Analysis of Imaging Features of Connective Tissue Diseases Involving the Respiratory System (Postprint)

Authors: Xu Xiaoli, Sui Ting, Song Lan, Huang Yao, Wang Xiao, Jin Zhengyu, Song Wei

Date: 2018-06-14T00:00:00+00:00

Abstract

Connective tissue diseases involving the respiratory system may manifest as interstitial lung disease, diffuse alveolar damage, alveolar hemorrhage, pulmonary vascular lesions, pleural lesions, and airway lesions, among others. Their clinical manifestations lack specificity, and pulmonary function tests and chest CT are the most commonly utilized diagnostic modalities. The imaging features of respiratory system involvement in different connective tissue diseases exhibit similarities while possessing distinct characteristics. This article provides an overview of the imaging manifestations associated with respiratory system involvement in connective tissue diseases, aiming to enhance readers' understanding and guide clinical practice.

Full Text

Imaging Manifestations of Respiratory Diseases Associated with Connective Tissue Diseases

Journal: Medical Journal of Peking Union Medical College Hospital (ChinaXiv Partner Journal)
Authors: XU Xiaoli, SUI Xin, SONG Lan, HUANG Yao, WANG Xiao, JIN Zhengyu, SONG Wei
Affiliation: Department of Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China
Corresponding Author: SONG Wei, Tel: 010-69154261, E-mail: cjr.songwei@vip.163.com

Abstract

Respiratory manifestations of connective tissue diseases (CTDs) include interstitial lung diseases, diffuse alveolar injury, alveolar hemorrhage, pulmonary vascular lesions, pleural lesions, and airway disease. These manifestations lack specific clinical symptoms, with pulmonary function tests and chest CT being the most frequently applied examinations. While different connective tissue diseases involving the respiratory system share common features, they also exhibit characteristic imaging patterns. This paper reviews the imaging manifestations of respiratory diseases associated with connective tissue diseases to improve readers' recognition of these diseases and guide clinical practice.

Keywords: respiratory system; connective tissue diseases; imaging

1. Imaging Manifestations of Connective Tissue Disease-Related Respiratory Diseases

1.1 Pulmonary Hypertension

Pulmonary hypertension is defined as a mean pulmonary artery pressure 25 mmHg (1 mmHg = 0.133 kPa) measured by right heart catheterization at rest. It most commonly occurs in systemic sclerosis (SSc), followed by mixed connective tissue disease (MCTD) and systemic lupus erythematosus (SLE). Pulmonary function tests typically show decreased diffusion capacity for carbon monoxide (DLCO). CT findings include enlargement of the pulmonary artery and its branches, with contrast reflux into the inferior vena cava and hepatic veins. In severe cases, pericardial effusion may be present. Zheng et al. reported that CT pulmonary angiography (CTPA) has a sensitivity of 90.8% and specificity of 66.7% for diagnosing pulmonary hypertension when the main pulmonary artery diameter exceeds 30 mm, and a sensitivity of 94.3% and specificity of 55.6% when using the ratio of main pulmonary artery to ascending aorta diameter. These CT measurements can effectively predict pulmonary hypertension. Magnetic resonance imaging can serve as a complementary examination to evaluate right ventricular structure, function, and pulmonary artery blood flow.

1.2 Interstitial Lung Disease

Interstitial lung disease (ILD) refers to a group of diffuse lung diseases primarily involving the pulmonary interstitium, including the alveolar spaces and small airways, but excluding diseases of bronchi larger than the terminal bronchioles. It can be classified into known causes, idiopathic interstitial pneumonias, and rare clinicopathologic entities. Ground-glass opacity (GGO) on high-resolution CT (HRCT) represents early alveolitis. Anaya et al. consider non-specific interstitial pneumonia (NSIP) to be the most common pattern in CTD-associated ILD. The most common chest CT findings include GGO, reticular opacities, and

traction bronchiectasis, typically showing symmetric distribution in the bilateral lower lobes and subpleural regions. The extent of disease on HRCT correlates significantly with forced vital capacity in one second (FEV1) and DLCO. Honeycombing and airspace consolidation are rare in early disease. Lower lobe volume loss may also be observed. While it is difficult to differentiate cellular from fibrotic NSIP radiologically, HRCT is the preferred method for assessing disease extent, activity, and response to treatment.

