



A Case of Interstitial Lung Disease in a patient with Rheumatoid Arthritis

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Article Info

Received: September 01, 2026

Accepted: September 10, 2026

Published: September 25, 2026

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Citation: Simoni Shah, Aneri Parikh, Aditi Parmar, Dev Desai and Jainam Shah. (2026) "A Case of Interstitial Lung Disease in a patient with Rheumatoid Arthritis." Journal of International Medical Sciences, 1(1); DOI: 10.61148/JIMS/001

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Abstract:

This case report presents a unique instance of interstitial lung disease (ILD) occurring in a 60-year-old female patient with a history of rheumatoid arthritis. Interstitial lung disease (ILD) refers to a group of disorders characterized by inflammation and scarring (fibrosis) of the interstitium, which is the tissue that surrounds the air sacs (alveoli) in the lungs which typically affects the lung's ability to function properly. The correlation between ILD and RA has garnered increasing attention in recent years, as studies have highlighted the significant impact of ILD on the morbidity and mortality of RA patients. Interstitial lung disease (ILD) is a recognized extra-articular manifestation of rheumatoid arthritis (RA), a chronic autoimmune disorder primarily affecting the joints. The patient presented with persistent dry cough and exertional dyspnea, graded as MMRC grade 2, with a gradual onset of symptoms. This case underscores the importance of vigilance for respiratory manifestations in patients with rheumatoid arthritis, particularly in those with multiple comorbidities, to ensure timely diagnosis and management of interstitial lung disease.

Keywords: interstitial lung disease; interstitium; fibrosis; dyspnea; rheumatoid arthritis

Introduction

Interstitial lung disease describes a large group of disorders, most of which cause progressive scarring of lung tissue. The scarring associated with interstitial lung disease eventually affects your ability to breathe and get enough oxygen into your bloodstream. Interstitial lung disease can be caused by long-term exposure to hazardous materials, such as asbestos. Some types of autoimmune diseases, such as rheumatoid arthritis, also can cause interstitial lung disease. In some cases, however, the causes remain unknown. Once lung scarring occurs, it's generally irreversible.

Medications may slow the damage of interstitial lung disease, but many people never regain full use of their lungs [1].

Rheumatoid arthritis (RA) is a systemic inflammatory disease primarily affecting synovial joints with possible involvement of other organs. It is most often diagnosed in the fourth and fifth decades of life, and women are affected three times as often as men. The lung is a common site of extra-articular disease. Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is one of the most feared manifestations and causes serious

morbidity and increased mortality [2].

Clinically, RA can essentially affect any lung compartment including: the parenchyma, manifesting as interstitial lung disease (ILD) or rheumatoid nodules; pleura, resulting in pleural inflammation and/or effusions; small and large airways (cricoarytenoiditis, constrictive or follicular bronchiolitis and bronchiectasis); and pulmonary vasculature (vasculitis and pulmonary hypertension). Though lung involvement in RA typically occurs following articular manifestations, pulmonary manifestations may occasionally precede joint symptoms [3].

The presented case report highlights the event of interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA), emphasizing the importance of early recognition and comprehensive management. Clinically, patients may present with a spectrum of pulmonary manifestations ranging from mild dry cough, occasional shortness of breath (especially on exertion) and mild fatigue to rapidly progressive and persistent dry cough, severe shortness of breath, difficulty performing daily activities, cyanosis, rapid weight loss and chronic respiratory failure [1,4]. Hence, it is crucial to exercise caution when managing patients with ILD associated with RA, as it poses significant risks and complications that can arise unexpectedly. Therefore, utmost care and vigilance are essential.

