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Pulmonary Nodules Mimicking Metastasis in a Patient with Rheumatoid Arthritis: A Puzzling Clinical Scenario

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Abstract

Background: Pulmonary nodules present a diagnostic dilemma, particularly in patients with systemic autoimmune diseases such as rheumatoid arthritis (RA), where radiologic appearances may mimic metastatic malignancies. Differentiating between malignant and inflammatory etiologies is essential to guide appropriate treatment.

Case Report: We present the case of a 66-year-old female with a known history of RA who developed multiple bilateral pulmonary nodules. Initial imaging and PET-CT raised strong suspicion for metastatic disease; however, no primary malignancy could be identified. Histopathologic evaluation of a lung biopsy revealed necrotic-inflammatory lesions with negative malignancy markers. The patient continued immunosuppressive therapy for RA, and follow up imaging demonstrated near-complete resolution of the nodules. The clinical, radiological, and histopathological findings ultimately supported a diagnosis of rheumatoid pulmonary nodules.

Conclusion: This case underscores the importance of considering RA patients presenting with pulmonary nodules. Multidisciplinary assessment and histologic confirmation are important to avoid misdiagnosis and unnecessary oncologic treatment.

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INTRODUCTION

Pulmonary nodules are common incidental radiologic findings with a wide differential diagnosis, that includes infectious, inflammatory, and neoplastic processes. In patients with rheumatoid arthritis (RA), necrobiotic nodules are a rare but known extra-articular manifestation. When present in multiple and cavitating forms, these nodules can closely mimic metastatic malignancy on imaging, contributing to significant diagnostic dilema (1).

This report presents a case of a patient with RA whose pulmonary nodules were initially suspected to be metastatic disease but were eventually confirmed to be rheumatoid in origin based on histopathological examination, Lung ct follow up evaluation and clinical response to therapy.

CASE PRESENTATION

A 66-year-old female from southern Albania presented to the regional hospital in September 2024 with fever, cough, exertional dyspnea, and generalized weakness. She had a known history of rheumatoid arthritis diagnosed eight months earlier, managed with methotrexate, methylprednisolone, and folic acid. The patient reported poor adherence to therapy and had completely discontinued it since April 2024, prior to the onset of pulmonary symptoms. Her comorbidities included hypertension and type 2 diabetes mellitus. A thoracic CT scan (fig1) obtained at the time of admission demonstrated multiple bilateral pulmonary nodules, raising suspicion for metastatic malignancy.She was than referred to our tertiary care hospital for further evaluation. On physical examination, she appeared clinically stable. Her blood pressure was 120/70 mmHg and her oxygen saturation on room air was 96%. No palpable lymphadenopathy was noted, and cardiopulmonary auscultation was unremarkable. Laboratory findings showed mild thrombocytopenia and elevated blood glucose. Inflammatory markers, including CRP, were within normal range and the sputum culture were negative.

Figure 1. Fisrt Lung CT

To fully evaluate this case, we performed a trans-parietal lung biopsy. Microscopic examination of the biopsy performed on September 16, 2024, revealed necrotic areas surrounded by inflammatory epithelioid-like cells. Immunohistochemistry showed negative expression for malignancy-related epithelial markers (CK5/6, TTF1, PanCK), while CD68 was strongly positive, indicating macrophage-mediated inflammation. Histopathologic images clearly demonstrated these features, supporting a necrotizing inflammatory lesion.

PET-CT performed on September 29, 2024, demonstrated intense hypermetabolic activity with a SUVmax of 15 in the pulmonary nodules, but no hypermetabolic lesions were found in the liver, adrenal glands, bones, or other organs. No mediastinal or retroperitoneal lymphadenopathy was detected, and no primary tumor was located in the ENT, thyroid, or urogenital regions. Tumor markers including CEA, AFP, and CA 19-9 were within normal limits, while CA-125 was mildly elevated at 38.8 U/mL. Autoimmune testing revealed a positive antinuclear antibody (ANA) titer of 1:160 with a speckled pattern, consistent with her known RA. Rheumatoid factor and anti-CCP antibodies were negative.

Facing this diagnostic dilemma, the patient was re-hospitalized in October 2024 for a repeat biopsy. Clinically, she remained stable and asymptomatic. Bronchoscopy was performed and showed slightly hyperemic mucosa with minimal secretions and no obstructive lesions. A repeat transthoracic biopsy under CT guidance was therefore decided. During the procedure, notable retraction of the nodules was observed on imaging (Fig2). Following further discussion with colleagues and the patient, a decision was made to continue with imaging follow-up.

Figure 2. Second Lung CT

A follow-up thoracic CT scan was performed on March 4, 2025. The scan showed significant regression of the previously noted nodular lesions (Fig3). No pleural effusion, lymphadenopathy, or thoracic wall lesions were present. Follow-up imaging demonstrated resolution of the pulmonary nodules, correlating with the immunosuppressive therapy continuation for rheumatoid arthritis. The radiologic findings were indicative of pulmonary involvement secondary to rheumatoid arthritis rather than metastatic disease.

