DIP) and lymphocytic interstitial pneumonia (LIP) are relatively rare[٢].

On histological bases the UIP was found in up to ٥٠-٦٠% of IP, while non specific interstitial pneumonia (NSIP) in up to ١٥-٣٥% & DIP in up to١٠- ١٥ %[٢-٤].

The American Thoracic Society (ATS) has issued new official clinical guidelines on the diagnosis and management of idiopathic pulmonary fibrosis (IPF) and published this Joint Statement in the March ١٥, ٢٠١١ issue of the *American Journal of Respiratory and Critical Care Medicine*. According to this recent publication diagnosis of idiopathic pulmonary fibrosis (IPF) requires exclusion of known causes of interstitial lung disease such as domestic and

occupational/environmental lung exposures, connective tissue disease, and drug toxicity. Diagnosis also requires the presence of a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) scan [٥]. The most recent definition of IPF is actually: Idiopathic pulmonary fibrosis (IPF) is a discrete clinicopathologic entity defined by the presence of usual interstitial pneumonia on high-resolution CT scan and/or open lung biopsy and the absence of an alternate diagnosis or exposure explaining these findings[٦].

In HRCT, UIP should be considered in patients who present with low lung volumes, subpleural reticular opacities, macrocystic honeycombing, and traction bronchiectasis, the extent of which increases from the apex to the bases of the lungs . In the typical patient with UIP, the disease is most extensive on the most basal section of the high-resolution CT examination. Ground-glass opacities are present in the majority of patients with UIP but are usually limited in extent . Typically, imaging findings are heterogeneous, with areas of fibrosis alternating with areas of normal lung [١].

So our aim is to elaborate the CT diagnostic criteria of usual interstitial pneumonia in patients with IPF.

Subjects & Methods:

Twenty four patients [١٤ females and ١٠ males] with ages ranging from ٣٨ to ٦٢ years (mean age ٤٣.٦years) were included in this study. Patients presented with clinical symptoms suggestive of interstitial lung disease including history of progressive dyspnea and chronic dry cough. They were all subjected to thorough history taking, clinical assessment and laboratory evaluation for search of evidence any collagen disease , chemotherapeutic administration or history suggestive of pneumoconiosis.

Inclusion criteria: Patients with clinical symptoms suggestive of interstitial lung disease and showed positive HRCT findings.

Exclusion criteria: The following cases were excluded from our study:

١. Cases with collagen disease, chemotherapy treatment for any disease or with suspected pneumoconiosis were excluded from this study.

٢. Patient with any known chest disease as asthma or tuberculosis.

٣. Smokers.

٤. Patients with normal HRCT.

HRCT chest examination was done in Kasr-Al-Aini Radiology Department using the protocol in table ١.

Table ١ : Protocol for HRCT examination in Kasr Al-Aini

Preparation :None needed. **IV contrast :** None needed. **CT scanning** : CT scan examinations were performed using GE Light Speed Multislice ٤ channels present in the radiology department at Kasr Al- Aini hospital. The examination is done in supine position . A scout is taken with Kv ١٢٠ and mA ١٢٠ ,then helical scanning is done in caudo-cranial direction to minimize respiration artifacts , using detector row ٤, helical thickness ١.٢٥, pitch ١.٥:١, speed (mm/rot) ٧.٥, Detector configuration ٤ X ١.٢٥, beam collimation ٥.٠٠mm, interval ١.٠٠, gantry tilt ٠.٠, FOV depends on the patients' body built ,but is about ٣٥cm , Kv ١٢٠-١٤٠, mA ١٢٠-١٦٠ , total exposure time ١٦-٢٠sec during breath hold in inspiration . **The images** acquired are then sent to a separate workstation to be processed , manipulated and reconstructed . **Reconstruction technique :** Reconstruction of the images are done using reconstruction software available at the workstation to attain HRCT axial, coronal and sagittal images . Also mediastinal window images are done for each case.

Results:

All cases (١٠٠%) showed bilateral fairly symmetrical predominantly basal sub-pleural coarse reticulation mounting to honey combing in ١٦ cases (٦٧%) . Few cases showed other features; six cases (٢٥%) showed superadded ground glass opacification .Two cases (٨.٣%) had evidence of air trapping and one case (٤.١٧%) had septal thickening .All cases (١٠٠%) showed decrease volume of both lungs and traction bronchiectasis. **See table ٢**

Table ٢: Summary of HRCT findings

HRCT FINDING	NUMBER OF CASES	%	NUMBER OF FEMALES	NUMBER OF MALES
COARSE RETICULATION	٢٤	١٠٠%	١٤	١٠
HONEY COMBING	١٦	٦٧%	١٠	٦
GROUND GLASS OPACIFICATION	٦	٢٥%	٥	١
THICKENED SEPTAL LINES	١	٤.١٧%	١	-
AIR TRAPPING	٢	٨.٣%	٢	-
VOLUME LOSS	٢٤	١٠٠%	١٤	١٠
TRACTION BRONCHIECTASIS,	٢٤	١٠٠%	١٤	١٠
IRREGULAR PERIVASCULAR THICKENIG	١٨	٧٥%	١٣	٥
MEDIASTINAL LYMPHADENOPATHY	٢٠	٨٣.٣%	١٢	٨

