Usual interstitial pneumonia: a pattern or a disease? A reflection upon the topic

Pneumonia intersticial usual: um padrão ou uma doença? Reflexão sobre o assunto

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"The history of medicine is the history of distinguishing one condition from another." Lester S. King

To the Editor:

There are many ways in which a set of biological variables (clinical, laboratory, or histological variables) can characterize a distinct disease. In modern medicine, a nosological entity is most commonly determined by the primary factor responsible for the disease. Nevertheless, when the etiologic factor is unknown, a syndromic approach is the surrogate approach for establishing a diagnosis.

The Brazilian Thoracic Association Guidelines for Interstitial Lung Diseases[1] have recently been published. In conformity with the official 2011 American Thoracic Society Statement, idiopathic pulmonary fibrosis (IPF) is defined as a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, occurring primarily in older adults, being limited to the lungs, and being associated with the histopathological/radiological pattern of usual interstitial pneumonia (UIP), the diagnosis of IPF requiring the exclusion of other forms of interstitial pneumonia.[1,2] It is a syndromic approach to diagnosis, given that the essential etiologic factor remains unknown.

Typically, guidelines on a given subject gather the most relevant information available at the time, providing an excellent opportunity for a critical analysis of the subject in question. In this context, we would like to spark off a debate by asking the following question: would UIP be considered a disease in its own right if the accumulated evidence were viewed in a different light?

Because UIP has such a peculiar histological pattern, chest HRCT is able to predict the histological features of UIP with a great degree of confidence in some typical cases, dispensing with a biopsy.[2]

The uniqueness of UIP is determined by the process of fibrosis formation (peripheral, with temporal and spatial heterogeneity, and minimal inflammation). It is a maladaptive repair process regardless of whether it is idiopathic or related to other diseases.[3] This unique fibrotic process is designated IPF when it is not associated with other diseases. However, from a nosological point of view, the real difference between UIP related to other conditions (such as collagen vascular diseases and hypersensitivity pneumonitis) and its "idiopathic" form is unclear.

We should now turn back to our initial considerations. When proposing that UIP be considered a disease in its own right, we took into consideration the characteristics that define a nosological entity. The histological features of UIP are distinctive enough to characterize a disease:

- A disease of the lung repair process, UIP results in a peculiar form of fibrotic deposition, regardless of its relationship with other diseases (such information, i.e., the context in which this occurs, being of minor importance).
- This peculiar form of fibrotic deposition can be diagnosed by histology and chest HRCT.

All of the abovementioned features are sufficient to characterize a disease in modern medicine, although the complete pathogenesis of UIP has yet to be fully understood.

Indeed, caution must be exercised when providing UIP with such a diagnostic power; correct recognition of UIP is imperative. It can be difficult for pathologists to differentiate between UIP and other, UIP-like, lesions in some cases.[4] A UIP-like pattern commonly has special features, including inflammation outside areas of honeycombing,[5] centrilobular fibrosis,[6] fewer areas of honeycombing,[7] higher scores for lymphoid hyperplasia,[5] and germinal centers.[7] Accurate differentiation between UIP and UIP-like lesions should be pursued diligently because UIP-like

lesions are manifestations of other diseases, which might respond to immunosuppressive therapy.

The consequences of considering UIP a disease in its own right are as follows:

- A recently published interim analysis showed higher mortality and hospitalization rates in the group of IPF patients treated with azathioprine, prednisone, and N-acetylcysteine than in that of those treated with placebo.[8] If immunosuppressive therapy is harmful to IPF patients, it might also be harmful to UIP patients who have not been diagnosed as having IPF simply because of the association of UIP with another disease, although they might present with the same fibrotic process as do those who have IPF. Unfortunately, it remains unclear in the literature whether this is the case. Therefore, caution is advised until new studies have determined whether UIP behaves as a disease and therefore responds uniformly poorly to immunosuppression regardless of whether it is idiopathic or not
- Drugs such as pirfenidone are currently being tested in IPF patients. If any such drug is proven to be beneficial, it can be tested and considered for use in UIP (lato sensu) patients as well.

In interstitial lung diseases, the concepts of patterns and diseases are constantly changing as the knowledge base increases. Thinking of UIP as a disease has a direct impact on current patient care, the use of immunosuppressive therapies requiring more caution and researchers having greater freedom to study the use of anti-IPF drugs in patients with UIP. Looking at UIP from this new perspective might improve the management of UIP as efforts to gain a deeper understanding of UIP continue. Many pieces of this puzzle are still missing, and the crucial question that needs to be answered so that UIP can be fully understood is the following: what is the driving force behind the peculiar and unrelenting proliferation of fibroblasts?

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