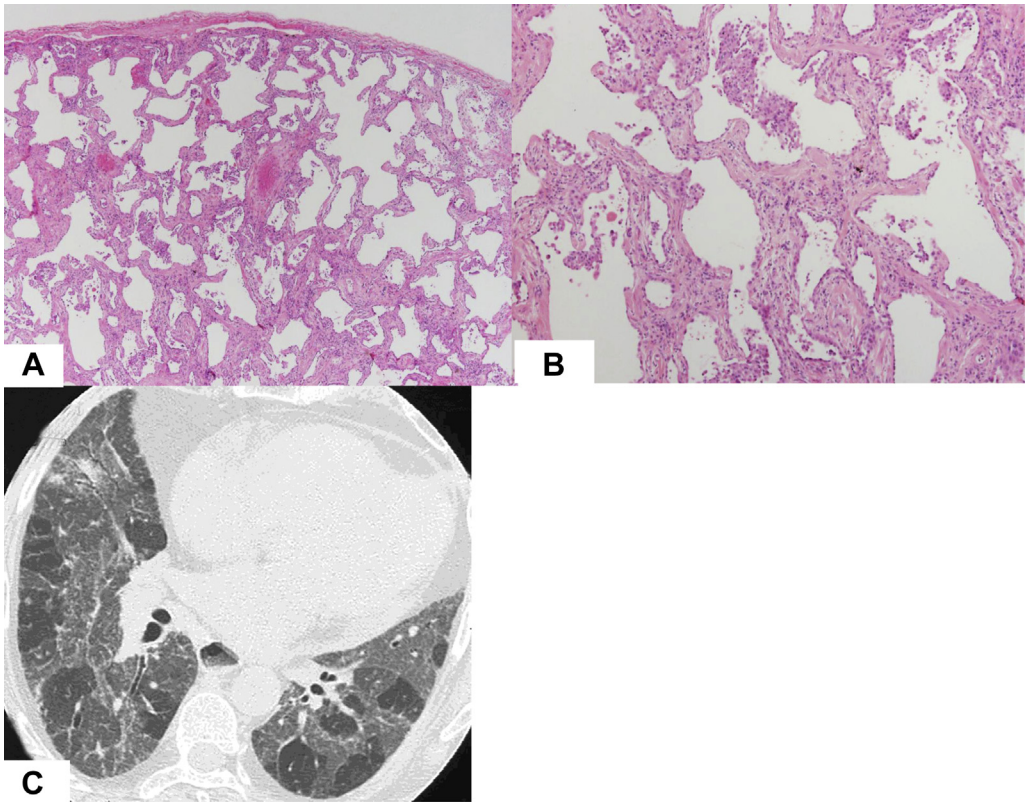

Figure 18 – ***Indeterminate for fibrotic hypersensitivity pneumonitis (HP) by surgical lung biopsy but typical fibrotic HP by CT imaging.*** *A, A fibrosing pattern of nonspecific interstitial pneumonia was seen in this biopsy with diffuse involvement of the alveolar parenchyma lacking any bronchiolocentric distribution. No granulomas or honeycombing are seen. B, The alveolar walls show uniform thickening by fibrosis with mild chronic inflammation. The CT scan showed the typical HP pattern.* ***Typical HP by CT imaging.*** *C, This CT scan is from the patient whose biopsy in panels A and B showed a fibrosing pattern of nonspecific interstitial pneumonia. It shows the three-density sign (predominant ground-glass attenuation with areas of normal attenuation and mosaic attenuation) with mild reticulation and traction bronchiectasis. This combination of findings provides strong support for the diagnosis of HP rather than idiopathic nonspecific interstitial pneumonia.*

Similar to nonfibrotic HP, the category of *indeterminate for fibrotic HP* pattern is based largely on a clinical finding or radiologic pattern suggesting fibrotic HP; however, a lung biopsy (Figs 17A-D, 18A-C) shows a pattern of fibrosing interstitial lung disease that by itself does not meet the pathologic criteria for the pattern of *typical fibrotic HP*, *compatible with fibrotic HP*, or an *alternative diagnosis*. This category can include cases that on biopsy show a pure UIP (Figs 17A-B) or NSIP pattern (Figs 18A-B) without features suggestive of fibrotic HP such as bronchiolocentricity or granulomas.[19,48,190,204] In such cases, HRCT findings can strongly favor HP rather than idiopathic NSIP (Fig 18C) or IPF (Figs 17C, 17D), respectively.

The category of *alternative diagnosis* is appropriate for biopsies that show definitive features of other interstitial lung diseases (Table 8).

Differential Diagnosis

The major differential diagnostic considerations for HP and their key histologic features are addressed in the category of Alternative Diagnoses. Table 9 lists several additional differential diagnoses that deserve special mention.

Diagnostic Approach

The presented diagnostic algorithm (Fig 1) illustrates a multidisciplinary team-based approach to the diagnostic process of HP based on seven diagnostic tenets and incorporating the evidence-based recommendations delineated in the guideline and expert panel report detailed in the previous section of this manuscript.

First, the diagnostic approach to HP is step-wise, patient-centered, and ideally based on multidisciplinary evaluation.

Second, while nonfibrotic HP cases with an identified IA may be solved by pattern recognition, complex cases including those with fibrotic HP may require a hypothetico-deductive diagnostic approach. Pending the availability of accurate and reliable precision medicine tools, this diagnostic approach includes the following