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Case report

# Progressive massive fibrosis in a patient with silicosis and rheumatoid arthritis

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## Abstract

We present a case of progressive massive fibrosis in a 58-year-old woman with prior history of a 6-year exposure to silica dust while working in a quartz crushing plant. She had developed symptoms of arthropathy after 5 years of silica exposure. A diagnosis of rheumatoid arthritis was made subsequently, and she was put on treatment with sulfasalazine, hydroxychloroquine, methotrexate and leflunomide. She noticed dyspnea 3 years later which progressed to modified Medical Research Council (mMRC) grade 4 where she presented to the respiratory wards to be diagnosed of accelerated silicosis with progressive massive fibrosis.

## Introduction

Progressive massive fibrosis (PMF) refers to a lung disease seen predominantly within the context of exposure to dust such as in silicosis [1]. Silicosis is the most common occupational disease worldwide [2]. It occurs due to the inhalation of crystalline silica and can lead to extensive pulmonary fibrosis [3]. Rheumatoid arthritis is a systemic inflammatory arthropathy with several extra articular manifestations. Pulmonary involvement is well known with one of the most common manifestations being interstitial lung disease [4]. Some of the medication given for the treatment of rheumatoid arthritis such as methotrexate and leflunomide are also known to have pulmonary complications such as pneumonitis leading to pulmonary fibrosis [5-7]. It has been suggested that silicosis may be associated with rheumatoid arthritis, scleroderma, lupus, and progressive systemic sclerosis [8,9].

## Case Report

A 58-year-old housewife presented to the respiratory wards of the National hospital Kandy with a complaint of a dry cough for the last four years which had worsened during the last four weeks. The cough was associated with a mild shortness of breath which was initially modified Medical Research Council (mMRC) grade one, but it gradually progressed to mMRC grade four over the past two weeks. She also complained of a low-grade fever in the evenings during the last two weeks with loss of appetite and loss of weight. This was also associated with mild joint pains in her wrists, hands, and knees.

She had been diagnosed with seropositive rheumatoid arthritis in 2016. For this she was prescribed sulfasalazine 500 mg twice a day, hydroxychloroquine 200 mg a day and methotrexate 17.5 mg weekly with folic acid supplementation. From 2018 onwards she had been prescribed leflunomide 20 mg daily at an exacerbation of arthropathy. Her disease was currently in remission prior to her current presentation.

She worked in a quartz crushing industry from the years 2010 to 2016. This plant exports finely powdered silica. She had worked almost seven days a week during this time from eight a.m. to four p.m. with an hour's break for lunch at midday. The workers were asked to wear clothes masks as the only personal protective equipment. She was not aware of any environmental control measures on this plant. She had stopped working after 2016 because she started to develop joint pains in her hands and knees which she found to be debilitating. She was diagnosed with rheumatoid arthritis shortly after she left her job.

No chest radiographs were done on her at the onset or during her employment time of 6 years. She was breathless at rest and

febrile with a temperature of 37.2 degrees Celsius on initial presentation. She had a blood pressure of 110/70 mmHg and a pulse rate of 110 beats per minute. Her oxygen saturation was 94%. There were a few scattered bilateral crepitations on auscultation of her lungs. She did not have clubbing. While she complained of joint pains, there was no evidence of any active inflammation or synovitis of the joints.

Her chest radiograph showed bilateral mass-like opacities with irregular margins across all lung fields but mainly in the upper and mid zones. No pleural effusions were seen. She had a white blood cell count of 11.50 10^3/µL with 78.7 per cent neutrophils, a C-reactive protein of 75 mg/L and an erythrocyte sedimentation rate of 70 mm/hour. A differential diagnosis of bilateral pulmonary fibrosis either due to rheumatoid arthritis associated interstitial lung disease [RAILD], drug induced lung disease or pulmonary tuberculosis and a secondary bacterial infection was considered. The patient was started on intravenous cefotaxime and clarithromycin with supplemental oxygen therapy. She started to improve with this treatment after three days.She was screened for tuberculosis. The tuberculosis screening with three morning sputum samples for acid fast bacilli, Mantoux and GeneXpert-MTB testing were negative.

A high-resolution computed tomography (HRCT) scan of the chest was carried out after 5days. It showed conglomerate masses mainly in bilateral upper zones associated with traction bronchiectasis, contraction of the upper lobes and hilar elevation on the right side. The lower lobes were involved to a lesser degree. The lung architecture was distorted. No cavitation or cysts were seen. Small rounded one-to-three-millimeter nodules were distributed throughout the lungs which were most numerous in the upper lobes. There was no tree-in-bud appearance. The hilar and mediastinal lymph nodes were enlarged with bilateral eggshell type calcification. Mosaic attenuation was seen with air trapping in the expiratory films. The HRCT was suggestive of a progressive massive fibrosis of the lungs with eggshell type mediastinal and hilar node calcifications compatible with silica exposure.

