Radiology: Cardiothoracic Imaging COMMENTARY

Interstitial Pulmonary Fibrosis in Systemic Lupus Erythematosus: Are There Variants of the Variant Fibrotic Patterns?

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Connective tissue disease (CTD) is a well-recognized cause of pleural and parenchymal disease, but the relative proportion of involvement in these two areas varies in relation to the specific entity. Conditions such as scleroderma, rheumatoid arthritis, and dermatopolymyositis disproportionately affect the lungs, whereas systemic lupus erythematosus (SLE) more often involves serosal surfaces such as the pleura and pericardium (1). A minority of patients with SLE demonstrate lung involvement. For this reason, it is not surprising that most investigations of CTD-related interstitial lung disease focus on scleroderma and other CTDs that preferentially involve the lung parenchyma.

Recent descriptions of CT findings have emphasized important differences between patients with idiopathic pulmonary fibrosis, who often demonstrate a "classic" usual interstitial pneumonia pattern, and those with CTD-related interstitial lung disease, who exhibit changes that have been termed *variant fibrosis*. CT findings in the spectrum of interstitial pulmonary fibrosis reported to have a higher association with CTD-related interstitial lung disease than idiopathic pulmonary fibrosis include the straight-edge sign (a sharp partition between lower-lung honeycombing with normal more superior lung parenchyma), the exuberant honeycombing sign (honeycombing affecting a large percentage of a lobe), and the anterior upper lobe sign (honeycombing extending into the lung from the anterior periphery of the upper lobes) (2). In 2018, a CT "four-corners" sign, said to be specific for scleroderma, was described (3). Moreover, at pathologic examination, it is recognized that some CTDs, including scleroderma, are more likely to manifest parenchymal disease as nonspecific interstitial pneumonia or organizing pneumonia rather than usual interstitial pneumonia. However, the image correlates of these various patterns and fibrotic lung disease in general have not been investigated thoroughly in patients with SLE. Thus, the contribution of the current article is its characterization of parenchymal findings on CT scans in a large cohort of patients with SLE and interstitial pulmonary fibrosis (4).

This retrospective study was performed at a large academic medical center using an electronic database that queried patients with SLE and lung fibrosis, identifying 50 patients (46 women) with a mean age of 49 years. A single thin-section CT scan was reviewed for each patient, either the scan acquired chronologically closest to pulmonary function testing or, if pulmonary function testing was not obtained, the most recent available CT scan. Two thoracic radiologists reviewed each thin-section CT scan and assessed the overall type of fibrosis (usual interstitial pneumonia vs another pattern) and whether variant patterns such as the straight-edge sign and others were present in patients who did not have a classic usual interstitial pneumonia pattern or another well-defined diffuse lung disease pattern such as fibrotic nonspecific interstitial pneumonia. In addition, they assessed two types of appearances that heretofore lacked a formal description in the literature. They defined the "heterogeneous lung destruction" sign to indicate heterogeneous areas of architectural distortion and geographical cicatrical emphysema that differ in appearance from typical subpleural honeycombing and "island-like fibrosis" to denote regions of peripheral wedge-shaped fibrosis with acute margins that extend toward the center of the lung and that are sharply demarcated from normal adjacent lung. In addition, a severity score for the amount of reticulation and consolidation was assigned based on total lung involvement to the nearest 5% with correlation to pulmonary function testing.

A consensus was reached by the two radiologists in 41 (82%) of the 50 patients. Twenty-two patients (44%) were characterized as having variant fibrosis (defined as showing any of the five signs described above), and 19 (38%) were deemed to have a fibrotic pattern of nonspecific interstitial fibrosis. When the two radiologists disagreed, the most common point of difference was the situation where one radiologist characterized the CT as showing fibrotic nonspecific interstitial pneumonia and the other a form of

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variant fibrosis. With respect to variant fibrosis, the most common signs identified by both readers were island-like fibrosis, the straight-edge sign, and the heterogeneous lung destruction sign, each accounting for 48% or more studies. Overall, severity scores showed an inverse correlation with two parameters on pulmonary function testing (forced vital capacity and diffusing capacity for carbon monoxide).

The study demonstrates that similar to other CTDs, a classic pattern of usual interstitial pneumonia is not the most common finding in SLE. In fact, it appears to be quite unusual, on the basis of the absence of any cases identified by the readers in this study. It would be interesting to determine if pathologic evaluation showed concurrent findings; however, only a few patients had such correlation. Among the seven patients who underwent open lung biopsy, none demonstrated a usual interstitial pattern, a result concordant with the imaging findings.

The authors' description of two new variant fibrosis patterns, the island-like fibrosis and heterogeneous lung destruction signs, is notable because they were identified in a large percentage of patients with SLE-related pulmonary fibrosis. At this stage, it is unclear how robust these patterns are in the context of CTD-related interstitial lung disease. The κ value for the island-like fibrosis pattern was inferior to that of the other patterns. Thus, the staying power of this sign is open to question. It will be of interest to determine if the newly described patterns reported in this article are reproducible and accepted by other researchers. It is also unknown how often these signs are encountered in other CTD-related interstitial lung disease. Nor can it as yet be determined the extent to which the signs are a marker for CTD-related interstitial lung disease rather than idiopathic pulmonary fibrosis. Finally, no pathologic correlate for these findings has been established. More broadly, a risk exists that the proliferation of signs will obfuscate the overall goal of classifying interstitial pulmonary fibrosis. This may be a particularly difficult task for general radiologists among whom the nuances of interstitial lung disease represent a frequent challenge.

As our understanding of CTD-related interstitial lung disease continues to expand, further information regarding the parenchymal manifestations of SLE is a welcome addition. It is hoped that this investigation will stimulate additional studies to show points of distinction between SLE-related pulmonary fibrosis and other CTD-related interstitial lung disease and determine the context and value of more established signs of variant fibrosis, as well as the newer CT findings described in this article.

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