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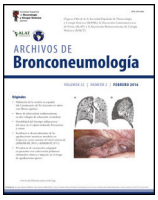

Editorial

Does Idiopathic Pulmonary Fibrosis Differ From Other Fibrosis? A Proposed Method for Identifying the Causes☆

¿Es la fibrosis pulmonar idiopática una entidad diferente del resto de las fibrosis? Propuesta para buscar las causas

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In 1969, Liebow[1] made the first classification of idiopathic interstitial pulmonary diseases (IPD). According to Saldaña, Professor Liebow often used to say, while visualizing IPD biopsies under the microscope: "put this report in the usual pile", meaning the group which did not have the characteristics of any of the other entities. This is where the moniker "usual" came from, and has led to the entity being called usual interstitial pneumonia (UIP).

The Path to UIP Characterization

In 2000, the ATS/ERS consensus on idiopathic pulmonary fibrosis (IPF) was published,[2] in which IPF was recognized as a separate clinical entity, defined as a disease of unknown origin, limited to the lung, with UIP histology, after ruling out collagen vascular disease, drug toxicity and environmental causes[2] (but not smoking). This classification excluded patients with fibrosis without histological criteria for UIP that are currently categorized under "Unclassifiable Interstitial Pneumonias",[3] or possible UIP or non-UIP.[4]

In the 2000 consensus,[2] the supporters of IPF based their recommendation for a surgical biopsy in most cases on some studies in which paradoxically only 33% of IPF patients had undergone surgical biopsy.

Persisting diagnostic doubts surrounding IPF led to the publication of new consensus guidelines in 2002 accepting that a picture of UIP can be seen on HRCT in cases of asbestosis, collagen disorders, hypersensitivity pneumonitis (HP), and in some advanced stages of sarcoidosis.[3]

Ten years later, in 2011, diagnostic difficulties persisted, a committee of experts drew up a new position statement[4] that graded the evidence available (high, moderate, low, or very low), and made a recommendation (yes or no, strong or weak), based on a majority vote.

The conclusion emerging from this democratic process was that after excluding the known causes of IPD, a patient can be diagnosed with IPF merely on the basis of a characteristic HRCT image (or a combination of HRCT and biopsy). Nonetheless, recognizing that HRCT images may not be so clear cut, the authors classify patterns as definitive UIP, possible UIP, and non-UIP. They also subdivide UIP histological patterns into definitive, probable or possible UIP and non-UIP.[4]

All these classifications and subdivisions underline the difficulty of making a definitive IPF diagnosis, even for experts. Indeed, we now know that diagnostic concordance in the interpretation of an HRCT pattern of UIP among radiologists,[5] or a UIP pattern among pathologists[6] is at most moderate. These diagnostic difficulties have led authors to call on radiologists, pathologists and pulmonologists at each hospital to establish a new multidisciplinary diagnostic consensus for the final classification of UIP or non-UIP.[4]

All these consensus or voted guideline recommendations, together with the need to subdivide the classification of images and to seek out multidisciplinary consensus, illustrate the difficulties encountered in differentiating between IPF/UIP and non-UIP fibrosis in routine clinical practice.

Bearing in mind that after a comprehensive diagnostic study at least 42% of patients with a diagnosis of IPF are found to have chronic hypersensitivity pneumonitis (HP),[7] IPF/UIP seems even less likely to be an independent clinical entity. The confusion increases further if we take into account that some IPF (UIP/emphysema) are caused by smoking.

What happens to patients with pulmonary fibrosis who do not meet the criteria for IPF? Do they have a different etiology, clinical laboratory tests or clinical course, or is the difference purely morphological? Indeed, both are idiopathic fibrosis (if not, they would have been diagnosed as HP or asbestosis, collagen disorders, fibrosis/emphysema, etc.), but, according to the guidelines, these patients would be diagnosed as having non-UIP pulmonary fibrosis or "Unclassifiable Idiopathic Interstitial Pneumonia".[8] Can this group be said to be different from the IPF group? And can

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we identify these patients and withhold the administration of corticosteroids, antifibrotics, etc., on the basis of such imprecise diagnostic criteria?

Given the Difficulty in Differentiating Between UIP and Non-UIP Histology and HRCT Patterns and Therefore in Identifying IPF, We Propose That

The etiology of the pulmonary fibrosis, whether it presents with UIP criteria or not, must be identified. To achieve this, a full case study must be performed in a tertiary hospital, consisting of a comprehensive, reiterative clinical history gathered by an expert, clinical laboratory test including a battery of anti-tissue antibodies and specific IgG antibodies (ELISA) to a panel of molds, serum (not stools) from various birds, and feather extracts, etc.[7] Naturally, HRCT, bronchoalveolar lavage, and cryobiopsies should be obtained systematically. If any material is suspected (feathers, mold patches on walls, etc.), these will be cultured for fungi. Finally, if there is good reason to suspect an organic etiology, a bronchial challenge test with that antigen will be performed, with the aim of confirming any causal relationship. The bronchial challenge test in pneumonitis (and in fibrosis) has been validated in several recent publications.[9]

Moreover, any relationship between the IPF and smoking must be ruled out using the diagnostic criteria recommended by experts.[10]

This systematic study will greatly reduce the need for surgical biopsy[11] and its associated drawbacks, complications, and possible death.

An etiological diagnosis of fibrosis, preferably without surgical biopsy, is essential to prevent new cases and avoid or reduce exposure to the antigen, thus improving prognosis[12], and tailor treatment. If chronic HP is diagnosed, corticosteroids are recommended.

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