The patient was assessed with pulmonary functions testing which showed a restrictive pattern with reduced diffusing capacity of 46% predicted for carbon monoxide (DLCO). A Doppler echocardiogram showed no evidence of pulmonary hypertension. With these clinical and investigative findings, a diagnosis of accelerated silicosis with progressive massive fibrosis presenting with an infective exacerbation was made.

**Discussion**

Progressive massive fibrosis (PMF) refers to the formation of large conglomerate masses of fibrosis in the upper zones of the lung [1]. These changes may be seen in the lower zones as well [8]. It occurs due to dust exposure, such as silica, and it may be confused with tuberculosis, other infections and malignancies [1]. PMF is a serious, debilitating condition and thus is a dreaded sequela of silicosis [8]. Silicosis refers to a variety of lung diseases caused by the inhalation of silica dust [3]. There are three different clinical presentations of silicosis, namely Acute silicosis, which is also known as silicoproteinosis, accelerated silicosis and chronic silicosis. Acute silicosis occurs within a few days of intense exposure to silica dust [9]. Patients present with an acute onset of respiratory symptoms with perhaps fever and pleuritic chest pain. The other, far more common presentation is that of chronic silicosis. This manifests ten years after the initial silica exposure [11]. It can present as simple silicosis, where the patients are usually asymptomatic or have some exertional dyspnea, or PMF, where the symptoms are more severe. Accelerated silicosis is diagnosed when the disease manifests within ten years from the initial exposure. It is more likely to happen when the patient is exposed to high levels of silica dust [12]. As our patient had an exposure history of 6 years, it is likely that she was having accelerated silicosis.

The International Labor Organization [ILO] identifies three criteria to diagnose silicosis. Namely an exposure history to silica containing dust, radiological manifestations compatible with silicosis and exclusion of any other condition mimicking silicosis.

In our patient with her acute presentation with fever and constitutional symptoms as well as her rheumatoid arthritis, we considered a differential diagnosis of rheumatoid lung and drug induced lung disease. Tuberculosis was also an important differential diagnosis to consider as silicosis itself is a well-known predisposing factor for tuberculosis [13].

Tuberculosis can present on the chest radiograph as unilateral or bilateral infiltrates commonly seen on the upper zones [14]. Our patient's chest radiograph had bilateral rounded mass-like opacities more prominently seen on the right upper and mid zones; resembling changes that may be seen in tuberculosis but there were no cavitary lesions. Her sputum acid fast bacilli, Mantoux and GeneXpert-MTB testing were repeatedly negative. Hence the likelihood of active tuberculosis was excluded [15,16].

Our patient also had rheumatoid arthritis which has several pulmonary manifestations including interstitial lung disease. The most common pattern of interstitial lung disease seen in rheumatoid arthritis is usual interstitial lung pneumonitis (UIP) followed by non- specific interstitial pneumonia (NSIP) [17]. However, the basal subpleural honeycombing that is seen in UIP nor the ground glass opacities seen in NSIP were seen in our patient's HRCT which made rheumatoid lung unlikely [18].

This patient was also on methotrexate and leflunomide for her rheumatoid arthritis. These drugs are also known to have various pulmonary manifestations such as fibrosis or pneumonitis [5-7]. Methotrexate is known to cause hypersensitivity pneumonitis which usually occurs in the first year of treatment [19,20]. Whether methotrexate can cause a more chronic fibrosis, as seen in our patient, is controversial. Leflunomide is known to be involved in the development of interstitial lung disease and is contraindicated when there is pre-existing interstitial lung disease [22].

However, leflunomide induced lung injury is rare, with a worldwide prevalence of 0.02 % and it generally occurs within the first twenty weeks after the initiation of the drug [22,23]. Since our patient had been on methotrexate since 2017 and leflunomide since 2018, it is difficult to attribute her chronic lung disease to her drugs.

It has been suggested that silicosis may be associated with autoimmune diseases like rheumatoid arthritis, scleroderma, lupus,

and progressive systemic sclerosis [8,9]. Since this patient developed the initial symptoms of arthritis with six years of silica exposure it is a possible association. In 1997, the International Agency for Research on Cancer (IARC) classified crystalline silica inhaled in the form of quartz or cristobalite from occupational sources as a human (Group 1) carcinogen. Our patient did not show clinical or radiological evidence of lung cancer.

