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CASE REPORT

Methotrexate-Induced Pulmonary Fibrosis in a Patient with Rheumatoid Arthritis: A Case Report

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Abstract

Methotrexate is a cornerstone in the treatment of rheumatoid arthritis (RA), offering immunosuppressive benefits that significantly reduce disease progression. However, rare adverse effects such as pulmonary fibrosis can be life-threatening. We report the case of a 66-year-old female with seropositive RA who developed progressive dyspnea and dry cough after 14 months of methotrexate therapy. Imaging and pulmonary function tests revealed restrictive lung disease, and high-resolution CT demonstrated interstitial changes consistent with drug-induced pulmonary fibrosis. Methotrexate was discontinued, and corticosteroid therapy was initiated, leading to partial symptomatic improvement. Clinicians must remain vigilant for methotrexate-induced pulmonary complications, particularly in patients presenting with new respiratory symptoms. Early recognition and intervention can mitigate irreversible damage.

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder primarily affecting joints but also associated with extra-articular manifestations (Conforti et al., 2021; Figus et al., 2021). Methotrexate (MTX), a folate antagonist, remains a first-line disease-modifying antirheumatic drug (DMARD) due to its proven efficacy in controlling inflammation and preventing joint destruction (Bedoui et al., 2019; Shafiq et al., 2025). However, its long-term use is associated with potential adverse effects, including hepatotoxicity, myelosuppression, and less frequently, pulmonary toxicity (Solomon et al., 2020; Wang et al., 2018).

MTX-induced pulmonary fibrosis is an uncommon but serious complication that may be irreversible (Kim et al., 2009) (Dawson et al., 2021). The incidence ranges from 0.3% to 11.6% in various cohorts, often presenting as nonspecific interstitial pneumonia (NSIP) or organizing pneumonia (Fragoulis et al., 2019). Diagnosis is largely clinical, based on the exclusion of infection, heart failure, or primary interstitial lung disease, and supported by radiologic and functional findings.

Here, we present a case of MTX-induced pulmonary fibrosis in a woman with RA, highlighting the clinical presentation, diagnostic process, and management strategies.

2. Case Report

A 66-year-old female with a 3-year history of seropositive rheumatoid arthritis presented to the rheumatology clinic with progressive shortness of breath and dry cough for the past six weeks. She denied fever, chest pain, or orthopnea. She was on weekly methotrexate (15 mg) orally, folic acid (5 mg daily), and prednisolone (5 mg/day). Her arthritis had been well-controlled for the last year (Table 1).

She had no prior history of lung disease, tuberculosis, or smoking. Physical examination revealed fine inspiratory crackles at bilateral lung bases without signs of fluid overload or cardiac dysfunction.

Bronchoscopy with lavage was negative for infectious causes, including tuberculosis and fungal pathogens. Cardiac workup including echocardiography was unremarkable.

Based on the temporal association with methotrexate, clinical exclusion of other causes, and typical radiographic findings, a diagnosis of methotrexate-induced pulmonary fibrosis was made.

Table 1: Baseline and Diagnostic Data

Parameter	Value	Reference Range	Interpretation
White blood cell count	7.2 $\times 10^3/\mu L$	4.0–11.0 $\times 10^3/\mu L$	Normal
ESR	28 mm/hr	<20 mm/hr	Mildly elevated
CRP	10 mg/L	<5 mg/L	Elevated
RF/Anti-CCP	Positive	Negative	Confirms RA
Chest X-ray	Bilateral reticular shadowing	—	Suggestive of ILD
HRCT chest	Ground-glass opacities, sub-pleural reticulation	—	Interstitial lung disease
Pulmonary function test	FVC 65%, DLCO 48%	>80% normal	Restrictive pattern

3. Discussion

Methotrexate-induced pulmonary toxicity is a well-documented but rare adverse effect, more common in elderly, female, and nonsmoking patients with RA (Crestani et al., 2015; Lopez-Olivo et al., 2025). The mechanism is believed to involve hypersensitivity reactions or direct alveolar damage due to oxidative stress and folate pathway disruption (Matouk et al., 2023).

Symptoms often develop insidiously, as in our case, or acutely with fever and hypoxia. A high index of suspicion is warranted when respiratory symptoms develop in patients on MTX, especially beyond six months of therapy.

High-resolution CT (HRCT) typically reveals bilateral interstitial changes, such as ground-glass opacities, septal thickening, and honeycombing in advanced cases (Schaefer-Prokop et al., 2001). Pulmonary function tests (PFTs) show a restrictive pattern with decreased diffusion capacity (DLCO) (Aduen et al., 2007).

In the present case, radiographic and functional findings, coupled with the exclusion of infection and cardiac pathology, were key to diagnosis. Although lung biopsy provides definitive histology, it is often avoided due to procedural risk, particularly in the elderly.

Management typically involves immediate discontinuation of methotrexate and administration of systemic corticosteroids. In our case, prednisone 40 mg/day was initiated, with gradual taper over 6 weeks. The patient's symptoms improved modestly, although some functional impairment persisted, consistent with partial fibrosis.

4. Conclusion

This case emphasizes the importance of recognizing methotrexate-induced pulmonary fibrosis in patients with RA presenting with new respiratory symptoms. Early diagnosis, exclusion of alternative causes, and drug withdrawal are critical to minimizing irreversible lung damage. Routine pulmonary monitoring and patient education may help in timely detection of this serious but preventable complication.

Declarations

Ethics approval statement

No ethical approval was required for the current study as it did not deal with any human or animal samples.

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

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Author contribution

Conceptualization, Data curation, Investigation, Formal analysis: A.S.S. Writing—review and editing: I.H. All authors have read and agreed to the published version of the manuscript

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