Transbronchial Biopsy and Usual Interstitial Pneumonia

A New Paradigm?

Usual interstitial pneumonia (UIP), the underlying histology of idiopathic pulmonary fibrosis (IPF), has a poor prognosis (median survival, 3 years), and to date there is no impressively effective therapy. Therefore, at least for prognosis, and in some cases for early transplant referral, it is important to confirm this diagnosis.

Expert radiologists and clinicians can accomplish this in approximately 50% of cases of UIP with a high degree of specificity. When typical radiologic features are present and tissue acquisition is deemed unnecessary, most clinicians feel that the disease is already advanced. However, there are a number of patients without typical radiologic findings, and also younger subjects, in whom a histologic diagnosis is often necessary. In addition, a number of treatment trials are in motion for IPF and a tissue diagnosis is required for inclusion in these trials.

Which type of biopsy is suitable for the diagnosis of UIP? In this issue of CHEST (see page 1126), Berbescu et al reviewed 22 patients with known UIP (21 cases diagnosed by surgical biopsy, 1 case diagnosed by clinical and radiologic features) and then retrospectively examined transbronchial biopsies (TBBs) from these patients. They concluded that a diagnosis of UIP was possible on the TBB in seven subjects, and in two others that the findings were consistent with UIP.

As a rationale for the use of TBB, Berbescu et al cite a report in which there was 17% mortality within 30 days following surgical lung biopsy for UIP. However, this has not been the experience of many interstitial lung disease centers across the world. In most studies, the morbidity and mortality from surgical lung biopsy is < 3%. Thus, we would not view potential complications as a major factor in deciding what type of lung biopsy to perform.

The question of which kind of biopsy should be performed to diagnose UIP has a long and controversial history. Surgical lung biopsy is accepted as the “gold standard,” but the role, if any, of TBB is contentious. The concept that TBB is useful for UIP and other forms of diffuse interstitial pneumonias was first addressed by Anderson. Of 939 TBBs, 39% were read as “chronic interstitial pneumonitis and fibrosis,” an observation that lead many to view TBB as a useful tool in this setting.

Subsequent reports challenged this idea. The most comprehensive is that of Wall et al, who compared TBB to open biopsy in the same patients with the TBB and open biopsies read, blinded, by an experienced pulmonary pathologist, the late Charles B. Carrington. Wall et al found that TBB findings read as normal or showing only a nonspecific pattern of interstitial inflammation and fibrosis missed cases of idiopathic interstitial pneumonias (mostly UIP) with a high frequency; conversely, TBB findings read as showing an idiopathic interstitial pneumonia were wrong in the vast majority of cases. Other reports, for example that of Wilson et al, demonstrated that the morphologic findings of interstitial inflammation and fibrosis in TBB appeared to have little relevance to subsequent clinical course (for more detail see Chung). Studies of this sort lead to a quiet campaign to discourage pulmonologists from relying on TBB to confirm the diagnosis of UIP as well as other forms of idiopathic interstitial pneumonias, a campaign that culminated in recent consensus statements from the American Thoracic Society/European Respiratory Society, which explicitly state that TBB has no role in the diagnosis of UIP.

Does the report of Berbescu et al overturn the current collective wisdom? To a pathologist, UIP is a diagnosis based to a great extent on low-power architecture because the individual features of UIP are not necessarily specific; rather, it is the repetitive combination of patchwork fibrosis, fibroblast foci, and microscopic honeycombing interspersed with unaffected lung and arranged in a peripheral and often perilobular distribution that leads to the diagnosis.

TBB does not allow assessment of the distribution of fibrosis within the lobe and lobule, nor does it allow one to determine whether the process is diffuse. For these reasons, Berbescu et al used the
combination of patchwork fibrosis, fibroblast foci, and microscopic honeycombing as criteria they considered diagnostic of UIP, and some of their illustrations do show fields that could be UIP. But as the authors acknowledge, none of these findings individually has diagnostic specificity, and even this combination could be the result of a variety of processes, including drug reactions, chronic hypersensitivity pneumonitis, connective tissue diseases, or asbestosis. Pathologically, one could also argue that the combination of only patchwork fibrosis and honeycombing (one of Berbescu’s acceptable combinations for diagnosing UIP) in a small specimen has much lower specificity, and it is now recognized that fibroblast foci, often but not exclusively found in areas of dense fibrosis, occur in other interstitial lung diseases. As a further complication, cases of unequivocal UIP can have focal areas that look like nonspecific interstitial pneumonia; this problem is readily addressed in surgical lung biopsies but likely to cause tremendous confusion in TBB.

The strength of the report by Berbescu et al2 is that they do provide detailed pathologic descriptions of what UIP might look like in TBBs, descriptions that are virtually nonexistent in the literature, and thus they offer a set of criteria that can be tested. As the authors note, the real issue is whether these criteria are accurate in patients with UIP established on surgical lung biopsy; rather, do they work applied in a prospective and blinded fashion? To this we would add two crucial questions: Do these criteria apply to patients who do not have the expected clinical and radiologic picture of IPF, because this is the setting in which a biopsy is of most importance, and are the features proposed by expert pathologists with a tremendous experience in this area usable by pathologists in the general medical community? These issues are worth investigating. But until such studies are performed, we suggest that the collective wisdom be followed and that TBB not be used to diagnose IPF/UIP.

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Neither of the authors has any conflicts of interest relating to this editorial.

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Pediatricians Are Not Just Small Internists

We pediatricians like to remind anybody who will listen that children are not just small adults. The diseases of childhood are those of growth and development, and response of the growing child to the external environment. Genetic diseases such as cystic fibrosis and primary ciliary dyskinesia are usually first diagnosed in the young child, and significant congenital abnormalities of the airways, thorax, and lung are diagnosed and treated initially in the first years of life. Therapy is directed at maximizing growth potential of the child, with the recognition by pediatricians that interventions early in life can benefit the growing child and the adult; the child is clearly the father to the man.

Not to put too fine an edge on it, diseases of adulthood and the elderly are often those of physiologic decay and chronic abuse. COPD, lung cancer, alcoholism, obesity-related disorders, coronary artery disease, and hypertension are all good examples. The goal of therapy in adults is often to slow the ravages of aging and to try and reverse the effects of too much food, drink, or tobacco smoke. Because of these differences, it is not unusual for the pediatr-