

Access this article online

Quick Response Code:



Website:  
https://eurasianj pulmonol.org

DOI:  
10.14744/ejp.2024.2004

# A case of mixed connective tissue disease following occupational silicosis: A potential association

Yusuf Samir Hasanlı

ORCID:

Yusuf Samir Hasanlı: 0000-0001-6514-6789

## Abstract:

Mixed connective tissue disease is a rare autoimmune rheumatological disorder of unclear etiology. Its association with silicosis is even rarer, but it is an intriguing relationship worthy of investigation. We present the case of a 45-year-old male patient who was diagnosed with silicosis after seven years of working in a quartz surface mine. Three years following his silicosis diagnosis, he developed rheumatological complaints and was subsequently diagnosed with mixed connective tissue disease. This case highlights the association of silicosis and mixed connective tissue disease. While rare, the available literature suggests that silica particles may contribute to the development of the disease.

## Keywords:

autoimmune, mixed connective tissue disease, silicosis

## Introduction

Autoimmune rheumatic diseases are a complex but relatively uncommon conditions that include various connective tissue diseases, each with distinct clinical findings. Characteristic signs, symptoms, and autoantibodies help to identify specific connective tissue diseases. Some patients may fulfill the criteria for more than one well-defined connective tissue disease, while others present with symptoms typical of autoimmune conditions that cannot be classified with certainty. Currently, classification criteria exist for five recognized autoimmune connective tissue diseases: systemic lupus erythematosus (SLE), scleroderma, myositis (polymyositis), rheumatoid arthritis (RA), and Sjögren's syndrome.

The presentation of all five connective tissue diseases is variable; however, the diagnosis of a specific connective tissue disease usually becomes apparent over time.<sup>[1]</sup> Conditions that fulfill the criteria for two or more defined autoimmune diseases are often referred to as "overlap syndromes." Mixed connective tissue disease (MCTD) is one such overlap syndrome.<sup>[1,2]</sup>

By definition, MCTD is a systemic connective tissue disease characterized by a combination of clinical features from the aforementioned diseases and the presence of high titers of anti-U1-ribonucleo-

Division of Occupational Diseases, Department of Internal Diseases, Ankara Etlik City Hospital, Ankara, Türkiye

## Address for correspondence:

Dr. Yusuf Samir Hasanlı,  
Division of Occupational Diseases, Department of Internal Diseases, Ankara Etlik City Hospital, Ankara, Türkiye.  
E-mail: dryusufsmrh@gmail.com

Received: 27-02-2024

Revised: 08-06-2024

Accepted: 29-07-2024

Published: 13-05-2025

**How to cite this article:** Hasanlı YS. A case of mixed connective tissue disease following occupational silicosis: A potential association. Eurasian J Pulmonol 0000;00:1-4.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** kare@karepb.com





**Figure 1:** Patient's lung X-ray and high-resolution computed tomography (HRCT) sections. (a) Millimetric, multiple micronodules and homogeneous opacities are observed in the upper zones of both lungs. (b) Millimetric, multiple micronodules and hyperdense lesions are observed in the upper regions of both lungs. (c) Multiple hilar and mediastinal lymphadenopathies, some of which are calcified (yellow arrow).

protein (U1-RNP) antibodies.<sup>[3]</sup> Mixed connective tissue disease was first described by Sharp et al. in 1972.<sup>[4]</sup> Although MCTD is conceptually an overlap syndrome, its overlapping features rarely appear together simultaneously, and it often takes years for the diagnostic criteria to be fully met. The onset of an autoantibody-mediated disease is the result of a complex interplay between genetic predisposition and environmental or occupational factors.<sup>[5]</sup> The association of silicosis and/or silica exposure with connective tissue diseases—especially systemic sclerosis, rheumatoid arthritis, and systemic lupus erythematosus—as well as serological abnormalities such as antinuclear antibodies (ANA) and immune complexes, has been demonstrated in several studies, with cases reported in the literature.<sup>[6]</sup> In this context, we aimed to contribute to the literature by presenting a case of MCTD that developed following silicosis.

