

# Rheumatoid arthritis with necrotic lung nodules

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## Abstract

Rheumatoid arthritis is a multisystemic inflammatory disease. Lungs are the commonest site of extra-articular involvement. Rheumatoid lung nodules occur infrequently and can undergo necrosis giving rise to necrobiotic lung nodules. Infections, malignancy and granulomatosis with polyangiitis are more common causes of cavitating lung nodules. Presence of rheumatoid factor, history of smoking and use of methotrexate increase the chances of developing rheumatoid lung nodulosis. Histopathological examination of the nodule is essential to make a correct diagnosis. We present a 74-year-old male with long-standing rheumatoid arthritis who had multiple cavitating lung nodules. Biopsy from the lung nodule could not be performed as the patient refused to consent. However, infection, malignancy and granulomatosis with polyangiitis were ruled out on the basis of blood investigations and bronchoscopy. He was empirically treated with a moderate dose of glucocorticoid along with conventional synthetic disease-modifying antirheumatic drugs. After three months of treatment, the lung nodules disappeared completely and his articular symptoms showed marked improvement.

**Keywords:** rheumatoid arthritis, cavitating lung nodules, steroids

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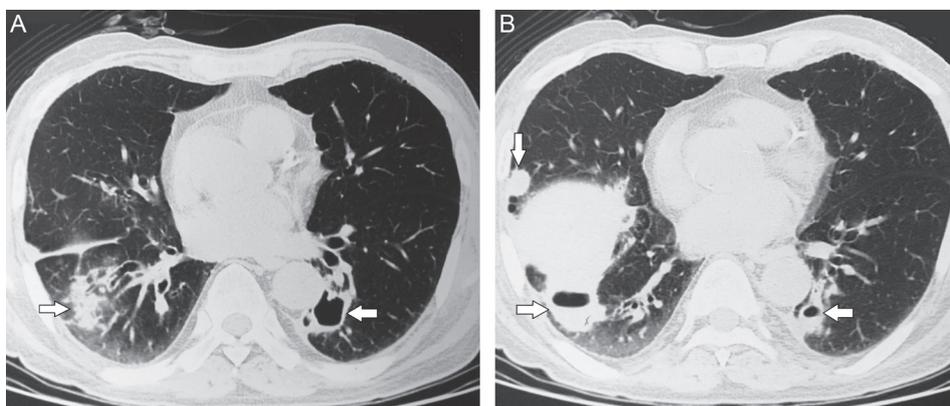
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## Case presentation

A 74-year-old male suffered from seropositive rheumatoid arthritis for 22 years and was treated with methotrexate. He presented with difficulty in breathing and a non-productive cough, progressing over the previous month. Examination revealed tubular bronchial breath sounds in the right infrascapular and infra-axillary areas. Synovitis was evident in metacarpophalangeal joints, wrists and shoulders along with deformities (clinical disease activity index [CDAI] 48).

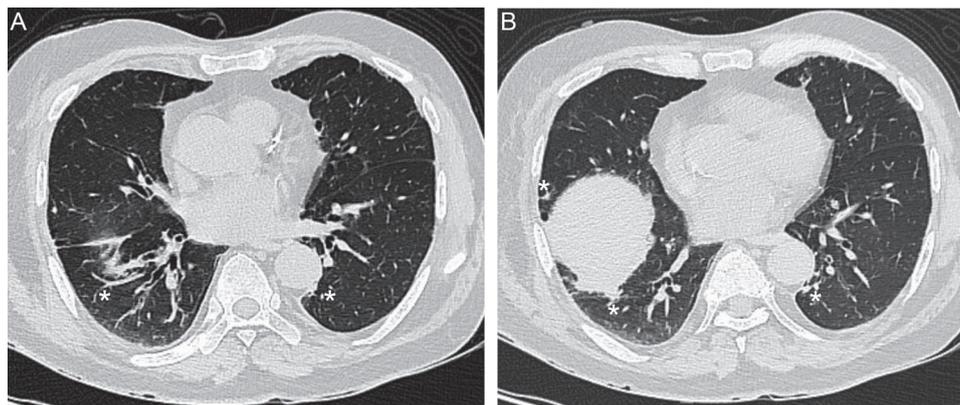
He did not have fever or other constitutional features. Radiograph of the chest showed a cavity in the right lower zone. Contrast-enhanced computed tomography (CECT) of the chest was remarkable for multiple nodules in both lungs with cavitation in some of them (Figure 1, arrows). There was no significant mediastinal lymphadenopathy. Bronchoscopy and bronchoalveolar lavage were negative for tuberculosis, fungus, bacterial infection, nocardiosis and malignant cells. CECT of the abdomen and pelvis did not show any evidence of primary malignancy. Blood investigations showed rheumatoid



**Figure 1** CECT of the chest at presentation showing cavitating and non-cavitating lung nodules (arrows in A and B).

CECT: contrast enhanced computed tomography

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**Figure 2** CECT of the chest 3 months after treatment showing disappearance of the nodules, marked by white asterisks corresponding to the areas marked by arrows in figure 1.

