Rheumatological Diseases in Denim Sandblasters with Silicosis: What Should Pulmonologists Look for?

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OBJECTIVE: Silica exposure is not only the cause of silicosis, also associated rheumatological diseases like rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and systemic sclerosis (SSc). This report will reveal the rheumatological diseases of silicosis patients who were exposed to silica while working as denim sandblasters. Additionally, we will describe some clinical and laboratory findings that will help pulmonologist suspect, recognize, and manage rheumatological diseases related to silica exposure in patients with silicosis.

MATERIAL AND METHODS: We reviewed the records of 142 sandblasters diagnosed with silicosis and found ten silicosis cases who also had rheumatological diseases between the years 2009 and 2017. The occupational characteristics, serological, functional and radiological data, were collected for patients of silicosis with rheumatological diseases.

RESULTS: Ten silicosis patients with concomitant rheumatological diseases were found. Six patients among our cases had diagnosed SSc (4.2%), three of them had RA (2.1%), and one of them was being monitored for SLE (0.7%). The mean silica exposure time of the cases was 4.3±1.9 years (min: 1 max: 8). We also found elevated LD, sedimentation and CRP levels in our cases.

CONCLUSION: It should be kept in mind that, in silicosis cases with arthralgia, joint tenderness or sclerosis at the fingertips may be indicative of rheumatological diseases related to silica exposure, and in these cases, the unexplained elevations of sedimentation and CRP levels may also be a result of silica-induced rheumatological diseases.

KEYWORDS: Silicosis, rheumatological diseases, silica, sandblasters

INTRODUCTION

Crystalline silica exposure is the cause of silicosis, which is an irreversible occupational pulmonary disease, characterized by parenchymal inflammation and fibrotic changes. Recent studies have reported that silica exposure is also associated with rheumatological diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and systemic sclerosis (SSc) [1-3]. It has also been shown that silica exposure may trigger the polyclonal activation of T cells that play a role in the pathogenesis and etiology of rheumatological diseases [4, 5]. This report aimed to study rheumatological diseases of patients with silicosis who were exposed to silica while working as denim sandblasters. In the 2000s, Turkey faced a devastating silicosis outbreak due to silica exposure in the new sector of denim sandblasting [6]. Although the relationship between silica exposure and rheumatological diseases is well-known, no notification has been made regarding denim sandblasters with silicosis and concomitant rheumatological diseases as yet. Additionally, we will delineate some clinical and laboratory findings that will help a pulmonologist suspect, recognize, and manage rheumatological diseases related to silica exposure in patients with silicosis.

MATERIAL AND METHODS

We reviewed the records of 142 sandblasters diagnosed with silicosis and found ten silicosis cases who also had rheumatological diseases between 2009 and 2017. The occupational characteristics and serological, functional, and radiological data were collected for patients with silicosis with rheumatological diseases.

RESULTS

Ten patients with silicosis and with concomitant rheumatological diseases were found (7.0% of all sandblasters in our records), and none of them had a rheumatological diagnosis before silica exposure. Their mean age was 31.8±5.1 years (min...
Case 6, a 40-year-old male patient had mMRC level 1 dyspnea, pain, coldness and cyanosis in the hands, and sclerodactyly. He had been diagnosed with silicosis six years ago. He had rheumatological complaints for four years and was diagnosed with SSc four years ago.

Silicosis with Rheumatoid Arthritis
Case 7, a 30-year-old male denim worker was referred for dyspnea eight years ago, and he diagnosed with silicosis. He started to have complaints of pain and swelling in his knees, joints of hands and feet three years later following the diagnosis of silicosis.

Case 8, a 28-year-old male patient presented with a history of exertional dyspnea for the past three years. He was also diagnosed with RA three years ago while he was working as a denim sandblaster.

Case 9, a 41-year-old male patient had mMRC level 2 dyspnea for five years. He also had complaints of arthralgia and swelling in his ankle joint. He was diagnosed with RA three years ago.

The RA cases also had high levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), which were unexplained by other clinical conditions. The patients were evaluated by using rheumatology and diagnosed with high levels of anti-cyclic citrullinated peptide (anti-CCP) and a positive rheumatoid factor (RF) test given in Table 2.

Silicosis with Systemic Lupus Erythematosus
Case 10, a 32-year-old man was referred for mMRC level 3 dyspnea, weight loss, and weakness three years ago, and he started to have complaints of diplopia three months ago. He also had high levels of LD, ESR, and CRP. The patient’s immunological laboratory test results were compatible with SLE. His neurological comorbidity was considered to be secondary to his immunological disease.

The diagnoses of silicosis of the cases that were classified according to the International Labor Organization (ILO) International Classification of Radiographs of Pneumoconiosis are given in Table 1. Apart from Case 10, all the cases had restrictions in respiratory function tests, whereas Case 4 had a mild obstruction. We determined that the majority of cases had inspiratory and/or expiratory crackles on lung auscultation because of severe interstitial lung disease.