2. Imaging Features of Different Connective Tissue Diseases Involving the Respiratory System

2.1 Systemic Lupus Erythematosus

SLE can involve multiple thoracic structures. Acute lung injury manifests as diffuse alveolar hemorrhage and acute lupus pneumonitis, which, although rare, are often fatal. Patients present with dyspnea and declining hemoglobin levels. HRCT shows diffuse or focal consolidations with GGO and interlobular septal thickening, predominantly in the lower lungs. Bronchoscopy is required for definitive diagnosis of alveolar hemorrhage. Chronic lung injury typically manifests as NSIP pattern. Pleural effusions are common and may be bilateral. SLE patients are prone to deep vein thrombosis; if chest pain occurs, contrast-enhanced CT should be performed to evaluate for pulmonary thromboembolism and infarction. Irregular linear opacities with septal thickening may indicate fibrosis. Since infection is the most common cause of pulmonary infiltrates in SLE, conditions such as acute lupus pneumonitis and alveolar hemorrhage must be distinguished from community-acquired pneumonia.

2.2 Rheumatoid Arthritis

RA frequently involves the pleura, manifesting as mild pleural thickening or unilateral pleural effusions that are often self-limiting. ILD patterns include usual interstitial pneumonia (UIP), organizing pneumonia (OP), and lymphocytic interstitial pneumonia (LIP), with NSIP being most common. HRCT findings consist of reticular opacities, GGO, intralobular interstitial thickening, and traction bronchiectasis, typically involving small areas in the lung bases with volume loss and architectural distortion. Airway disease is common, including bronchiectasis, bronchiolitis obliterans, and follicular bronchiolitis. Bronchiolitis obliterans presents as mosaic attenuation on CT, while follicular bronchiolitis appears as centrilobular nodules with ground-glass density. Rheumatoid nodules are common, typically located in the peripheral upper and middle lungs, varying in size, and may appear and resolve spontaneously. Caplan' s syndrome, characterized by multiple calcified pulmonary nodules, is most frequently seen in male smokers with RA and coal worker' s pneumoconiosis.

2.3 Systemic Sclerosis

SSc has the highest incidence of ILD among CTDs (80% of patients). NSIP is the most common pattern, though UIP may also be seen. HRCT demonstrates peripheral reticular opacies in the lower lobes with traction bronchiectasis. Disease progression correlates negatively with DLCO. Esophageal involvement predisposes to aspiration pneumonia. Pulmonary vascular involvement can lead to persistent pulmonary hypertension. Patients with progressive systemic sclerosis have an increased risk of malignancy, particularly breast cancer, requiring careful follow-up.

2.4 Polymyositis/Dermatomyositis

ILD occurs in 30-58% of PM/DM patients and is a major cause of mortality. HRCT findings include patchy consolidations, GGO, septal thickening, irregular bronchovascular bundle thickening, and bronchiectasis. Honeycombing may be seen in advanced disease. The anti-Jo-1 antibody is present in 50-70% of patients with ILD, while those negative for Jo-1 may also develop ILD. Irregular bronchovascular bundle thickening is often reversible after treatment, whereas the presence of parenchymal bands or subpleural lines may progress to honeycombing. PM/DM patients have an increased risk of malignancy, particularly lung cancer; any new pulmonary nodules during follow-up require careful evaluation.

2.5 Sjögren' s Syndrome

Sjögren' s syndrome can involve airways (bronchiectasis) and lung parenchyma, with LIP and NSIP being common patterns. HRCT shows multiple thin-walled cysts with centrilobular nodules, predominantly in the lower lungs. Bronchovascular bundle thickening and peribronchovascular nodules may be present, while honeycombing and consolidation are rare. Patients have an increased risk of lymphoma, particularly mucosa-associated lymphoid tissue (MALT) lymphoma. When solid nodules or pleural effusions develop, lymphoma should be considered.

2.6 Mixed Connective Tissue Disease

MCTD is characterized by overlapping features of SLE, SSc, and PM/DM with extremely high titers of circulating anti-nuclear antibodies. Thoracic involvement most commonly manifests as pulmonary hypertension, pleural thickening, ILD, and pericardial effusion. The most common ILD pattern is NSIP, appearing as bilateral subpleural GGO and septal thickening.

2.7 Ankylosing Spondylitis

Pulmonary involvement in ankylosing spondylitis typically occurs in patients with long disease duration, manifesting as upper lobe fibrosis, paraseptal em-

physema, and bronchiectasis. The apical location can make differentiation from tuberculosis difficult. Centrilobular nodules are less common.

