Diagnosis Of Interstitial Pulmonary Fibrosis-An Update

Adesh Kumar * , Ashish Kumar Gupta, Mohd Haroon Khan*****

*Associate Professor, **Assistant Professor, , ***Assistant Professor, *,**Department of Pulmonary Medicine, Rural Institute of Medical Sciences & Research Safai, Etawa U.P.India.***Department of Community Medicine, SHKM Govt. Medical College, Nalhar,(Mewat) Haryana. India.

Abstracts: The most common and most lethal type of idiopathic interstitial pneumonia (IIP) is idiopathic pulmonary fibrosis (IPF), which accounts for 55% of lung diseases classified as IIPs. Diagnosis of IPF requires precision and a multidisciplinary approach .Indeed, an early and accurate diagnosis of IPF is critical for a better outcome, especially with the advent of new specific treatments for this disease. The previous guidelines using major and minor criteria for the clinical (i.e. non-pathological) diagnosis of IPF have been discarded, as it is now clear that, in an appropriate clinical setting, the presence of a classical UIP pattern on the HRCT scan is sufficient for a diagnosis of IPF to be made. In the presence of the four classical features, that together accurately identify a Usual interstitial pneumonia (UIP) pattern, a definitive diagnosis of IPF can be made. Guidelines emphasizes the importance of multidisciplinary discussion between clinicians, radiologists and pathologists to improve diagnostic confidence. The course of disease in IPF is unpredictable, but the importance of an early diagnosis is clear, as individuals with less severe lung function abnormalities have a better prognosis. [Adesh K NJIRM 2014; 5(3) :122 - 125]

Key Words: Idiopathic interstitial pneumonia, idiopathic pulmonary fibrosis, acute interstitial pneumonitis

Author for correspondence: Dr. Mohd. Haroon Khan**;** Community Medicine, SHKM Govt. Medical College, Nalhar (Mewat) Haryana India, 122107. M: 08199001421; Email: drharoonkhan99@yahoo.com

Interstitial Pulmonary Fibrosis (IPF) is characterized by an inexorable progression of interstitial fibrosis resulting in restrictive lung disease and worsening gas exchange leading to death from respiratory failure within 5 years of diagnosis.

Historical Perspective: Reviewing the history of IPF will both clarify the present terminology and distinguish contemporary nomenclature from the outmoded terms encountered in earlier literature.

Fibrosis of the lung was long recognized in association with infection or dust inhalation. In te nineteenth century pulmonary fibrosis was known as cirrhosis of the lung.

In 1944 Louis Hamman and Arnold Rich[1] published a paper describing acute diffuse interstitial fibrosis of the lung. Hamman and Rich reported a series of unusual cases that showed a unique clinical presentation featuring idiopathic sub acute respiratory failure followed by death. Their report was complete with pathological finding from autopsy. They described thicking of alveolar interstitial cases of Hamman and Rich best fit a diagnosis of the fibrosing interstitial pneumonia known as acute interstitial pneumonitis. So it remained for the next three decades.

In 1969 Liebow and Corringto[1] heralded the modern era of interstitial lung disease histopathology with the notion that idiopathic interstitial pneumonia could be split into separate pathological subtype.

In 2002 a panel of expert of American Thoracic Society and the European Respiratory Society[2] released an official statement for the purpose of providing a new and comprehensive classification of IIPs that considered all clinical radiographic and pathological features.

Previously, in the absence of surgical lung biopsy (SLB), the presence of all four major criteria and three out of four minor criteria were required in order to determine that the diagnosis was consistent with IPF[2]. The four major criteria were (1) exclusion of other known causes of interstitial lung disease, such as certain drug toxicities environmental exposure and connective tissue disease (2) abnormal lung function studies that include evidence of restriction (reduced VC, often with an increased forced expiratory volume in 1s/FVC ratio) and impaired gas exchange (increased alveolar-arterial oxygen tension difference with rest or exercise or decrease diffusing capacity of the lung for carbon mono-oxide) (3) High resolution computed tomography (HRCT) scans showing bibasilar reticular

abnormalities with minimal ground glass opacities and (4) transbronchial lung biopsy TBB or bronchoalveolar lavage showing no features to support on alternative diagnosis.

The four minor criteria were (1) age>50 yr (2) insidious onset of otherwise unexplained dyspnea (3) duration of illness of 3 months and (4) bibasilar, inspiratory crackle dry or "Velcro" type in quality.