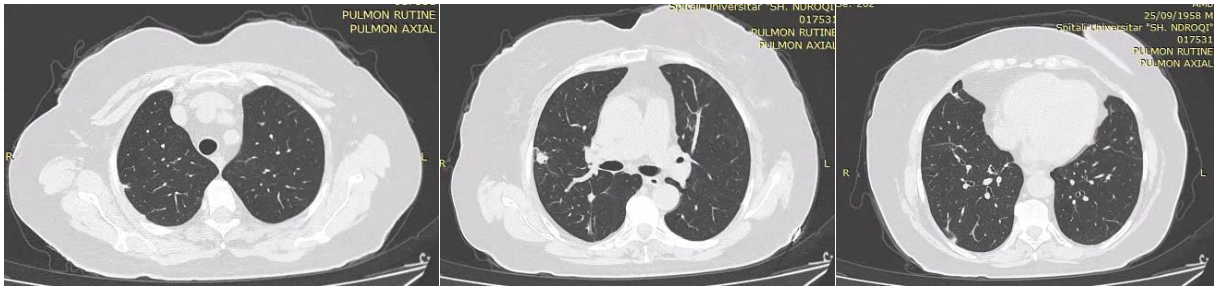

Figure 3. Third Lung CT

The differential diagnosis for multiple pulmonary nodules in this patient enters a broad range of possibilities, including metastatic pulmonary disease, infectious granulomatous processes, lymphoma, and rheumatoid pulmonary nodules. Metastatic disease was initially considered due to the radiologic appearance of multiple bilateral nodules, some with cavitation. However, the absence of a primary malignancy, normal tumor marker profiles, and the complete resolution of the nodules without oncologic intervention decreased the likelihood of metastasis. The importance of biopsy in differentiating these from malignancy is underlined at many reports by *Alhajery (2,3) and León Sierra (4).*

Infectious etiologies, such as tuberculosis or fungal infections, were also considered. However, there were no systemic signs of infection, sputum cultures and inflammatory markers were not consistent with an active infectious process, making this diagnosis less likely.

Lymphoma was another differential consideration. However, this was ruled out based on a negative PET-CT scan, lack of systemic lymphadenopathy, and clinical stability.

The most plausible diagnosis was that of rheumatoid pulmonary nodules, an uncommon extra-articular manifestation of rheumatoid arthritis. This conclusion was supported by the patient's underlying RA, the histopathological findings and the complete radiographic resolution of the nodules responding the immunosuppressive therapy. Other cases highlights the occurrence of pulmonary nodules early in the disease course and the importance of considering RA in the differential diagnosis (5).

The patient continued her RA treatment regimen, including methotrexate, low-dose methylprednisolone, and folic acid; the same therapeutic scheme was resumed as previously prescribed, since the patient had not been taking the medication. No oncologic or antimicrobial therapies were initiated. Concomitant treatment for her hypertension and diabetes was maintained. She remained clinically stable so the radiologic resolution of the nodules confirmed their inflammatory nature.

DISCUSSION

This case raises concern in the diagnostic challenges when evaluating pulmonary nodules

in patients with autoimmune conditions. In patients with rheumatoid arthritis, particularly those undergoing treatment with methotrexate, pulmonary nodules may develop or progress (6,7), presenting radiologic features that look alike secondary malignancy nodules. Although our patient was not under leflunomide therapy, literature reports suggest that even under methotrexate or leflunomide treatment, RA-associated pulmonary nodules may develop or progress. This emphasizes the fact that such manifestations can occur during therapy, further complicating the diagnostic process, highlighting the need for careful monitoring during treatment (3). These nodules can exhibit high metabolic activity on PET-CT scans complicating the differentiation from metastatic disease.

Definitive diagnosis requires histopathological evaluation to exclude a neoplastic processes. In this case, biopsy findings demonstrated CD68 positivity, sugesting of macrophage-rich inflammation, and absence of epithelial markers excluding carcinoma. Additionally, the presence of antinuclear antibodies supported the underlying autoimmune pathology. The complete radiographic resolution of the nodules following the immunosuppressive therapy for RA confirmed their non malignant inflammatory nature.

Recognition of rheumatoid nodules as a potential cause is important in order to prevent misdiagnosis and unnecessary oncologic therapy (8). This case emphasizes the importance of a multidisciplinary approach involving pulmonology, rheumatology, radiology, and pathology in accurately diagnosing pulmonary nodules, with histopathological examination being the definitive tool for establishing the correct diagnosis.

CONCLUSION

Pulmonary nodules in patients with rheumatoid arthritis may clinically and radiologically resemble metastatic disease. This case illustrates the importance of a multidisplinary diagnostic approach, including histopathology, imaging, autoimmune evaluation, and clinical follow-up. In this patient, the nodules were ultimately determined to be rheumatoid in origin concluding through continued immunosuppressive therapy. This case underscores the indispensable value of lung biopsy, with histopathologic confirmation serving as the definitive diagnostic tool in differentiating rheumatoid nodules from malignancy, thereby averting misdiagnosis and inappropriate oncologic interventions.

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Conflict of Interest Statement: The authors declare that they have no conflict of interest.

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