The LD level was found to be high in the four SSc cases. The LD level of case 5 was high, about four times the upper limit. All SSc cases had high levels of ESR and CRP, which were unexplained by other clinical conditions. The median ESR was 57 mm/h (0-10 mm/h; min 26, max 81), and the median CRP level was 31.6 mg/l (0-0.5 mg/l; min 3.5, max 119.8).

The patients who had been evaluated by using rheumatology and diagnosed with high levels of anti-Scl 70 (anti-DNA topoisomerase I) and positive anti-nuclear antibody (ANA) as a result of the tests are shown in Table 2.

CONCLUSIONS
The cases of rheumatological diseases diagnosed in workers with silica exposure in different sectors are found in the literature with or without silicosis. In addition to miners and drillers, stonemasons [7], dental technicians [8, 9], and pot
tery makers [10] are examples of some of the affected worker groups diagnosed with silicosis and/or rheumatological diseases so far. This study shows another under-risk group of workers who were exposed to silica and diagnosed with various rheumatological diseases and silicosis due to their work in denim sandblasting.

The frequency of rheumatological diseases due to silica exposure in different studies shows a wide variety. A study among fifty scouring powder factory workers reported SSc prevalence as 10% (5/50), SLE prevalence as 6% (3/50), and overlap syndrome (SLE/SSc) prevalence as 10% (5/50) [11]. A cross-sectional study that was carried out in Israel showed that 23% (9/40) of workers who had silica exposure had various rheumatological diseases, and one-third of them had SSc [12]. A report from the state of Michigan Surveillance System for Silicosis evaluated 790 silicosis cases and reported the prevalence of rheumatological diseases as 5.5% (44/790), RA prevalence as 4.2% (33/790), SSc prevalence as 0.3% (2/790), and SLE prevalence as 0.1% (1/790) [13]. In our series, 7% of all recorded denim sandblasters had rheumatological diseases. Six patients among the cases in our study were diagnosed with SSc (4.2%), three of them had RA (2.1%), and one of them was being monitored for SLE (0.7%).

Most of the published data show that the effects of chronic silica exposure (mean exposure time differences between 14.9 and 20 years) are associated with rheumatological diseases [13-16], while there is a limited number of studies on the acute effects of silica exposure [7-11]. A case series from Algeria [7] reported that mean exposure time in nine stone-masons was 4.8±1.1 years. Similarly, in our series, we describe acute silica exposure of 4.3±1.9 years (min 1, max 8) in sandblasters. The mean duration of exposure in scouring powder factory workers with rheumatological diseases [11] was 6.1 years. In contrast, we showed a longer latency period from last exposure until the appearance of symptoms as

| Case number | Silicosis Diagnosis age | Duration of exposure (years) | Radiographic findings by chest radiograph | ILO International Classification of Radiographs of Pneumoconiosis | FEV1% Predicted | FVC% Predicted | FEV1/FVC Predicted | DLCO | TLC |
|-------------|------------------------|-----------------------------|------------------------------------------|---------------------------------------------------------------|----------------|--------------|-------------------|------|-----|
| 1           | 26                     | 8                           | Diffuse reticulonodular imaging, massive fibrosis in right lung | qr 2/2 with opacity A | 60%            | 69%          | 76                | 56%            |
| 2           | 25                     | 1                           | Diffuse reticulonodular imaging, mediastinal lymphadenopathy, egg-shell calcification | pq 2/2                  | 66%            | 78%          | 71                | 69%            |
| 3           | 30                     | 5                           | Diffuse reticulonodular imaging with upper lobe dominancy | qr 3/3 with C opacity | 44%            | 40%          | 92                | 45% 46%        |
| 4           | 37                     | 5                           | Diffuse reticulonodular imaging, progressive massive fibrosis, mediastinal lymphadenopathy with calcification | rr 3/3                  | 69%            | 81%          | 73                | -              |
| 5           | 33                     | 5                           | Diffuse reticulonodular imaging, mediastinal lymphadenopathy | qq 2/2 with opacity A | 96%            | 122%         | 67                | 74% 92%        |
| 6           | 46                     | 5                           | Diffuse reticulonodular imaging, mediastinal lymphadenopathy | qq 3/2                  | 77%            | 84%          | 75                | -              |
| 7           | 30                     | 2                           | Diffuse nodular imaging | qq 2/3                  | 82%            | 86%          | 80                | 93% 82%        |
| 8           | 28                     | 4                           | Diffuse reticulonodular imaging | pp 2/2                  | 81%            | 94%          | 90                | 72%            |
| 9           | 41                     | 2                           | Diffuse reticulonodular imaging with upper lobe dominancy | ps 2/2                  | 92%            | 88%          | 77                | -              |
| 10          | 25                     | 3                           | Diffuse reticulonodular imaging, progressive massive fibrosis, mediastinal lymphadenopathy with calcification | qq 3/3 with opacity A | 63%            | 74%          | 72                | -              |
9.5±3.8 years (min 3, max 15) for the rheumatological symptoms and 6.8±3.8 years (min 1, max 13) for the respiratory symptoms.

The latency period from the first exposure until the appearance of symptoms of rheumatological diseases in stonemasons was found to be 5.8±1.3 years. The difference in the latency periods may be due to various factors such as amount of exposure, individual factors, and genetic factors.