3. Summary

The imaging manifestations of CTD-related respiratory disease are diverse and overlapping. Diagnosis requires integration of clinical presentation, laboratory findings (particularly autoantibodies), and imaging features. HRCT is the primary imaging modality for evaluating disease extent, activity, treatment response, and prognosis. It is essential to first exclude drug-related complications and opportunistic infections. Recognizing the characteristic chest imaging patterns of specific CTDs enables more accurate diagnosis and comprehensive patient assessment.

References

[1] Ohno Y, Koyama H, Yoshikawa T, et al. State-of-the-Art Imaging of the Lung for Connective Tissue Disease (Ctd) [J]. Curr Rheumatol Rep, 2015, 17: 69.

[2] Akira M, Sakatani M, Hara H. Thin-section CT findings in rheumatoid arthritis-associated lung disease: CT patterns and their courses [J]. J Comput Assist Tomogr, 1999, 23: 941-948.

[3] Karampitsakos T, Tzouvelekis A, Chrystikos S, et al. Pulmonary Hypertension in Patients with Interstitial Lung Disease [J]. Pulm Pharmacol Ther, 2018. doi: 10.1016/j.pupt.2018.03.002. [Epub ahead of print].

[4] Zheng Y, et al. Clinical analysis of autoimmune diseases complicated with pulmonary hypertension [J]. Chinese Journal of Rheumatology, 2006, 10: 97-100.

[5] Bazan IS, Mensah KA, Rudkovskaia AA, et al. Pulmonary arterial hypertension in the setting of scleroderma is different than in the setting of lupus: A review [J]. Respir Med, 2018, 134: 42-46.

[6] Zheng Y, et al. Role of main pulmonary artery diameter measurement in HRCT for diagnosis of pulmonary hypertension [J]. Chinese Journal of Clinicians, 2014, 8: 31-35.

[7] Pamboucas C, Nihoyannopoulos P. Cardiovascular magnetic resonance: its role in the diagnosis and evaluation of pulmonary arterial hypertension [J]. Rev Esp Cardiol, 2006, 59: 755-760.

[8] Anaya JM, Diethelm L, Ortiz LA, et al. Pulmonary involvement in rheumatoid arthritis [J]. Semin Arthritis Rheum, 1995, 24: 242-254.

[9] Antin-Ozerkis D, Rubinowitz A, Evans J, et al. Interstitial Lung Disease in the Connective Tissue Diseases [J]. Clin Chest Med, 2012, 33: 123-149.

[10] Tazelaar HD, Viggiano RW, Pickersgill J, et al. Interstitial lung disease in polymyositis and dermatomyositis: clinical features and prognosis as correlated with histologic findings [J]. Am Rev Respir Dis, 1990, 141: 727-733.

[11] Remy-Jardin M, Remy J, Cortet B, et al. Lung changes in rheumatoid arthritis: CT findings [J]. Radiology, 1994, 193: 375-382.

[12] Kligerman SJ, Groshong S, Brown KK, et al. Nonspecific interstitial pneumonia: radiologic, clinical, and pathologic considerations [J]. RadioGraphics, 2009, 29: 73-87.

[13] Mayberry JP, Primack SL, Müller NL. Thoracic manifestations of systemic autoimmune diseases: radiographic and high-resolution CT findings [J]. RadioGraphics, 2000, 20: 1623-1635.

[14] Fenlon HM, Doran M, Sant SM, et al. High-resolution chest CT in systemic lupus erythematosus [J]. AJR Am J Roentgenol, 1996, 166: 301-307.

[15] Wan SA, Teh CL, Jobli AT. Lupus Pneumonitis as the Initial Presentation of Systemic Lupus Erythematosus: Case Series from a Single Institution [J]. Lupus, 2016, 25: 1485-1490.

[16] Weinrib L, Sharma OP, Quismorio FP. A long-term study of interstitial lung disease in systemic lupus erythematosus [J]. Semin Arthritis Rheum, 1990, 20: 48-56.

[17] Gladman DD, Urowitz MB. Venous syndromes and pulmonary embolism in systemic lupus erythematosus [J]. Ann Rheum Dis, 1980, 39: 340-343.

[18] Mittoo S, Fell CD. Pulmonary Manifestations of Systemic Lupus Erythematosus [J]. Semin Respir Crit Care Med, 2014, 35: 249-254.

[19] Bankier AA, Kiener HP, Wiesmayr MN, et al. Discrete lung involvement in systemic lupus erythematosus: CT assessment [J]. Radiology, 1995, 196: 835-840.