Diagnostic criteria for IPF: The first step, based on background investigation and physical examination, is to exclude known causes of ILD, e.g. certain drug toxicities, environmental exposures and connective tissue disease-associated ILD. Another important step based on thoracic CT and pathology consists of differentiating IPF from other IIPs, particularly nonspecific interstitial pneumonia (NSIP), but also desquamative interstitial pneumonia, respiratory bronchiolitis-associated ILD, acute interstitial pneumonia, cryptogenic organising pneumonia and lymphocytic interstitial pneumonia[2,3] Findings on chest radiographs (CXR) of patients with IPF include peripheral reticular opacities that are most profuse at the lung bases[4]. However, several studies have evidenced the superior accuracy of high-resolution CT (HRCT) compared to CXR, since HRCT can identify abnormalities before they become visible on a CXR and confer more specificity[5], due to thin-section HRCT which increases spatial resolution and facilitates the visualisation of parenchymal detail to the level of the pulmonary lobules. The finding of a usual interstitial pneumonia (UIP) pattern on HRCT may be sufficient to diagnose IPF, with no need for surgical lung biopsy (SLB).

A UIP Pattern On HRCT Relies On The Following Four Criteria: 1) Subpleural basal predominance; 2) reticular abnormality; 3) Honeycombing with or without traction bronchiectasis; 4) Absence of features known to be inconsistent with the UIP pattern, e.g. condensations, nodules or pre-eminent ground glass [6-7].

In 2011, the American Thoracic Society (ATS), the European Respiratory Society (ERS), the Japanese Respiratory Society (JRS) and Latin American Thoracic Society (ALAT) issued an official joint statement providing guidance for the diagnosis and management of IPF[3]. These guidelines include a revision of the diagnostic criteria (1) Exclusion of other known caused of ILD (domestic and occupational environmental exposure, connective tissue disease and drug toxicities) (2) The presence of a usual interstitial pneumonia (UIP) pattern on the HRCT scans in individual not subjected to SLB and (3) specific combination of HRCT and SLB pattern in individual subjected to SLB.

The previous guidelines using major and minor criteria for the clinical diagnosis of IPF have been discarded, as it is now clear that, in an appropriate clinical setting, the presence of a classical UIP pattern on the HRCT scans is sufficient for the diagnosis of IPF to be made[2].

Radiological Features of IPF: The features of a classical UIP pattern on HRCT require (1) the presence of sub-pleural abnormalities predominantly at the based, (2) Reticular abnormality, (3) honeycombing with or without traction bronchiectasis and (4) the absence of features that are inconsistent with UIP pattern (upper or middle lobe predominance, peribronchovascular predominance, extensive ground glass abnormality greater than reticular abnormality, profuse micronodules, discrete multiple cysts away from areas or honeycombing, diffuse mosaic attenuation /air trapping, or consolidation in bronchopulmonary segments/lobes[8]. If honeycombing with or without traction bronchiectasis is absent then the diagnosis using HRCT can only be possible. Notably, for those individual with HRCT scans features falling into the category of "possible UIP patterns" or inconsistent with UIP pattern, further diagnostic evaluation is required[3].

Histopathological Features Of IPF: The histopathological pattern of UIP is characteristically heterogeneous, predominantly sub-pleural, basal, bilateral and patchy in appearance[3]. For the definitive diagnosis of UIP, the following features are required to be present (1) marked fibrosis/architectural distortion with or without honeycombing in a predominantly sub-pleural/paraseptal distribution (2) patchy

involvement of lung parenchyma by fibrosis and (3) presence of fibroblast foci.

Probable UIP Pattern Include Following Criteria (1) evidence of marked fibrosis/architectural distortion ± honeycombing (2) absence of either patchy involvement or fibroblastic foci, but not both (3) absence of features against a diagnosis of UIP suggesting an alternative diagnosis or (4) honeycombing changes only.

Criteria For Possible UIP Pattern are (1) patchy or diffuse involvement of lung parenchyma by fibrosis with or without interstitial inflammation (2) absence of other criteria for UIP (3) absence of features against a diagnosis if UIP.

Features Against The UIP Pattern are (1) hyaline membrane (2) organizing pneumonia (3) granulomas (4) marked interstitial inflammatory cell (5) predominantly airway centered changes (6) other features suggestive of an alternative diagnosis.

Diagnosis Algorithm For IPF: The 2011 guidelines provide a diagnostic algorithm for IPF[3]. Individual with suspected IPF (i.e. individual with unexplained dyspnea or exertion and or cough with evidence of ILD) should be carefully evaluated for identifiable causes of ILD. In the absence of an identifiable cause for ILD, a HRCT demonstrating a UIP pattern is diagnostic of IPF. In the absence of a UIP pattern on HRCT, IPF can be diagnosed by the combination of specific HRCT and histopathological patterns.