We also found elevated LD, ESR, and CRP levels in our cases. LD is an intracellular enzyme which increases in blood plasma when tissues are damaged by an injury or disease. A case-control study reported that denim sandblasters with complicated silicosis have a high levels of LD in comparison with those with simple silicosis and healthy groups, and they suggested that LD levels might be considered as a marker of pulmonary parenchymal involvement in patients (17). Similarly, four of five complicated silicosis cases in our series (cases 1, 3, 5, 9 and 10) had high levels of LD. Moreover, all cases had high levels of ESR and CRP, which were unexplained by other clinical conditions.

This report is valuable not only for showing 10 silicosis cases caused by denim sandblasting with three different comorbid rheumatological diseases related to silica exposure but also for describing elevated ESR and CRP levels, which could not be explained by other reasons in patients with silicosis and may be indicators of rheumatological diseases associated with silica exposure. We also recommended that the workers' compensation rates be calculated again as rheumatological diseases related to silica exposure affect the level of workers' compensation.

It should be kept in mind that silicosis cases with arthralgia, joint tenderness, or sclerosis at the fingertips may be indicative of rheumatological diseases related to silica exposure, and in these cases, the unexplained elevation of ESR and CRP levels may also be a result of silica-induced rheumatological diseases.
Informed Consent: Written informed consent was obtained from the patients or relatives of dead patients.

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REFERENCES

1. Blanc PD, Järvholm B, Torén K. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. Am J Med 2015;128:1094-101. [CrossRef]
2. Miller FW, Alfredsson L, Costenbader KH, et al. Epidemiology of environmental exposures and human autoimmune diseases: Findings from a national institute of environmental health sciences expert panel workshop. J Autoimmun 2012;39:259-71. [CrossRef]
3. Lee S, Hayashi H, Mastuzaki H, et al. Silicosis and autoimmunity. Curr Opin Allergy Clin Immunol 2017;17:78-84. [CrossRef]
4. Lee S, Matsuzaki H, Kumagai-Takei N, et al. Silica exposure and altered regulation of autoimmunity. Environ Health Prev Med 2014;19:322-9. [CrossRef]
5. Pollard KM. Silica, silicosis, and autoimmunity. Front Immunol 2016;7:97. doi: 10.3389/fimmu.2016.00097. eCollection 2016. [CrossRef]
6. Akgun M, Araz O, Yilmazel Ucar E, et al. Silicosis appears inevitable among former denim sandblasters: A 4-year follow-up study. Chest 2015;148:647-54. [CrossRef]
7. Slimani S, Ben Ammar A, Ladjouze-Rezig A. Connective tissue diseases after heavy exposure to silica: A report of nine cases in stonemasons. Clin Rheumatol 2010;5:531-3. [CrossRef]
8. Iannello S, Camuto M, Cantarella S, et al. Rheumatoid syndrome associated with lung interstitial disorder in a dental technician exposed to ceramic silica dust: A case report and critical literature review. Clin Rheumatol 2002;1:76-81. [CrossRef]
9. Astudillo L, Sailler L, Ecolﬁer M, et al. Exposure to silica and primary Sjögren’s syndrome in a dental technician. Rheumatology 2003;10:1268-9. [CrossRef]
10. Turner S, Cherry N. Rheumatoid arthritis in workers exposed to silica in the potter Industry. Occup Environ Med 2000;57:443-7. [CrossRef]
11. Sanchez-Roman J, Wichmann I, Salaberri J, et al. Multiple clinical and biological autoimmune manifestations in 50 workers after occupational exposure to silica. Ann Rheum Dis 1993;52:534-8. [CrossRef]
12. Shtraichman O, Blanc PD, Ollech JE, et al. Outbreak of autoimmune disease in silicosis linked to artificial stone. Occup Med 2015;65:444-50. [CrossRef]
13. Makol A, Reilly MJ, Rosenman KD. Prevalence of connective tissue disease in silicosis (1985-2006): A report from the state of Michigan surveillance system for silicosis. Am J Ind Med 2011;4:255-62. [CrossRef]
14. Aminian O, Sharifian S, Mehrdad R, et al. Antinuclear antibody and rheumatoid factor in Silica-Exposed workers. Arh Hig Rada Toksikol 2009;2:185-90. [CrossRef]
15. Stolt P, Källberg H, Lundberg I, et al. Silica exposure is associated with increased risk of developing rheumatoid arthritis: Results from the Swedish EIRA study. Ann Rheum Dis 2005;4:582-6. [CrossRef]
16. Miranda AAM, Nascimento AC, Peixoto IL, et al. Erasmus syndrome: silicosis and systemic sclerosis. Rev Bras Reumatol 2013;53:310-3. [CrossRef]
17. Deniz O, Gumus S, Ors F, et al. Serum lactate dehydrogenase levels significantly correlate with radiological extent of disease and spirometric values in patients with silicosis due to denim sandblasting. Clin Chem Lab Med 2012;50:483-8. [CrossRef]