[20] Zamora MR, Warner ML, Tuder R, et al. Diffuse alveolar hemorrhage and systemic lupus erythematosus: clinical presentation, histology, survival, and outcome [J]. Medicine (Baltimore), 1997, 76: 192-202.

[21] Kinder BW, Freemer MM, King TE, et al. Clinical and genetic risk factors for pneumonia in systemic lupus erythematosus [J]. Arthritis Rheum, 2007, 56: 2679-2686.

[22] Chansakul T, Dellaripa PF, Doyle TJ, et al. Intra-Thoracic Rheumatoid Arthritis: Imaging Spectrum of Typical Findings and Treatment Related Complications [J]. Eur J Radiol, 2015, 84: 1981-1991.

[23] Remy-Jardin M, Remy J, Cortet B, et al. Lung changes in rheumatoid arthritis: CT findings [J]. Radiology, 1994, 193: 375-382.

[24] Lee HK, Kim DS, Yoo B, et al. Histopathologic pattern and clinical features of rheumatoid arthritis-associated interstitial lung disease [J]. Chest, 2005, 127: 2019-2027.

[25] Hakala M, Pääkkö P, Sutinen S, et al. Association of bronchiolitis with connective tissue disorders [J]. Ann Rheum Dis, 1986, 45: 656-662.

[26] Aquino SL, Webb WR, Golden J. Bronchiolitis obliterans associated with rheumatoid arthritis: findings on HRCT and dynamic expiratory CT [J]. J Comput Assist Tomogr, 1994, 18: 555-558.

[27] Müller-Leisse C, Bussmann A, Meyer O, et al. Pulmonary manifestations in rheumatoid arthritis: high-resolution computed tomography in correlation with skeletal changes and laboratory chemical changes [J]. Röfo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr, 1996, 165: 438-444.

[28] Kelly CA, Saravanan V, Nisar M, et al. Rheumatoid Arthritis-Related Interstitial Lung Disease: Associations, Prognostic Factors and Physiological and Radiological Characteristics—a Large Multicentre UK Study [J]. Rheumatology (Oxford), 2014, 53: 1676-1682.

[29] Silva CI, Müller NL, Lynch DA, et al. Chronic hypersensitivity pneumonitis: differentiation from idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia by using thin-section CT [J]. Radiology, 2008, 246: 288-297.

[30] Srinivas S, Dhelaria R, Pai D, et al. Multiple calcified pulmonary nodules: an unusual presentation of rheumatoid lung [J]. Clin Radiol, 2007, 62: 274-276.

[31] Caplan A. Certain unusual radiological appearances in the chest of coal-miners suffering from rheumatoid arthritis [J]. Thorax, 1953, 8: 29-37.

[32] Solomon JJ, Olson AL, Fischer A, et al. Scleroderma Lung Disease [J]. Eur Respir Rev, 2013, 22: 6-19.

[33] Fujita J, Yoshinouchi T, Ohtsuki Y, et al. Non-specific interstitial pneumonia as pulmonary involvement of systemic sclerosis [J]. Ann Rheum Dis, 2001, 60: 281-283.

[34] Wells AU, Steen V, Valentini G. Pulmonary complications: one of the most challenging complications of systemic sclerosis [J]. Rheumatology (Oxford), 2009, 48: iii40-iii44.

[35] Tashkin DP, Elashoff R, Clements PJ, et al. Cyclophosphamide versus placebo in scleroderma lung disease [J]. N Engl J Med, 2006, 354: 2655-2666.

[36] Mayberry JP, Primack SL, Müller NL. Thoracic manifestations of systemic autoimmune diseases: radiographic and high-resolution CT findings [J]. RadioGraphics, 2000, 20: 1623-1635.

[37] Remy-Jardin M, Remy J, Wallaert B, et al. Pulmonary involvement in progressive systemic sclerosis: sequential evaluation with CT, pulmonary function tests, and bronchoalveolar lavage [J]. Radiology, 1993, 188: 499-506.

[38] Kim EA, Johkoh T, Lee KS, et al. Interstitial pneumonia in progressive systemic sclerosis: serial high-resolution CT findings with functional correlation [J]. J Comput Assist Tomogr, 2001, 25: 757-763.

[39] Shah RM, Jimenez S, Wechsler R. Significance of ground-glass opacity on HRCT in long-term follow-up of patients with systemic sclerosis [J]. J Thorac Imaging, 2007, 22: 120-124.

