Lung Involvement in Rheumatologic Patients

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Contents

Chapters i
Authors iii
Preface v

CHAPTERS

Chapter 1 - Rheumatoid Arthritis-Associated Interstitial Lung Disease 1
Seda ÇOLAK, Emre TEKGÖZ, Sedat YILMAZ

Chapter 2 - Sjögren's Syndrome and Interstitial Lung Disease 11
Ayşenur YALÇINTAŞ KANBUR, Ahmet Eftal YÜCEL

Chapter 3 - Systemic Sclerosis Related Interstitial Lung Diseases 21
Emre TEKGÖZ, Seda ÇOLAK, Sedat YILMAZ

Chapter 4 - Vasculites 33
Derya HOŞGÜN, Ümit KARATEPE

Chapter 5 - Inflammatory Myopathy Related Interstitial Lung Disease 51
Alper SARI

Chapter 6 - Interstitial Lung Disease Associated with Systemic Lupus Erythematosus 59
Tuğba İZCİ DURAN

Chapter 7 - Interstitial Lung Disease Associated with Mixed Connective Tissue Disease 65
Çağdaş Şahap OYGÜR, Ahmet Eftal YÜCEL

Index 73

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Preface

We believe that the light of science always illuminates all darkness and opens all doors. Recent advances show that pulmonary involvement in rheumatic diseases can have a chance for early diagnosis and treatment, primarily with the awareness of physicians and even patients. In our book, we aimed to shed light on all our colleagues in this field, especially in the branches of chest diseases and rheumatology.

Many thanks to our contributing authors and editors. We hope that this work will be useful to our colleagues

Sincerely,

Zeynep ERAYMAN ÖZEN
MD, Editor
2023, Ankara

Rheumatoid Arthritis-Associated Interstitial Lung Disease

1 Chapter

Seda ÇOLAK, Emre TEKGÖZ, Sedat YILMAZ

Rheumatoid arthritis (RA) is the most common, chronic and systemic inflammatory arthritis. The frequency of RA in the general population varies between 0.5% and 2%. Interstitial lung disease (ILD) is one of the most important causes of morbidity and mortality in RA patients, and its frequency has been reported to vary between 4% and 48%. However, it has been shown that this rate can be found to be even higher if high-resolution computed tomography (HRCT) is performed in RA patients who are not pulmonary asymptomatic. ILD is often detected years after the joint findings of RA, and less frequently, simultaneously with the joint findings. However, in approximately 10% of patients, ILD findings precede joint findings. Although RA is more common in women than in men, RA-related ILD is more common in men.

ETIOLOGY AND PATHOGENESIS

Although the etiology of RA-associated ILD is not clearly known, it is thought that fibrosis, which develops because of chronic inflammation and endothelial dysfunction, which starts with the trigger of environmental factors in genetically susceptible individuals, plays a role in the pathogenesis. Among the genetic factors, HLA-B54, HLA-DQB1*0601, HLA-B40, HLA-DR4 and site encoding α-1 protease inhibitor are accused in the development of ILD in RA patients. In addition, RPA3-UMAD1 and MUC5B gene polymorphisms were also associated with an increased risk of RA-related ILD in different populations. It has been shown that these gene polymorphisms increase the risk of usual interstitial pneumonia (OIP) more than other ILD patterns. Although not used in clinical practice, some cytokines and chemokine (Interleukin (IL)-18, IL-33, matrix metalloproteinase-7, surfactant protein D, etc.) have been shown to be associated with the development of ILD in RA patients.

Anti-cyclic citrullinated peptide antibodies (ACPA) play a role both in the pathogenesis of RA and in the pathogenesis of RA-associated ILD, and its effect is more clearly known than other factors. Citrullination is the conversion of arginine to citrulline because of post-translational modification. Immune activation triggered by citrullination leads to the formation of antibodies against citrulline proteins. Although ACPA is detected at high levels in the blood and synovium of patients with RA, it can also be detected at high levels in bronchoalveolar lavage samples of patients with RA-related ILD. There are two hypotheses that ACPA is responsible for the pathogenesis of RA-associated ILD. According to the first hypothesis, inflammation initiated by passaging ACPA antibodies formed in the

4 Chapter

Vasculites

Derya HOŞGÜN, Ümit KARATEPE

Vasculitides are defined as the presence of inflammatory leukocytes that cause reactive damage to the vessel wall. Deterioration of vascular integrity leads to bleeding, ischemia, and necrosis. Depending on the type of vasculitis, the size, type and location of the affected vessel differ. It may be idiopathic or because of an underlying disease. With the exclusion of alternative diagnoses, the treatment is generally immunosuppressive therapy. The classification system developed by the international Chapel Hill Consensus Conference is used for non-infectious vasculitides. It is classified as large vessel, medium vessel, and small vessel vasculitis (**Table 1**).

