International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1221-1225 www.ijprajournal.com ISSN:2456-4494

Rituximab-Induced Interstitial Lung Disease: A Case Report

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Date of Submission: 03-08-2026 Date of Acceptance: 15-08-2026

ABSTRACT

Rituximab-induced interstitial lung disease (RTX-ILD) is a rare but clinically significant complication. It is an anti-CD20 monoclonal antibody used in non-Hodgkin lymphoma, chronic lymphocytic leukemia, and autoimmune diseases such as rheumatoid arthritis. Its prevalence varies widely, with clinical trials reporting <0.03% (approximately 1 in 3,000–3,500 patients), while real-world studies show higher rates of 3.7–10%, reaching up to 14% in high-risk groups. Clinically, it presents with progressive dyspnea (80–90%), dry cough (60–70%), and fever (40–60%), and is often underdiagnosed due to nonspecific features.

RTX-ILD typically develops after repeated exposure, most commonly between the third and fifth treatment cycles, with a delayed onset occurring weeks after infusion. In this context, a 69-year-old female with non-Hodgkin lymphoma developed RTX-ILD after the fourth cycle of chemotherapy. She was receiving a regimen consisting of INJ.CYCLOPHOSPHAMIDE (700 mg), INJ. DOXORUBICIN (40 mg), INJ. VINCRISTINE(1mg), and INJ. RITUXIMAB (600mg), INJ. PREDNISOLONE (40mg). She presented with abdominal discomfort, vomiting, fever, and dry cough. The diagnosis was established based on clinical features, radiological evidence of interstitial lung involvement, and exclusion of infectious causes.

Management involves immediate discontinuation of rituximab, with systemic corticosteroids recommended in moderate to severe cases. Clinical and radiological improvement is commonly observed with early intervention; however, delayed recognition may result in respiratory failure and increased mortality. Given its nonspecific presentation and potential severity, heightened clinical awareness and early diagnostic consideration are essential for optimizing patient outcomes.

Keywords: Rituximab, Interstitial lung disease, Non-Hodgkin lymphoma

I. Introduction

Rituximab is a chimeric monoclonal antibody that targets the CD20 antigen on mature B lymphocytes and is widely used to treat B-cell malignancies, including non-Hodgkin lymphoma and chronic lymphocytic leukemia, as well as autoimmune disorders. By inducing B-cell depletion through complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity, and apoptosis, rituximab has significantly improved patient outcomes. Although generally well tolerated, rituximab has been associated with adverse effects such as infusion reactions, infections, hepatitis B reactivation, hematological abnormalities, and rare pulmonary toxicities. RTX-ILD is an uncommon but potentially life-threatening complication. Its exact pathogenesis remains unclear, with proposed mechanisms including cytokine-mediated inflammation and immune dysregulation. RTX-ILD typically develops within days to weeks after treatment and presents with nonspecific symptoms including dyspnea, dry cough, fever, and hypoxemia. HRCT commonly shows bilateral ground-glass opacities or diffuse interstitial infiltrates. Early diagnosis is essential, as prompt discontinuation of rituximab and corticosteroid therapy can improve outcomes.

II. Case Presentation

A 69-year-old female presented to the emergency department with complaints of generalized weakness, progressive fatigue, and

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multiple episodes of non-bilious, non-bloody vomiting for three days. The fatigue had progressively worsened over the preceding days and significantly limited her ability to perform routine daily activities. There was no history of hematemesis, melena, abdominal pain, diarrhea, or other gastrointestinal complaints.

The patient was a known case of follicular non-Hodgkin lymphoma and had been receiving chemotherapy with the R-CHOP regimen comprising INJ.CYCLOPHOSPHAMIDE (700 mg), INJ. DOXORUBICIN (40 mg), INJ. VINCRISTINE(1mg), and INJ. RITUXIMAB (600mg), INJ. PREDNISOLONE (40mg) . She had successfully completed four cycles of chemotherapy, with the last cycle administered on 2 January 2026. A fifth cycle had initially been planned; however, it was deferred by the treating oncologist because of her clinical condition. The patient also had a significant family history of lymphoma, with her brother having previously been diagnosed with the disease.