[40] Panchabhai TS, Farver C, Highland KB. Lymphocytic Interstitial Pneumonia [J]. Clin Chest Med, 2016, 37: 463-474.

[41] Marasini B, Concia E, Belloli L, et al. Systemic sclerosis and cancer [J]. Int J Immunopathol Pharmacol, 2009, 22: 573-578.

[42] Yang Y, Fujita J, Tokuda M, et al. Chronological evaluation of the onset of histologically confirmed interstitial pneumonia associated with polymyositis/dermatomyositis [J]. Clin Rheumatol, 2009, 28: 757-765.

[43] Hallowell RW, Ascherman DP, Danoff SK. Pulmonary manifestations of polymyositis/dermatomyositis [J]. Semin Respir Crit Care Med, 2014, 35: 239-248.

[44] Tazelaar HD, Viggiano RW, Pickersgill J, et al. Interstitial lung disease in polymyositis and dermatomyositis: clinical features and prognosis as correlated with histologic findings [J]. Am Rev Respir Dis, 1990, 141: 727-733.

[45] Verschakelen JA, Verbeken EK, Demedts MG. Pulmonary involvement in polymyositis [J]. J Belge Radiol, 1995, 78: 317-321.

[46] Akira M, Hara H, Sakatani M. Interstitial lung disease in association with polymyositis-dermatomyositis: long-term follow-up CT evaluation in seven patients [J]. Radiology, 1999, 210: 333-338.

[47] Bonnefoy O, Ferretti G, Calaque O, et al. Serial chest CT findings in interstitial disease associated with polymyositis-dermatomyositis [J]. Eur J Radiol, 2004, 49: 235-244.

[48] Fataar S, Johkoh T, Kwon OJ, et al. High-resolution CT findings in patients with polymyositis and dermatomyositis [J]. J Thorac Imaging, 1996, 11: 250-259.

[49] Chen MH, Chou HP, Lai CC, et al. Lung involvement in primary Sjögren' s syndrome: correlation between high-resolution computed tomography score and mortality [J]. J Chin Med Assoc, 2014, 77: 75-82.

[50] Flament T, Bigot A, Chaigre B, et al. Pulmonary Manifestations of Sjögren' s Syndrome [J]. Eur Respir Rev, 2016, 25: 110-123.

[51] Parambil JG, Myers JL, Lindell RM, et al. Interstitial lung disease in primary Sjögren syndrome [J]. Chest, 2006, 130: 1489-1495.

[52] Lynch DA. Lung disease related to collagen vascular disease [J]. J Thorac Imaging, 2009, 24: 299-309.

[53] Koyama M, Johkoh T, Honda O, et al. Pulmonary involvement in primary Sjögren' s syndrome: spectrum of pulmonary abnormalities and computed tomography findings in 60 patients [J]. J Thorac Imaging, 2001, 16: 94-98.

[54] Yachoui R, Leon C, Sitwala K, et al. Pulmonary malt lymphoma in patients with Sjögren' s syndrome [J]. Clin Med Res, 2017, 15: 6-12.

[55] Honda O, Johkoh T, Ichikado K, et al. Differential diagnosis of lymphocytic interstitial pneumonia and malignant lymphoma on high-resolution CT [J]. AJR Am J Roentgenol, 1999, 173: 71-74.

[56] Bodolay E, Szekanecz Z, Dévényi K, et al. Evaluation of interstitial lung disease in mixed connective tissue disease (MCTD) [J]. Rheumatology (Oxford), 2005, 44: 656-661.

[57] Fagundes MN, Caleiro MT, Navarro-Rodriguez T, et al. Esophageal involvement and interstitial lung disease in mixed connective tissue disease [J]. Respir Med, 2009, 103: 854-860.

[58] Lee-Chiong TL. Pulmonary manifestations of ankylosing spondylitis and relapsing polychondritis [J]. Clin Chest Med, 1998, 19: 747-757.

[59] Hallowell RW, Ascherman DP, Danoff SK. Pulmonary manifestations of polymyositis/dermatomyositis [J]. Semin Respir Crit Care Med, 2014, 35: 239-248.

[60] Minai OA. Pulmonary manifestations of ankylosing spondylitis [J]. Clin Pulm Med, 2013, 20: 68-72.

[61] Cottin V. Idiopathic interstitial pneumonias with connective tissue diseases features: A review [J]. Respirology, 2016, 21: 245-258.

Note: Figure translations are in progress. See original paper for figures.