Case presentation:

A 60-year-old woman, hailing from a lower socioeconomic background, presented at the outpatient department accompanied by her husband, reporting dry cough and exertional dyspnoea (graded as MMRC grade 2), which gradually developed over the past two and a half to three months. She had been asymptomatic three months prior. Initially, she experienced nocturnal dry cough, which progressively extended to mornings despite attempting traditional remedies such as hot water, honey, ginger tea, steam inhalation, warm liquids, and avoiding cold foods like ice cream and cold water, as well as gargling with warm salt water, all of which provided no relief. Subsequently, she began experiencing shortness of breath, initially only during light physical activities such as household chores, but rest would alleviate her symptoms, leading her to dismiss them. Over time, her symptoms worsened, with breathlessness occurring during activities such as shopping for groceries, rushing to catch a bus, or climbing stairs. Despite attributing her fatigue and breathlessness to her busy lifestyle and physical exertion, she noticed her reduced walking pace compared to peers of similar age, particularly evident during a recent family outing to a local fair. Concerned by her declining functional capacity, she sought medical attention at L.G. Hospital's outpatient department. There is no associated fever, headache, dizziness, vomiting, diarrhoea, difficulty swallowing, abdominal pain or blood in stool.

Past history:

The patient has a confirmed history of rheumatoid arthritis for the past decade. Additionally, she has been diagnosed with diabetes for the past six years and hypothyroidism for the past three years.

Physical examination:

The patient was conscious, oriented to place and person and responding to verbal commands. She was vitally stable; physical examination showed a temperature of 97.9 F, pulse rate of 86/min, blood pressure of 130/80 mm Hg, SpO₂ 95% on room air, and RBS of 140 mg/dl. Grade 2 clubbing was seen bilaterally, on both the fingers (specifically on index fingers of both hands). There was no evidence of jaundice, anemia, edema, lymphadenopathy or cyanosis on physical examination. Respiratory examination revealed bilateral fine Velcro creps which were evident in the infrascapular region. On cardiovascular examination, S1 and S2 were heard with a loud P2 at the pulmonary area. On GI examination, abdomen was non-distended non-tender with normal bowel sounds. On neurological examination, the patient was alert; reflexes and tone in the upper and the lower limbs was normal. Therefore, other than her respiratory concerns, no other abnormalities were noted during our comprehensive systemic examination.

Lab investigations:

- Blood examination (Hb, WBC + WBC differential counts, RBC, Haematocrit, platelet counts), Liver Function Test, Renal Function Test, Lipid Profile were within the normal range [Table 1-4].

Test	Observed Value	Reference Range
Hemoglobin	12 g/dl	(12-18)
WBC	10.00 kU/L	(5.2-12.4)
RBC	4.5 * 10 ⁶ /ul	(4.5-5.5)
Hematocrit	40.3%	(40-50)
Platelet counts	294 kU/L	(130-400)
Neutrophile	75 %	(49-74)
Lymphocyte	27%	(26-46)
Monocyte	05%	(2-12)
Eosinophil	01%	(0-5)
Basophil	00%	(0-2)

Table 1: Blood examination.

Test	Observed Value	Reference Range
SGPT serum	30 U/L	(10-49 U/L)
SGOT serum	27 U/L	(0-34 U/L))
Alkaline Phosphatase Serum	46 U/L	(45-129 U/L)
Total Bilirubin	0.40 mg/dl	(0.3-1.2 mg/dl)
Direct Bilirubin	0.20 mg/dl	(0-0.3 mg/dl)
Indirect Bilirubin	0.34 mg/dl	-

Table 2: Liver Function Test.

Test	Observed Value	Reference Range
Blood Urea	20.0 mg/dl	(15-45 mg/dl)
Creatinine serum	0.80 mg/dl	(0.5-1.1 mg/dl)
Sodium serum	140 mmol/L	(132-146 mmol/L)
Potassium serum	4.24 mmol/L	(3.5-5.5 mmol/L)
Chlorine serum	105 mmol/L	(99-109 mmol/L)

Table 3: Renal Function Test.

