Comments

Lessons from the interstitial lung disease-India registry: A proposed practical scheme of classification of diffuse parenchymal lung diseases in the Indian subcontinent

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Abstract

The revelation of interstitial lung disease India registry leads one to consider a revisit into the classification of diffuse parenchymal lung disease that would be clinically relevant for the Indian subcontinent. The author ponders that a simple clinical classification based on steroid sensitivity may be worthwhile.

KEY WORDS: Diffuse parenchymal lung disease, hypersensitivity pneumonitis, high-resolution computed tomography chest, CTD-ILD(connective tissue disease associated ILD), Sarcoidosis

Introduction

The interstitial lung disease India registry has made us understand that diffuse parenchymal lung disease (DPLD) in India, unlike the western world, is mostly secondary to hypersensitivity pneumonitis (HP)[1] that forms a roughly 70% bulk of all DPLDs with Connective tissue disease (CTD) - associated DPLD and sarcoidosis.[1] The common qualities of these three conditions are (a) predominantly lymphocytic parenchymal inflammation and (b) their treatability with steroid. This makes us rethink of DPLD and question our approach regarding whether should we move from an idiopathic pulmonary fibrosis-dominated algorithm to a HP-dominated one.

One may propose to classify all acquired DPLD far simply as steroid sensitive, steroid nonsensitive, and with unknown steroid sensitivity [Table 1]. The former (the “steroid-sensitive” group) consists of entities with confirmed or possible diagnosis of sarcoidosis, chronic HP and connective tissue disease (CTD) -associated DPLD.

On the contrary, IPF and fibrotic nonspecific interstitial pneumonia (NSIP) remain clearly “steroid nonsensitive.”

This proposed approach to classify a DPLD patients should start from history and clinical exercises already well elaborated in standard texts and should be followed by radiological interpretation, especially from high-resolution computed tomography (HRCT) chest [Figure 1]. IPF is clearly delineated into confident and possible on HRCT criteria.[2] The diagnosis of chronic HP is often not difficult as HRCT chest can confidently discriminate HP from other DPLDs[3] as certain HRCT features are found highly suggestive of HP-associated DPLD.[4,5] The HRCT features of collagen vascular diseases especially when unaccompanied by clinical clues poses difficulty in diagnosis. A recently published American Thoracic Society (ATS) - European Respiratory Society statement has tried to characterize these members of DPLD (with suspected but not having the classical features of CTD)

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with a name as interstitial pneumonia with autoimmune features (IPAF). This entity of IPAF may thus qualify to be the “possible” collagen vascular disease (CVD) related DPLD. Incidentally, the so-called “sure” or “possible” abnormality pattern is already proposed for sarcoidosis (as typical and atypical) and upcoming for HP. The left out cases of DPLD consisting of the “unknown” or “difficult to classify” patients should be dealt with multidisciplinary discussion (MDD). This identification of the DPLD with such “sure” or “possible” connotation certainly finds scope of support from the serological tests for sarcoidosis (serum angiotensin-converting enzyme), HP (IgG precipitin tests), and CVD (rheumatoid factor, antinuclear antibody, and further profile of autoantibodies).

This approach to classification can be strengthened further with fiberoptic bronchoscopy and bronchoalveolar lavage fluid (BALF) analysis for all and selective transbronchial lung biopsy plus-minus transbronchial needle aspiration in cases of suspected sarcoidosis or malignancy. Incidentally, the use of BALF is still not popular although it helps to diagnose DPLD from occupational exposures to inorganic dust, malignancy, hematological disease, drug-induced lung disease, and pulmonary alveolar proteinosis with confidence and sarcoidosis or HP with very high accuracy. In addition, its role for detection or exclusion of infection is unambiguous. Once tuberculosis and fungal infections are ruled out, BAL lymphocytosis with differential count of lymphocytes as over 25% is very likely caused by sarcoidosis or HP or drug toxicity although such lymphocyte count is also observed in cryptogenic organizing pneumonia, cellular type of NSIP, lymphoid interstitial pneumonia (LIP), or non-LIP

![Figure 1](image-url)

**Figure 1:** Flowchart showing the diagnostic algorithm for diffuse parenchymal lung disease with interpretations (abbreviations used are HP: Hypersensitivity pneumonitis, CTD-ILD: Connective tissue disease-associated interstitial lung disease, IPF: Idiopathic pulmonary fibrosis, NSIP: Nonspecific interstitial pneumonia, BALF: Bronchoalveolar lavage fluid, FOB: Fiberoptic bronchoscopy, TBLB: Transbronchial lung biopsy, SACE: Serum angiotensin-converting enzyme)
lymphoproliferative disorders.[10] Even in the face of classical HRCT diagnosis of usual interstitial pneumonia, BALF lymphocytosis >30% is a strong indicator of an alternate diagnosis than IPF.[10] Ideally, the workup for DPLD should not spare even a single patient who is not steroid resistant. Further to lymphocytosis, the CD4 to CD8 ratio in BALF may be of use since it gets skewed in favor of CD4 cells in sarcoidosis while the opposite is found in HP-associated DPLD.[11,12] Incidentally, lymphocyte count may not rise in BALF of chronic HP and on the contrary can be raised in exposed asymptomatic individuals without having the disease.[13] The BALF lymphocytosis should better be interpreted in the light of clinical and HRCT features as the BALF cellularity-related information and issues are vast and variable.[14] The BALF cellularity-based algorithm in DPLD forwarded by the ATS, therefore, demands judicious application to ensure its usefulness.[14]

Once the diagnostic exercise remains inconclusive after clinical, HRCT, serological, and bronchoscopic evaluations, one should resort to lung biopsy (open or thoracoscopy guided) preferably with concurrence from an MDD, whenever possible.

The identification of steroid sensitivity makes the treatment approach simpler. While the steroid-sensitive patients will be treated with systemic steroid with or without immunosuppressive agents, the steroid-nonsensitive patients will be treated with antifibrotic drugs (pirfenidone or nintedanib) with or without antioxidant N-acetyl cysteine.

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Conflicts of interest
There are no conflicts of interest.

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