Discussion

UIP is the most common form of chronic interstitial pneumonitis (١٠ to ٢٠ times more prevalent than DIP). Most cases occur sporadically, although familial forms have been reported. Patients typically present between the ages of ٥٠-٧٠ years with progressive dyspnea and a dry cough [٧] , Men are affected slightly more frequently than women [٨]. These were the most common clinical presentations in our study , however,

our age group was rather younger and we had more female than male cases.

UIP produces very characteristic findings on HRCT which can permit the proper diagnosis without the requirement for a lung biopsy [٧]. The American Thoracic Society and the European Respiratory Society concluded that the presence of characteristic features of IPF or UIP at thin-section CT allows a confident diagnosis and precludes the need for surgical biopsy [٩]. In about ٥٠% of cases, HRCT scan is sufficient to allow a confident diagnosis of IPF and lung biopsy can be avoided [٨]. The sensitivity of CT for the diagnosis of IPF is about ٦٣% and the specificity is about ٧٠% [٨]. The positive predictive value of a HRCT diagnosis of UIP is between ٧٠-١٠٠% [٧].

According to Muller-Mang and his colleagues the interstitial changes of UIP are predominantly peripheral. A hallmark of UIP is it's **patchy distribution** with a predilection for the lung bases particularly the sub-pleural regions of the posterobasal segments of the lower lobes (the central lung zones are spared until late in the course of the disorder). **Intra**lobular interstitial thickening is most commonly seen in patients with idiopathic pulmonary fibrosis and it produces a reticular or web-like pattern characteristically in the sub-pleural lung periphery. [١] These findings were clearly demonstrated in all our cases. They also described associated irregular septal thickening and intralobular (centrilobular) bronchovascular thickening that are sometimes noted. Irregular perivascular interstitial thickening is common and produces irregular interfaces between the lung and the pulmonary vessels. Septal thickening was recognized in only one of our case (٤.١٧%) while irregular perivascular thickening was detected in ١٨ of our cases (٧٥%). Subpleural lines can be seen, and may resolve following initiation of therapy-possibly representing resolution of atelectatic changes due to decreased lung compliance. None of our cases (٠%) showed this finding.

Dixon and Benamore, ٢٠١٠, [١٠] declared that the main aim of HRCT is to separate patients with typical features of IPF-UIP from the other IIPs. If the typical features are present, radiologists can make a confident diagnosis of UIP in greater than ٩٠% when compared to surgical lung biopsy as the reference standard, justifying non-invasive diagnosis. The typical features are reticulation, honeycombing and traction bronchiectasis, with basal and subpleural predominance. In the early stages there may only be

irregularity seen at the pleuraeparenchymal border at the lung bases, whilst extensive honeycombing is characteristic
in end-stage disease. Honeycombing is the strongest indicator of UIP on CT (with a ٩٠% positive predictive value, PPV), occurring in ٧٠-٨٠% of cases. Pathologically, honeycombing represents
destroyed and fibrotic lung tissue, with cystic air spaces (from a few millimetres to several centimetres) with thick fibrous walls, indicating end-stages of the disease. This correlates on HRCT with clustered cystic air spaces of varying sizes with well-defined walls in a subpleural, predominantly lower zone location.

In the setting of interstitial lung disease the presence of areas of ground glass opacity have been shown to reflect active parenchymal inflammation (in ٦٥-٨٥% of cases), provided that these areas are **not** associated with evidence of fibrosis, traction bronchiectasis, or bronchiolectasis. Which is according to Flaherty and colleagues , and Lynch and colleages, is because ground glass attenuation may merely reflect chronic interstitial fibrosis which appears as ground glass density due to partial volume averaging with cystic changes that may be too small to be resolved anatomically [١١,١٢]. This was actually the case with our six patients (٢٥%) that showed ground glass opacification on top of the coarse reticulation pattern.

Late in the disorder there is honeycombing, traction bronchiectasis, and considerable architectural distortion. Honeycombing can be found in up to ٩٦% of patients with end-stage idiopathic pulmonary fibrosis. The honeycomb cysts usually range from ٢ to ٢٠ mm, typically share walls, and frequently occur in several layers in the sub-pleural lung[١٣-١٦].

Pleural disease is not a feature of UIP. Occasionally, dense subpleural pulmonary fibrosis may mimic pleural thickening [١٤]. None (٠ %) of our cases showed pleural lesions.

Enlarged mediastinal nodes can be found in ٥٥% to ٦٦% of patients with idiopathic pulmonary fibrosis [١٧,١٨]. Sub centimetric right paratracheal lymph nodes were seen in ٢٠ of our cases (٨٣.٣%). No larger lymph nodes were detected, none showed calcification or breaking down, they were all discrete and were considered insignificant by CT.