Test	Observed Value	Reference Range
Total cholesterol	198mg/dL	(<200 mg/dl)
Triglycerides	140mg/dL	(<150 mg/dl)
HDL cholesterol	42mg/dL	(>40 mg/dl)
Non-HDL cholesterol	120mg/dL	(<130 mg/dl)
VLDL cholesterol	27mg/dL	(<30 mg/dl)
CHOL/HDL ratio	4.7	(0-4.97)

Table 4: Lipid Profile.

- Other Investigations:**

- 2D Echocardiography:** Right ventricular systolic pressure (RVSP): 45 mm Hg
Right Atrium and Right Ventricle: Dilated
Moderate to severe tricuspid regurgitation noted
Left ventricular ejection fraction (LVEF): 55%
- C-reactive protein (CRP):** >9.6, positive
- Rheumatoid Arthritis factor (RA factor):** positive
- Anti-cyclic citrullinated peptide (anti-CCP):** positive
- ECG:** P Pulmonale is seen

- HRCT of Thorax:** Thorax HRCT revealed subpleural honeycombing with adjacent fibrotic changes seen in bilateral lower lung fields highly suggestive of Usual Interstitial Pneumonia (UIP) pattern.

Diagnosis:

The patient presented with signs and symptoms concerning for Interstitial Lung Disease as evidenced in the HRCT of the Thorax. After ruling out other causes of Interstitial Lung Disease like smoking, exposure to dust or asbestos, exposure to mold, toxins or pollutants such as grain dust, bird and animal droppings, certain chemotherapeutic drugs, anti-biotics and idiopathic causes, a correlation was established between Rheumatoid Arthritis and Interstitial Lung Diseases. Furthermore, investigations like RA factor and anti-CCP played an important role in confirming the diagnosis of Interstitial Lung Disease due to Rheumatoid Arthritis.

Management:

The patient's treatment regimen was augmented with Pirfenidone, an anti-fibrotic medication, in addition to the existing medications for Rheumatoid Arthritis, namely Leflunomide, Methotrexate, and Hydroxychloroquine. Upon discharge, the patient was prescribed Mycophenolate, a cytotoxic agent.

She had already been taking thyroxine for her hypothyroidism, amlodipine for hypertension, and a combination of Glimison M2, VogzM, and Vildagliptin for diabetes mellitus.

Lung transplantation is a viable therapeutic approach for eligible patients with progressive disease that is not responsive to medical therapy.

Discussion:

Interstitial lung diseases (ILDs) encompass a diverse group of disorders characterized by inflammation and fibrosis of the lung interstitium, the tissue and space around the alveoli in the lungs. Common types of ILD include Idiopathic Pulmonary Fibrosis (IPF), a chronic, progressive fibrotic disorder with no known cause; Sarcoidosis, a multisystem granulomatous disease often involving the lungs; Hypersensitivity Pneumonitis, an inflammatory syndrome caused by inhaled organic dusts; Connective Tissue Disease-Associated ILD, which includes conditions like rheumatoid arthritis and systemic sclerosis; and Occupational and Environmental ILD, resulting from exposure to hazardous materials such as asbestos and silica [5]. Symptoms typically include a persistent dry cough, shortness of breath (dyspnea), fatigue, weight loss, and chest discomfort. Diagnosis involves a detailed patient history and physical examination to identify potential exposures or underlying diseases, pulmonary function tests (PFTs) to assess lung volumes and gas exchange, high-resolution CT (HRCT) scans of the chest to identify patterns of lung involvement, lung biopsies in selected cases to confirm diagnosis and determine the specific type of ILD, and blood tests to rule out autoimmune diseases or other conditions. Treatment options include medications such as anti-fibrotic agents (e.g., pirfenidone, nintedanib) for IPF, corticosteroids, and immunosuppressants for inflammatory ILDs, oxygen therapy for patients with significant hypoxemia, pulmonary rehabilitation involving exercise training, education, and support, and lung transplant for advanced cases refractory to medical treatment [2,6]. The prognosis of ILD varies widely depending on the specific type and severity; some forms, like IPF, have a poor prognosis with a median survival of 3-5 years after diagnosis, while others, like sarcoidosis, may have a more benign course or even resolve spontaneously. Interstitial lung diseases are complex pulmonary disorders requiring a multidisciplinary approach for diagnosis and management, and early recognition and appropriate treatment are crucial to improving patient outcomes and quality of life [7].