### Case Report

We report a 43-year-old male who spent seven years of his 22-year working life as a packaging worker in a quartz surface mine. His job involved filling quartz, which had been ground and collected in silos, into sacks and paper packages, averaging up to 20 per day. He transported the filled sacks using a forklift and occasionally swept dust from the floor with a dry brush. He was exposed to concentrated quartz dust and did not consistently use a dust mask due to inadequate implementation of occupational health and safety measures. In the final years of his work in the mine, he began experiencing shortness of breath, cough, and pain with swelling in his hand joints. Silicosis was detected during a periodic examination in the seventh year of his employment at the surface mine, prompting him to

leave the job and start working as a bus driver. He presented to our hospital with increasing pain in his hand joints and dry mouth, which had worsened over the past three years. The patient had a 12 pack-year smoking history, and his mother had diabetes mellitus. On physical examination, there was swelling in the small joints of his hands and feet; however, examinations of other systems, including the respiratory system, were unremarkable. His oxygen saturation on room air was 96%. Spirometry and diffusion test results were as follows: forced expiratory volume in 1 second (FEV<sub>1</sub>): 2.93 L (76%), forced vital capacity (FVC): 3.90 L (83%), FEV<sub>1</sub>/FVC ratio: 76.9%, diffusing capacity of the lung for carbon monoxide (DLCO): 13.9 (43%), and DLCO adjusted for alveolar volume (DLCO/VA): 2.7 (59%). A chest X-ray revealed large homogeneous opacities along with bilateral millimetric round opacities, consistent with silicosis. High-resolution computed tomography (HRCT) showed findings of chronic complicated silicosis accompanied by hilar calcified lymphadenopathy, also known as progressive massive fibrosis (PMF) [Fig. 1]. The patient was referred to the rheumatology department due to his joint complaints and dry mouth. Laboratory investigations revealed the following: ANA: 1/5120 (granular pattern), anti U1-RNP: (+++), anti-Smith antibody (anti-SM): (++), sedimentation rate: 49 mm, C-reactive protein (CRP): 1.2 mg/dL, minor salivary gland biopsy lymphocyte score: 3, and Shirmer test: 20–16 mm. There were no abnormalities in the comparative hand, wrist, and elbow films, except for a diffuse osteopenic signal increase in the bones. Based on these findings, the patient was diagnosed with mixed connective tissue disease accompanying silicosis. Steroid treatment was initiated, an appropriate occupational disease report was prepared, and the patient was placed under follow-up.

## Discussion

We present the case of a quarry worker who developed silicosis due to prolonged exposure to quartz dust under poor occupational safety conditions and was subsequently diagnosed with mixed connective tissue disease. With this case, we aim to highlight once again that silica exposure and/or silicosis can lead to rheumatological diseases. Therefore, it is imperative to conduct thorough rheumatological evaluations and examinations of individuals with silicosis and/or silicon dioxide exposure.

The etiology of MCTD is unclear. No clear risk factors have been identified so far, although it is thought that immune activation due to environmental or occupational factors plays a role in individuals with a genetic predisposition. Some viruses, such as Human Immunodeficiency Virus (HIV), and certain chemicals have been found to be associated with the disease. It is a rare condition with an as yet undetermined incidence.<sup>[7]</sup> Interstitial lung disease, particularly a nonspecific interstitial pneumonia (NSIP) pattern, is observed in 35% to 67% of patients with MCTD.<sup>[8]</sup> Our case aligns with silicosis in terms of exposure history and radiological findings, and the association of silica exposure or silicosis with certain rheumatological diseases has been previously described. Erasmus Syndrome, defined as the coexistence of silica exposure and/or silicosis with systemic sclerosis,<sup>[9,10]</sup> and numerous examples of the relationship between rheumatoid arthritis and silica exposure, can also be cited.<sup>[11]</sup>