Conclusion

Confident UIP diagnosis by HRCT can be made. The presence of coarse

reticular abnormalities with bibasilar and sub-pleural predilection, honeycombing, that may be accompanied with minimal ground glass opacities on HRCH scan are diagnostic criteria of UIP. Thus, because of the high degree of accuracy of HRCT, no biopsy will be needed except in the minority of cases where atypical patterns are present.

References

١. Muller-Mang C, Grosse C. ,Schmid K,et al.What Every Radiologist Should Know About Idiopathic Interstitial Pneumonia. Radiographics ٢٠٠٧; ٥٧:٥٩٥-٦١٥.

٢. Katzenstein AL, Myers JL. Idiopathic pulmonary fibrosis: clinical relevence of pathologic classification. Am J Respir Crit Care Med ١٩٩٨; ٥٧:١٣٠١-١٣١٥.

٣. Bjoraker J, Ryu J,Edwin, et al. prognostic significance of histopathologic subsets in idiopathic pulmonary fibrosis. Am J, Respir Crit Care Med ١٩٩٨,١٥٧:١٩٩-٢٠٣.

٤. Nicholson AG, Colby TV, du Bois RM, et al. the prognostic significnae of the histologic pattern of interstitial pneumonia in patients presenting with the clinical entity of cryptogenic fibrosing alveolitis. Am J Respir Crit Care Med ٢٠٠٠, ١٦٢: ٢٢١٣-٢٢١٧.

٥. Raghu G,Collard HR, Egan JJ, et al. American Thoracic Society Documents An official ATS/ERS/JRS/ALAT Statement: idiopathic pulmonary fibrosis : evidence-based guideline for diagnosis and management. Am J Respir Crit Care Med ٢٠١١ ,١٨٣(٦): ٧٨٨-٨٢٤.

٦. Gan Y, Herzog EL,Gomer RH. Pirfenidone treatment of idiopathic pulmonary fibrosis. Ther Clin Risk Manag. ٢٠١١; ٧: ٣٩–٤٧.

٧. Lynch DA , Newel JD Jr, Cool C ,et al. Idiopathic interstitial pneumonia : CT features. Radiology ٢٠٠٥;٢٣٦:١٠-٢١.

٨. Souza CA, Műller NL ,Flint J. ,et al. Idiopathic pulmonary fibrosis :spectrum of High –resolution CT findings. AJR ٢٠٠٥; ١٨٥:١٥٣١-١٥٣٩.

٩. Sumikawa H, Johkoh T, Ichikado K, et al . Usual interstitial pneumonia and chronic idiopathic interstitial pneumonia : analysis of CT appearance in ٩٢ patients. Radiology ٢٠٠٦; ٢٤١:٢٥٨-٢٦٦.

١٠. Dixon S and Benamore R. The idiopathic interstitial pneumonias: understanding key radiological features. Clinical radiology ٢٠١٠, ٦٥ ٨٢٣-٨٣١.

١١. Flaherty KR, Toews GB, Travis WD, et al. clinical significance of histological classification of idiopathic interstitial pneumonia. Eur Respir J ٢٠٠٢,١٩:٢٧٥-٢٨٣.

١٢. Lynch DA . International concensus of idiopathic interstitial pneumonia. Society of Thoracic Radiology Course Syllabus ٢٠٠٠; ٥٢-٥٦.

١٣. Hyland RH , Gordon DA, Broden I ,et al. A systematic controlled study of pulmonary abnormalities in rheumatoid arthritis. Chest ١٩٩٥;١٠٨:١٠٩-١١٥.

١٤. Johkoh T, Muller NL, Cartier Y, et al, idiopathic interstitial pneumonias: diagnostic accuracy of thin section CT in

١٢٩ patients. Radiologiy ١٩٩٩, ٢١١:٥٥٥-٥٦٠.

١٥. Hunninghake GW, Lynch DA, Calvin JR, et al. radiologic findings are strongly associated with a pathologic diagnosis of usual interstitial pneumonia. Chest ٢٠٠٣,١٢٤:١٢١٥-١٢٢٣.

١٦. Akira M, Hamada H, Sakatani M, et al. CT findings during phase of accelerated deterioration in patients with idiopathic pulmonary fibrosis AJR Am j Roentgenol ١٩٩٧,١٦٨:٧٩-٨٣.

١٧. Jung JI, Kin HH, Jung YJ, et al. mediastinal lymphadenopathy in pulmonary fibrosis: correlation with diasease severity. J comput assist tomogr ٢٠٠٠,٢٤:٧٠٦-٧١٠.

١٨. Souza CA, Muller LN ,Lee KS, et al. Idiopathic interstitial pneumonia :prevelance of lymph ,nodes enlargement in ٢٠٦ patients. AJR ٢٠٠٦, ١٨٦; ١٩٥-١٩٩.