Post-treatment radiological assessment demonstrated regression of the previously enlarged lymph nodes, suggesting a favorable response to chemotherapy. However, imaging also revealed morphological features consistent with liver cirrhosis. In addition, a suspicious hepatic lesion measuring approximately 2.0 × 1.8 cm was identified, necessitating further evaluation by the gastroenterology team.

On admission, the patient was conscious, alert, and oriented. Her vital signs revealed a pulse rate of 107 beats/min, blood pressure of 128/86 mmHg, respiratory rate of 18 breaths/min, and peripheral oxygen saturation (SpO_2) of 94% on room air. General physical examination demonstrated bilateral pedal edema. Respiratory system examination revealed severe bilateral wheezing with associated progressive breathing difficulty, while cardiovascular examination was unremarkable. Examination of the remaining systems did not reveal any significant abnormalities.

Baseline laboratory investigations showed mild leukocytosis, with a total white blood cell count of 12,080 cells/µL, which gradually decreased to 9,510 cells/µL during hospitalization following treatment. The platelet count was 1.40 × 10^5/µL. Although the erythrocyte sedimentation rate remained within normal limits, the C-reactive protein level was elevated at 20.3 mg/L, indicating an ongoing inflammatory process.

Biochemical evaluation demonstrated evidence of hepatic dysfunction. Total bilirubin was elevated at 3.75 mg/dL on admission and subsequently decreased to 3.08 mg/dL after four days of treatment. Direct bilirubin improved from 2.40 mg/dL to 1.71 mg/dL, while indirect bilirubin remained relatively stable. Serum AST was elevated at 95 U/L initially and showed a slight decline to 91 U/L. ALT increased from 40 U/L to 85 U/L during hospitalization, whereas ALP decreased from 140 U/L to 116 U/L. Serum electrolyte analysis revealed mild hyponatremia, with a sodium level of 131 mmol/L, while the potassium level remained within the normal range at 4.8 mmol/L.

Despite supportive management, the patient's respiratory symptoms progressively worsened, with persistent wheezing and increasing dyspnea. In view of the worsening respiratory status, a computed tomography (CT) scan of the chest was performed, which demonstrated a few areas of pulmonary consolidation. To further characterize these abnormalities, a high-resolution computed tomography (HRCT) scan of the chest was obtained. HRCT revealed diffuse bilateral ground-glass opacities with multifocal areas of consolidation and interlobular septal thickening. Based on these radiological findings, the possibility of drug-related pulmonary toxicity was suggested.

Considering the temporal relationship between recent administration of rituximab-containing chemotherapy and the development of progressive respiratory symptoms, together with the characteristic HRCT findings, of diffused bilateral ground glass densities, few consolidations and areas of interlobular septal thickening rituximab-induced interstitial lung disease was considered the most likely diagnosis. The patient was subsequently reffered to the Department of Oncology for further evaluation and management.

They started CORTICOSTEROID therapy with intravenous METHYLPREDNISOLONE (500 mg) once daily for three consecutive days. INJ. FUROSEMIDE (20 mg) twice daily was administered to manage fluid overload, while nebulization with LEVOSALBUTAMOL and BUDESONIDE every six hours was initiated to relieve bronchospasm and improve respiratory function.

As infectious pneumonia remained a differential diagnosis at presentation, empirical antimicrobial therapy with INTRAVENOUS MEROPENEM (1g) every 8 hours and INJ. AZITHROMYCIN (500 mg) once daily was commenced, latter the INJ.AZHITHROMYCIN was stopped afer 7 days. Following completion of pulse CORTICOSTEROID therapy, the patient was transitioned to oral T.PREDNISOLONE (20 mg) in a

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2-1-0 dosing schedule, which was planned to be continued for one month with further adjustment based on her clinical response.

Considering the concomitant diagnosis of liver cirrhosis and the presence of a hepatic lesion, supportive management included T.URSODEOXYCHOLIC ACID (300 mg) twice daily, LACTULOSE SYRUP (20 mL), and INJ. VITAMIN K (10 mg) once daily for 10 days. Following stabilization, the patient was discharged on maintenance therapy with T.FUROSEMIDE 20 mg and SPIRONOLACTONE (50 mg) once daily for edema associated with chronic liver disease.