Other Investigation In Diagnosis: BAL cellular analysis has been used for many years in the diagnosis of several ILDs. When evaluating individual with suspected IPF, BAL is useful in excluding other conditions, especially chronic HP, for which a diagnosis is suggested by lymphocytosis >40%[3]. The 2011 guideline recommend, however, that BAL cellular analysis should not be performed in the diagnosis evaluation of IPF in the majority of individual, but may be appropriate for a minority. The evidence regarding whether or not BAL adds significantly improved diagnostic specificity is presently unclear [3].

TBB has been shown to be useful in the evaluation of conditions that are predominantly bronchocentric and that can be diagnosed from the relatively small samples that can be obtained by TBB, for examples sarcoidosis, especially in those relatively rare instances when the disease mimics IPF by having a UIP pattern on HRCT[9-11]

With regard to the use of TBB as a diagnostic procedure in IPF, its sensitivity and specificity are unknown, even when the biopsy material shows histological features of UIP[12].

The 2011 guidelines do not recommend the use of TBB in the evaluation of IPF in the majority of individual, but it may be helpful in a minority[3].

Serological testing for connective tissues diseases is recommended for the diagnostic evaluation of IPF in the majority of individuals even in the absence of sign or symptoms of connective tissue disease, but may not be appropriate for all individual. In addition, there is very low quality evidence for the use of serological testing. However, it is valuable to exclude connective tissue disease, as this may present with a UIP pattern and it is recognized that this group of individual generally have a better outcome than those who have idiopathic disease[13].

Conclusion: The previous guidelines using major and minor criteria for the clinical diagnosis of IPF have been discarded, as it is now clear that, in an appropriate clinical setting, the presence of a classical UIP pattern on the HRCT scan is sufficient for a diagnosis of IPF to be made Early diagnosis of IPF is, therefore, a critical factor for improved prognosis, as individuals with early disease have less severe lung function abnormalities. Multidisciplinary discussions between experts in pulmonology, radiology and pathology will remain the cornerstone to improving the confidence in diagnosing IPF early and accurately, and facilitating the early use of effective therapies as they emerge from the pipeline.

References:

1. Eric B.Meltzer, Paul W.Noble: Idiopathic pulmonary fibrosis, Fishman's pulmonary

diseases and disorders 4th edition vol I 2008;1143-1160.
2. American Thoracic Society, European Respiratory Society. American Thoracic Society/ European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med 2002;165: 277-304.
3. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med 2011; 183: 788-824.
4. Nishimura K, Kitaichi M, Izumi T, et al. Usual interstitial pneumonia: histologic correlation with high-resolution CT. Radiology 1992; 182: 337-342.
5. Aziz ZA, Wells AU, Bateman ED, et al. Interstitial lung disease: effects of thin-section CT on clinical decision making. Radiology 2006; 238: 725–733
6. Schmidt SL, Sundaram B, Flaherty KR. Diagnosing fibrotic lung disease: when is high-resolution computed tomography sufficient to make a diagnosis of idiopathic pulmonary fibrosis? Respirology 2009; 14: 934–939.
7. Sumikawa H, Johkoh T, Colby TV, et al. Computed tomography findings in pathological usual interstitial pneumonia: relationship to survival. Am J Respir Crit Care Med 2008; 177: 433–439.
8. Hansell DM, Bankier AA, Macmohan H, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008; 246: 697-722.
9. Hunninghake GW, Zimmerman MB, Schwartz DA, et al. Utility of a lung biopsy for the diagnosis of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2001; 164: 193-196.
10. Raghu G, Mageto YN, Lackhart D, et al. The accuracy of the clinical diagnosis of new-onset idiopathic pulmonary fibrosis and other interstitial lung disease: a prospective study. Chest 1999; 116: 1168-1174.
11. Flaherty KR, Thwaite EL, Kazerooni EA, et al. Radiological versus histological diagnosis in UIP and NSIP: survival implications. Thorax 2003; 58: 143-148.
12. Berbescu EA, Katzenstein AA, Snow JL, et al. Transbronchial biopsyin usual interstitial pneumonia. Chest 2006; 129: 1126-1131.
13. Park JH, Kim DS, Park IN, et al. Prognosis of fibrotic interstitial pneumonia: idiopathic versus collagen vascular disease-related subtypes. Am J Respir Crit Care Med 2007; 175: 705-711.

Conflict of interest: None
Funding: None