CECT: contrast enhanced computed tomography

factor 240 IU/ml, anti-cyclic citrullinated peptide 200 U/ml, erythrocyte sedimentation rate (ESR) 75 mm in first hour and C-reactive protein 54 mg/l. Haemogram, serum calcium, alkaline phosphatase and prostate specific antigen were normal as well as liver and kidney function tests. Antinuclear antibody, antineutrophil cytoplasmic antibody, serology for human immunodeficiency virus, Mantoux test and interferon-gamma release assay were negative. CT-guided biopsy from one of the lung nodules was planned, but the patient refused to consent. In view of the bilateral cavitating lung nodules, with no evidence of infection or malignancy in the investigations performed, the patient was diagnosed with necrobiotic lung nodules of rheumatoid arthritis with active disease. He was given prednisolone (0.5 mg/kg body weight in tapering doses), leflunomide (20 mg daily) and hydroxychloroquine (5 mg/kg body weight); methotrexate was discontinued. After three months of treatment, his synovitis and respiratory symptoms improved remarkably (CDAI 3). ESR and C-reactive protein (CRP) became normal and the lung nodules disappeared in the repeat CT scan of the chest (Figure 2, white asterisks).

## Discussion

Lungs are the commonest site of extra-articular involvement in rheumatoid arthritis. Interstitial lung disease is the most common manifestation of lung involvement. Lung nodules are seen in about 0.4% of patients on imaging and occur mostly in males who are positive for rheumatoid factor.<sup>1,2</sup> Smoking and treatment with methotrexate and tumour necrosis factor alpha inhibitors further increase the risk.<sup>2,3</sup> Leflunomide has also been implicated in a few case reports. However, our patient improved remarkably with it.<sup>4</sup> Rheumatoid lung nodules are frequently associated with subcutaneous nodules. Rarely, nodules can be present in unusual locations like cardiac valves.

Rheumatoid lung nodules are usually bilateral, predominantly in the subpleural areas. Pleural effusion and ground glass opacity may also be seen. Necrosis frequently occurs in the nodules giving rise to cavitation.<sup>5</sup> Multiple cavitating nodules may coalesce giving rise to bizarre shaped cavities.<sup>5</sup> Rupture into the pleural cavity can lead to pneumothorax.

Treatment with immunomodulators increases the risk for developing infections in patients with rheumatoid arthritis. Tuberculosis and fungal infections are the most important differential diagnoses of cavitating lesions in the lungs. Granulomatosis with polyangiitis and lung metastases can also present with similar lesions. Infections are usually associated with constitutional features. Presence of 'tree-in-bud' opacities, mediastinal lymphadenopathy and air-bronchogram on imaging are additional pointers towards an infective aetiology. Sharp projections from the margins of the nodules in the form of spiculations are commonly observed in neoplastic causes.<sup>6</sup> Histopathological examination helps in confirming the diagnosis and ruling out infection and malignancy. Chronic inflammatory cells comprising fibroblasts, lymphocytes and epithelioid cells surrounding an area of fibrinoid necrosis are seen on histopathology.<sup>2</sup>

In our patient, there was no evidence of infection, vasculitis or malignancy on blood investigations, bronchoscopy and imaging. However, biopsy of the lung nodule could not be performed because the patient refused. Empirical treatment with disease-modifying antirheumatic drugs and glucocorticoid led to marked improvement and resolution of lung nodules. This served as a surrogate for histopathological diagnosis of necrotic lung nodulosis of rheumatoid arthritis. Glucocorticoids, rituximab and tocilizumab have been shown to be effective in the treatment. Successful treatment leads to significant resolution of nodules, as seen in our patient. **1**

## References

- 1 Yousem SA, Colby TV, Carrington CB. Lung biopsy in rheumatoid arthritis. *Am Rev Respir Dis* 1985; 131: 770–7.
- 2 Ziff M. The rheumatoid nodule. *Arthritis Rheum* 1990; 33: 761–7.
- 3 Toussiot E, Berthelot JM, Pertuiset E et al. Pulmonary nodulosis and aseptic granulomatous lung disease occurring in patients with rheumatoid arthritis receiving tumor necrosis factor- $\alpha$  blocking agent: A case series. *J Rheumatol* 2009; 36: 2421–7.
- 4 Rozin A, Yigla M, Guralnik L et al. Rheumatoid lung nodulosis and osteopathy associated with leflunomide therapy. *Clin Rheumatol* 2006; 25: 384–8.
- 5 Alpay Kanitez N, Çelik S, Yilmaz Öner S et al. Cavitory pulmonary nodules in rheumatoid arthritis; case reports and review of the literature. *Eur J Rheumatol* 2018; 5: 65–8.
- 6 Zwirwich CV, Vedal S, Miller RR et al. Solitary pulmonary nodule: high-resolution CT and radiologic-pathologic correlation. *Radiology* 1991; 179: 469–76.