Following treatment, the patient's respiratory symptoms improved gradually, with reduction in wheezing and improvement in her overall clinical status. She remained hemodynamically stable throughout the remainder of her hospital stay and was discharged with advice to continue the prescribed medications. She was scheduled for follow-up after 10 days in both the Oncology and Gastroenterology outpatient departments for reassessment of her pulmonary status, lymphoma, liver cirrhosis, and hepatic lesion.

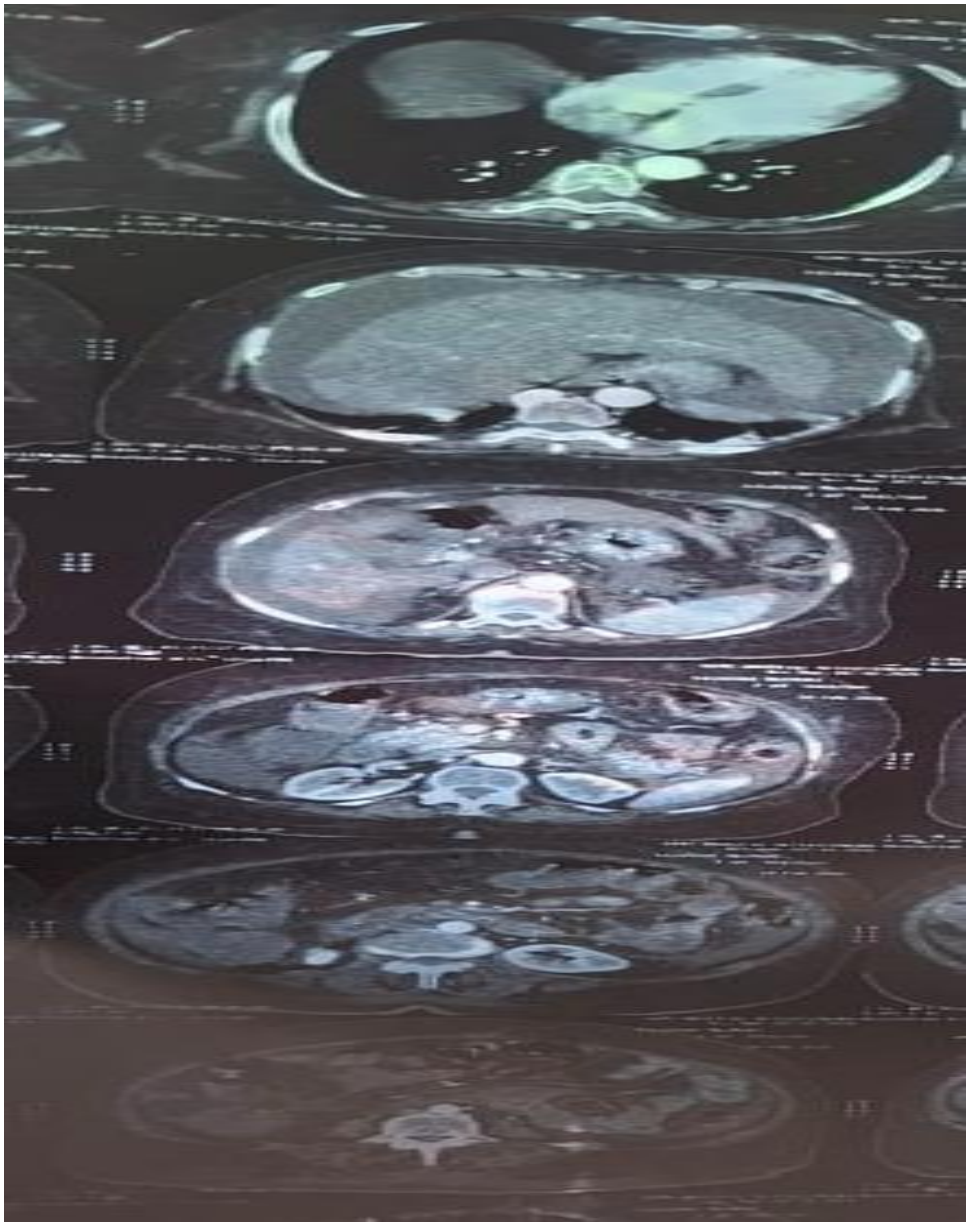

Fig 1: HRCT SCAN

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III. Discussion

Rituximab is an integral component of treatment for B-cell malignancies, particularly non-Hodgkin lymphoma, owing to its ability to improve response rates and overall survival when combined with conventional chemotherapy. Although generally well tolerated, rituximab has been associated with rare but potentially life-threatening pulmonary adverse effects, including rituximab-induced interstitial lung disease (RI-ILD). Increasing reports in the literature suggest that RI-ILD is likely underrecognized because of its nonspecific clinical presentation and the difficulty in differentiating it from other pulmonary complications encountered in patients receiving chemotherapy.

The onset of RI-ILD is variable, typically occurring within days to several weeks after rituximab administration, particularly following multiple treatment cycles. Patients commonly present with progressive dyspnea, dry cough, fever, fatigue, hypoxemia, and, in severe cases, acute respiratory failure. Since these manifestations closely resemble infectious pneumonia, pulmonary edema, pulmonary embolism, and pulmonary involvement by the underlying malignancy, clinicians should maintain a high index of suspicion in patients receiving rituximab who develop new respiratory symptoms.

High-resolution computed tomography (HRCT) is the preferred imaging modality for evaluating suspected RI-ILD. The most frequently reported findings include bilateral ground-glass opacities, patchy or diffuse consolidation, interlobular septal thickening, reticular opacities, and organizing pneumonia patterns. Although these findings are not specific, they strongly support the diagnosis when interpreted alongside the patient's clinical history and recent rituximab exposure.

There are no universally accepted diagnostic criteria for RI-ILD, and the diagnosis remains one of exclusion. It is established through a compatible temporal relationship with rituximab therapy, characteristic HRCT findings, and careful exclusion of infectious and noninfectious causes of diffuse pulmonary infiltrates. Additional investigations, including microbiological cultures, inflammatory markers, and bronchoalveolar lavage when indicated, may assist in excluding alternative diagnoses.