To date there is no curative treatment for silicosis emphasizing the importance of prevention of occupational dust exposure.

## References


1. Castranova V, Vallyathan V. Silicosis and coal workers' pneumoconiosis. 2000Aug24;108(Suppl 4):675–84.
2. Hoy R, Chambers D. Silica-related diseases in the modern world. 2020;75(11):2805–17.
3. Hamilton RJ, Thakur S, Holian A.Silica binding and toxicity in alveolar macrophages. 2008;44(7):1246–58.
4. Olson A, Swigris J, Sprunger D, Fischer A, Fernandez-Perez E, Solomon J, et al. Rheumatoid arthritis-interstitial lung disease-associated mortality. 2011;183(3):372–8.
5. Bullock J, Rizvi S, Saleh A, Ahmed S, Do D, Ansari R, et al. Rheumatoid Arthritis: A Brief Overview of the Treatment. 2018;27(6):501–7.
6. Vinay V, Munjal S, Verma P, Jain S, Yadav B, Sharma A. Methotrexate induced pneumonitis - A case report and review of literature. 2022;11(8):4844–6.
7. Goldenberg M. Leflunomide, a novel immunomodulator for the treatment of active rheumatoid arthritis. 1999;21(11):1837–52.
8. Makol A, Reilly M, Rosenman K. Prevalence of connective tissue disease in silicosis (1985-2006)-a report from the state of Michigan surveillance system for silicosis. 2011;54(4):255–62.
9. de Miranda A, Nascimento A, Peixoto I, Scrignoli J, Cardoso MS, Ribeiro S. Erasmus syndrome: silicosis and systemic sclerosis. 2013;53(3):310–.
10. Attfield M, Castranova V, Hale JM, Suarthana E, Thomas KC, Wang ML. Coal mine dust exposures and associated health outcomes; a review of information published since 1995. 2011;.
11. Duchange L, Brichet A, Lamblin C, Tillie I, Tonnel A, Wallaert B. Silicose aiguë. Caractéristiques cliniques, radiologiques, fonctionnelles et cytologiques du liquide broncho-alvéolaire. A propos de 6 observations. 1998;15(4):527–34.
12. Goodman G, Kaplan P, Stachura I, Castranova V, Pailes W, Lapp N. Acute silicosis responding to corticosteroid therapy. 1992;101(2):366–70.
13. Kreiss K, Zhen B. Risk of silicosis in a Colorado mining community. 1996;30(5):529–39.
14. Levin K, McLean C, Hoy R. Artificial stone-associated silicosis: clinical- pathological-radiological correlates of disease. 2019;7(7):e00470.
15. Hnizdo E, Murray J. Risk of pulmonary tuberculosis relative to silicosis and exposure to silica dust in South African gold miners. 1998;55(7):496–502.
16. Khan M, Kovnat D, Bachus B, Whitcomb M, Brody J, Snider G. Clinical and roentgenographic spectrum of pulmonary tuberculosis in the adult. 1977;62(1):31–8.
17. Natarajan AS, Gajalakshmi L, Karunakaran S. Accelerated silicosis in a silica flour mill worker. 1992;10(1):33–7.
18. Sharma N, et al. Silicosis and silicotuberculosis in India. 2016;94(10):777.
19. de Lauretis A, Veeraraghavan S, Renzoni E. Review series: aspects of interstitial lung disease: connective tissue disease-associated interstitial lung disease: how does it differ from IPF? How should the clinical approach differ?. 2011;8(1):53–82.
20. Raghu G, Collard H, Egan J, Martinez F, Behr J, Brown K, et al.Committee on Idiopathic Pulmonary Fibrosis. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. 2011;183(6):788–824.
21. Barrera P, et al. Methotrexate-related pulmonary complications in rheumatoid arthritis. 1994;53(7):434.
22. Cavagna L, Monti S, Grosso V, Boffini N, Scorletti E, Crepaldi G, et al. The multifaceted aspects of interstitial lung disease in rheumatoid arthritis. 2013;2013:759760.
23. Dawson JK, et al. Investigation of the chronic pulmonary effects of low- dose oral methotrexate in patients with rheumatoid arthritis: a prospective study incorporating HRCT scanning and pulmonary function tests. 2002;41(3):262–7.
24. Raj R, Nugent K. Leflunomide-induced interstitial lung disease (a systematic review). 2013;30(3):167–76.
25. Chikura B, Lane S, Dawson J. Clinical expression of leflunomide-induced pneumonitis. 2009;48(9):1065–8.


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