However, the literature reports very few cases of the coexistence of these two diseases (silicosis and Sharp syndrome). One case was reported from India, involving a person working in the stone crushing industry who developed MCTD six years after being diagnosed with silicosis.<sup>[12]</sup> Another case described a woman who contracted acute silicosis after inhaling cleaning powder containing silicon dioxide and subsequently developed connective tissue disease five years after exposure.<sup>[13]</sup> It is well known that silicon dioxide causes fibrotic events in lung tissue through various mechanisms. Although there are strong suspicions that silicon dioxide particles and nanoparticles contribute to autoimmune diseases, the exact mechanism remains unknown.<sup>[14]</sup>

Currently, it is not possible to draw definitive conclusions about the etiology of autoimmune diseases. How-

ever, the potential role of factors such as silica dust can be inferred. Naturally, this does not establish a definitive relationship. This case highlights once again that individuals exposed to silica or diagnosed with silicosis should undergo rheumatological evaluations during periodic workplace examinations.

## Informed Consent

Written informed consent was obtained from the patient, who agreed to the use of his medical images and information for publication.

## Conflicts of Interest

There are no conflicts of interest.

## Use of AI for Writing Assistance

No AI technologies utilized.

## Financial Support and Sponsorship

Nil.

## Peer-review

Externally peer-reviewed.

## References

1. Pepmueller PH. Undifferentiated Connective Tissue Disease, Mixed Connective Tissue Disease, and Overlap Syndromes in Rheumatology. *Mo Med* 2016;113(2):136–40.
2. Ciang NC, Pereira N, Isenberg DA. Mixed connective tissue disease-enigma variations? *Rheumatology (Oxford)* 2017;56(3):326–33. [\[CrossRef\]](#)
3. Ferrara CA, La Rocca G, Ielo G, Libra A, Sambataro G. Towards Early Diagnosis of Mixed Connective Tissue Disease: Updated Perspectives. *Immunotargets Ther* 2023;12:79–89. [\[CrossRef\]](#)
4. Alves MR, Isenberg DA. “Mixed connective tissue disease”: a condition in search of an identity. *Clin Exp Med* 2020;20(2):159–66. [\[CrossRef\]](#)
5. Marwa K, Anjum F. Undifferentiated Connective Tissue Disease. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
6. Pollard KM. Silica, Silicosis, and Autoimmunity. *Front Immunol* 2016;7:97. [\[CrossRef\]](#)
7. Sapkota B, Al Khalili Y. Mixed Connective Tissue Disease. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
8. Lee CT, Strek ME. The other connective tissue disease-associated interstitial lung diseases: Sjogren’s syndrome, mixed connective tissue disease, and systemic lupus erythematosus. *Curr Opin Pulm Med* 2021;27(5):388–95. [\[CrossRef\]](#)
9. Lomanta MJ, Atienza MA, Gonzales JRM, Amante EJB, Urquiza SC, Lucero-Orillaza H, et al. Erasmus Syndrome: A Case Report and Literature Review. *Am J Case Rep* 2022;23:e937061. [\[CrossRef\]](#)
10. Magalhães A, Moreira I, Pinheiro S, Borba A. Erasmus Syndrome: An Underrecognized Entity. *Acta Med Port* 2023;36(2):122–6. [\[CrossRef\]](#)
11. Mehri F, Jenabi E, Bashirian S, Shahna FG, Khazaei S. The association Between Occupational Exposure to silica and Risk of De-

- veloping Rheumatoid Arthritis: A Meta-Analysis. *Saf Health Work* 2020;11(2):136–42. [\[CrossRef\]](#)
12. Khanna A, Suri JC, Ray A, Sharma RK. Silica associated mixed connective tissue disorder in a stone crusher. *Indian J Occup Environ Med* 2013;17(2):76–7. [\[CrossRef\]](#)
13. Vincent M, Pouchelle C, Martinon S, Gerard F, Arthaud Y. Connective tissue disease due to intentional inhalation of scouring powder. *Eur Respir J* 1996;9(12):2688–90. [\[CrossRef\]](#)
14. Baum L, Arnold TC. Silicosis. *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.