Management primarily involves immediate discontinuation of rituximab and early initiation of systemic corticosteroids. Although standardized treatment guidelines are lacking, published case reports and systematic reviews consistently support the use of high-dose intravenous methylprednisolone in moderate-to-severe disease, followed by oral corticosteroids with gradual tapering according to the patient's clinical and radiological response. Supportive measures, including oxygen therapy, bronchodilators, and ventilatory support when required, are essential. Empirical broad-spectrum antibiotics are frequently administered until infectious causes have been reasonably excluded.

The prognosis of RI-ILD largely depends on early recognition and prompt treatment. Most patients demonstrate significant clinical and radiological improvement following withdrawal of rituximab and corticosteroid therapy, whereas delayed diagnosis may lead to respiratory failure, irreversible pulmonary fibrosis, or death. Therefore, clinicians should maintain a high index of suspicion for RI-ILD in patients receiving rituximab who present with unexplained respiratory symptoms. Early HRCT evaluation, multidisciplinary assessment, and timely corticosteroid therapy remain the cornerstone of successful management and improved patient outcomes.

IV. Conclusion

Rituximab-induced interstitial lung disease is a rare but potentially life-threatening adverse drug reaction that should be considered in patients receiving rituximab-containing chemotherapy who develop new or worsening respiratory symptoms. Because its clinical presentation is nonspecific and may mimic infectious or malignant pulmonary conditions, early recognition, prompt HRCT evaluation, and exclusion of alternative etiologies are essential for timely diagnosis. Immediate discontinuation of rituximab, initiation of systemic corticosteroid therapy, and appropriate supportive care remain the cornerstone of management and are associated with favorable clinical outcomes when instituted early. This case highlights the importance of maintaining a high index of suspicion, multidisciplinary collaboration, and vigilant monitoring to facilitate early diagnosis and improve patient outcomes. Further reporting of similar cases is warranted to enhance understanding of this uncommon adverse reaction and to strengthen the evidence guiding its diagnosis and management.

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Volume 11, Issue 4, Jul.-Aug.2026, pp:1221-1225 www.ijprajournal.com ISSN:2456-4494

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