Imaging of Pulmonary Manifestations of Connective Tissue Diseases

Jitesh Ahuja, MD[a,*], Deepika Arora, MD[b], Jeffrey P. Kanne, MD[c], Travis S. Henry, MD[d], J. David Godwin, MD[a]

KEYWORDS

• Connective tissue disease • Interstitial lung disease • Autoimmune lung disease

KEY POINTS

- Connective tissue diseases (CTDs) are a heterogeneous group of systemic inflammatory disorders characterized by the presence of circulating autoantibodies and autoimmune-mediated organ damage.
- The lung is a frequent target and more than one thoracic compartment can be involved, including the airway, lung parenchyma, pulmonary vasculature, pleura, and pericardium.
- Interstitial lung disease (ILD) and pulmonary arterial hypertension are the most common thoracic manifestations, and they increase morbidity and mortality in patients with CTDs.
- The most common histopathologic patterns of ILD are nonspecific interstitial pneumonia, usual interstitial pneumonia, organizing pneumonia, and lymphoid interstitial pneumonia.
- The radiologic and histopathologic features of ILD in patients with CTDs are similar to those with idiopathic ILD. Extrapulmonary manifestations, demographic features, and serology can help distinguish CTD-ILD from idiopathic ILD.

INTRODUCTION

Connective tissue diseases (CTDs), also called collagen vascular diseases, are a heterogeneous group of systemic inflammatory disorders characterized by the presence of circulating autoantibodies (**Table 1**) and autoimmune-mediated organ damage. The lung is a frequent target, and more than one thoracic compartment can be involved, including the airways, lung parenchyma, pulmonary vasculature, pleura, and pericardium. The CTDs that often involve the respiratory system are rheumatoid arthritis (RA), scleroderma or system sclerosis (SSc), Sjögren syndrome (SS), polymyositis (PM)/dermatomyositis (DM), systemic lupus erythematosis (SLE), mixed CTD (MCTD), and undifferentiated CTD (UCTD).

Interstitial lung disease (ILD) and pulmonary arterial hypertension are the most common thoracic manifestations, and they increase morbidity and mortality in patients with CTD.[1,2] Thoracic abnormalities usually follow systemic

[a] Department of Radiology, University of Washington, 1959 Northeast Pacific Street, Seattle, WA 98195, USA; [b] Division of Rheumatology, Multicare Health System, Allenmore Medical Center Building A, 1901 South Union Avenue, Suite A221, Tacoma, WA 98405, USA; [c] Department of Radiology, School of Medicine and Public Health, University of Wisconsin, 600 Highland Avenue, Madison, WI 53792, USA; [d] Department of Radiology and Biomedical Imaging, University of California, 505 Parnassus Avenue M391, Box 0628, San Francisco, CA 94143, USA

* Corresponding author. Department of Radiology, University of Washington, 1959 Northeast Pacific Street, Box 357115, Seattle, WA 98195.
E-mail address: ahujaj@uw.edu

Radiol Clin N Am ■ (2016) ■–■
http://dx.doi.org/10.1016/j.rcl.2016.05.005
0033-8389/16/$ – see front matter

Table 1
Autoantibodies in CTDs

Autoantibody	CTD
ANA	Various CTDs (SLE, SSc, SS, PM/DM) Nucleolar staining suggests SSc
Anti-dsDNA antibody	SLE
Anti-Ro antibody	SLE, SS
Anti-La antibody	SS, SLE
Anti-topoisomerase I (anti-Scl-70)	SSc
RF	RA, SS
Anti-CCP antibody	RA
Anti-RNP	MCTD
Anti-tRNA synthetases (Jo-1, MDA-5)	PM/DM/ antisynthetase syndrome

Abbreviations: ANA, antinuclear antibody; CCP, cyclic citrullinated peptide; dsDNA, double-stranded DNA; MCTD, mixed connective tissue disease; PM/DM, polymyositis/dermatomyositis; RA, rheumatoid arthritis; RF, rheumatoid factor; RNP, ribonucleoprotein; SLE, systemic lupus erythematosis; SS, Sjögren syndrome; SSc, systemic sclerosis.

manifestations of the CTDs but occasionally precede extrathoracic manifestations by months or even years.[1,3,4]

The pattern and frequency of thoracic diseases vary depending on the underlying CTD (**Table 2**). The most common histopathologic patterns of ILD are nonspecific interstitial pneumonia (NSIP), usual interstitial pneumonia (UIP), organizing pneumonia (OP), and lymphoid interstitial pneumonia (LIP).

The radiologic and histopathologic features of ILD in patients with CTDs are similar to those with idiopathic interstitial pneumonia.[5,6] However, close evaluation of the chest radiograph and high-resolution computed tomography (HRCT) scans can offer clues to the underlying CTD. For example, arthropathy suggests RA; esophageal dilation and pulmonary artery enlargement out of proportion to lung fibrosis suggest SSc; soft tissue calcification suggests DM or SSc; and pleural or pericardial effusion or thickening suggests SLE.

Extrapulmonary manifestations, demographic features, and serology can help distinguish CTD-ILD from idiopathic interstitial pneumonia.[5,7] Mediastinal lymphadenopathy is frequent in CTD and should not be considered malignant in the absence of known neoplasm. Treatment complications, including drug toxicity and opportunistic infection, can confuse the radiologic appearance and make diagnosis more difficult.

This article focuses on the thoracic manifestations of CTDs and briefly discusses complications caused by treatment.

PATTERNS OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONNECTIVE TISSUE DISEASES

Nonspecific Interstitial Pneumonia

NSIP is the most common pattern of ILD in CTDs,[8,9] and NSIP associated with CTD is far more common than idiopathic NSIP.[10,11] Some patients who are initially thought to have idiopathic NSIP later manifest CTD. Hence, CTDs should be thoroughly investigated in patients who present with an NSIP pattern of ILD without extrathoracic manifestations of CTD.[12,13]

NSIP pattern can occur with any CTD but particularly in SSc, PM/DM, and MCTD.[1,14] Spatial and temporal homogeneity are the pathologic hallmarks of NSIP.[15] Depending on the degree of interstitial inflammation and fibrosis, NSIP is divided into 2 categories, cellular and fibrotic, the latter with a worse prognosis.[15,16] On HRCT, ground-glass opacity (GGO) is the predominant abnormality with mild reticulation and traction bronchiectasis and bronchiolectasis (**Table 3**). The abnormality is concentrated in lower lobes, often in a peribronchovascular distribution (**Fig. 1**). Another distinctive feature of NSIP is that fibrosis may to some extent spare the immediately subpleural lung zone; some degree of sparing has been found in 20% to 64% of patients with NSIP.[1,6,12,17–19] Reticulation and traction bronchiectasis and bronchiolectasis increase with more advanced fibrotic NSIP. Honeycombing develops in advanced stages, but is uncommon initially.[6,17]

Usual Interstitial Pneumonia

UIP is the second most common pattern of CTD-ILD and the most common pattern of RA-ILD.[6,17] Pathologically, UIP is characterized by spatial and temporal heterogeneity.[15] Radiologic and pathologic features of UIP in CTDs are similar to those in idiopathic pulmonary fibrosis (IPF), except that fibroblastic foci may be less frequent than in IPF, which may account for the better prognosis of UIP in CTD than in IPF.[20]

HRCT features of UIP include peripheral and lower lobe predominance of reticulation, traction bronchiectasis, and honeycombing (**Fig. 2**). Coronal reformatting helps to display this distribution. Honeycombing needs to be distinguished from paraseptal emphysema and traction bronchiolectasis. Honeycombing is identified by peripheral