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized by inflammation of the synovial joints, leading to progressive joint damage, pain, and disability. It occurs when the immune system mistakenly attacks the synovium, resulting in inflammation that thickens the synovium and can eventually destroy cartilage and bone within the joint. The exact cause of RA is unknown, but genetic, environmental, and hormonal

factors are believed to play a role [8]. Symptoms include persistent joint pain, tenderness, and swelling, typically in the hands, wrists, and feet, morning stiffness lasting more than 30 minutes to an hour, symmetrical joint involvement, fatigue, fever, and loss of appetite, and rheumatoid nodules. Diagnosis involves clinical evaluation, laboratory tests (including rheumatoid factor and anti-CCP antibodies, elevated ESR, and CRP), and imaging (X-rays, ultrasound, or MRI). Treatment options include NSAIDs for pain relief, corticosteroids for acute flares, DMARDs such as methotrexate to slow disease progression, and biologic agents for patients unresponsive to traditional DMARDs. Supportive measures include physical and occupational therapy, regular exercise, a healthy diet, and patient education and support groups. Although RA is a chronic condition with no cure, early diagnosis and appropriate treatment can help many patients achieve remission or low disease activity, improving outcomes and quality of life. Regular monitoring and treatment adjustments are essential to manage disease activity and prevent complications [4,9].

Rheumatoid arthritis (RA) is a systemic autoimmune disorder primarily affecting the joints but can also involve various extra-articular organs, including the lungs. Interstitial lung disease (ILD) is one of the most significant pulmonary complications associated with RA. The exact mechanisms linking RA and ILD are not fully understood, but it is believed that the same autoimmune processes causing joint inflammation in RA can also target lung tissue, leading to chronic inflammation, fibrosis, and scarring of the lung interstitium. RA-associated ILD (RA-ILD) occurs in approximately 10% of RA patients, though subclinical or mild interstitial changes can be found in up to 30-40% of patients using high-resolution imaging techniques. Symptoms of RA-ILD include a persistent dry cough, shortness of breath on exertion, fatigue, chest discomfort, and joint symptoms consistent with RA [3,10]. Diagnosis involves clinical evaluation, pulmonary function tests, high-resolution CT scans, and occasionally lung biopsies and blood tests. Treatment options include immunosuppressive agents, corticosteroids, anti-fibrotic agents, oxygen therapy, and pulmonary rehabilitation, with close monitoring by pulmonary and rheumatology specialists. The prognosis of RA-ILD varies, with some patients experiencing slow progression and others having rapidly progressive disease leading to significant morbidity and mortality. The presence of ILD in RA patients generally indicates a worse overall prognosis, highlighting the need for early detection and a multidisciplinary approach for optimal management to improve outcomes and quality of life [11].

Conclusion:

The intersection of RA and ILD presents a complex clinical challenge, emphasizing the need for heightened awareness and early detection among healthcare providers. This patient's case underscores the importance of comprehensive diagnostic evaluations, including high-resolution imaging and pulmonary function tests, to identify and monitor ILD in RA patients. Additionally, it illustrates the critical role of a multidisciplinary approach in managing such cases, integrating rheumatology, pulmonology, and radiology expertise to optimize patient outcomes. Further research is warranted to better understand the pathophysiological mechanisms linking RA and ILD, and to

develop tailored therapeutic strategies that can effectively address both conditions. This case adds to the growing body of evidence on RA-associated ILD, offering valuable insights for clinicians and contributing to the ongoing efforts to improve the care of patients with this dual diagnosis.

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