Table 1: Classification of vasculitis (Classification of the Chapel Hill Consensus Conference)
Great Vessel Vasculitis: Giant cell arteritis, Takayasu arteritis
Mid-Vessel Vasculitides: Kawasaki disease, Polyarteritis nodosa
Small Vessel Vasculitides • **ANCA-Associated Vasculitides:** Granulomatous polyangitis (GPA) (Wegener), microscopic polyangitis (MPA), eosinophilia granulomatous polyangiitis (EGPA) (Churg-Strauss) • **Immunocomplex Vasculitis:** Anti-glomerular basement membrane (GBM) disease, cryoglobulinemic vasculitis, immunoglobulin (Ig) A Vasculitis
Variable Vasculitis: Behçet's disease, Cogan's syndrome
Single Organ Vasculitides: Cutaneous leukocytoclastic vasculitis, cutaneous arteritis, primary central nervous system (CNS) vasculitis, isolated arteritis
Systemic Disease-Associated Vasculitides: Systemic lupus erythrematosus (SLE), rheumatoid arthritis (RA), sarcoidosis
Vasculitides Associated with Etiology: Hepatitis B, syphilis, drug-induced and cancer-related

1-LARGE VESSEL VASCULITES

Giant Cell Arteridis

It is one of the most common vasculitides over the age of 50; It peaks at age 70. It is 2 times more common for females. It is characterized by granulomatous inflammation in the walls of large and medium arteries. It is categorized as cranial and extracranial.

It is characterized by headache, jaw pain, and vision problems. Nonspecific symptoms, such as subfebrile fever, anorexia, weight loss, myalgia are frequently detected. Vision problems are seen in 14-70%, they are severe and irreversible. Polymyalgia rheumatica is 40-60%. Extracranial involvement is in the proximal aorta, subclavian, axillary, proximal bronchial artery, abdominal aorta, and lower extremity arteries.

Interstitial Lung Disease Associated with Systemic Lupus Erythematosus

6 Chapter

Tuğba İZCİ DURAN

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of unknown cause that can affect almost every organ in the body. Immunological abnormality, especially the production of antinuclear antibodies (ANA), is a distinctive feature of the disease. Patients present with clinical features ranging from mild joint and skin involvement to life-threatening kidney, hematological, respiratory system, or central nervous system involvement. Many patients develop symptoms secondary to pulmonary involvement in SLE during their disease. Pulmonary manifestations of SLE are pleurisy, pneumonia, interstitial lung disease, pulmonary hypertension, Shrinking Lung Syndrome, and alveolar hemorrhage. Pleurisy, nonproductive cough, and/or dyspnea are often the first clues to lung involvement. However, abnormal PFT findings and/or chest radiographs sometimes can be detected in asymptomatic patients. Patients with SLE and lung involvement should always be evaluated for infection, especially due to bacteria or viruses. Given that many patients with SLE are immunosuppressive due to underlying disease or ongoing medications, opportunistic infections (e.g., mycobacteria or fungi) should also be considered in the differential diagnosis.

Interstitial lung disease in patients with systemic lupus erythematosus is presented in detail below.

INTERSTITIAL LUNG DISEASE

The true prevalence of chronic SLE-associated interstitial lung disease (SLE-ILD) is unknown, but its prevalence has been reported at between 3 and 9 percent and is rarely severe. Its prevalence in studies using HRCT is estimated to reach 70%. As with other rheumatic diseases, the types of SLE-IAD are similar to the histopathology of various idiopathic interstitial pneumonias. Non-specific interstitial pneumonia (NSIP), usual interstitial pneumonia (UIP), organizing pneumonia, lymphocytic interstitial pneumonia (LIP), follicular bronchiolitis, and nodular lymphoid hyperplasia have been reported in association with SLE. Initially, there is lymphocytic infiltration of the alveolar wall with the formation of a reticular pattern on high-resolution computed tomography (HRCT) imaging. While the NSIP pattern is the most commonly observed pattern in SLE, the UIP pattern is rarely seen.

Clinic in patients with interstitial lung disease typically presents with insidious onset of chronic nonproductive cough, dyspnea, and decreased exercise tolerance, but some patients may be asymptomatic. Physical examination typically reveals basilar rales at the end of inspiration.