INTERNAL MEDICINE

□ CASE REPORT □

Non-smoking Chronic Obstructive Pulmonary Disease Attributed to Occupational Exposure to Silica Dust

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Abstract

An 85-year-old, never-smoking man presented with exertional dyspnea. He had been exposed to silica dust in the work place. Chest computed tomography revealed bronchial wall thickening without emphysema. A pulmonary function test showed airflow obstruction without impaired gas transfer. Airway hyperresponsiveness and reversibility were not evident. A transbronchial lung biopsy showed findings suggestive of mineral dust exposure, such as fibrosis and slight pigmentation of bronchioles. He was diagnosed with non-smoking chronic obstructive pulmonary disease (COPD) due to occupational exposure to silica dust. His symptoms were improved using an inhaled long-acting bronchodilator. The clinical characteristics of non-smoking COPD are discussed in this report.

Key words: non-smoking chronic obstructive pulmonary disease, occupational chronic obstructive pulmonary disease, silica dust

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by the presence of airflow limitation that is not fully reversible, with or without symptoms. Although cigarette smoking is the major risk factor for COPD, other risk factors for developing COPD are increasingly being recognized. These risk factors include occupational and environmental exposures, such as dusts and fumes, in developed and developing countries, as well as indoor biomass fuel burning in many developing countries (1).

Information about the clinical characteristics of non-smoking COPD is still limited (2-4). We herein report and discuss the clinical features in a case of non-smoking COPD due to occupational exposure to silica dust.

Case Report

An 85-year-old man was referred to our hospital for further evaluation of exertional dyspnea for 6 months with a modified Medical Research Council (mMRC) dyspnea scale of grade 1. Four years prior, he had complained of a few weeks' history of coughing, pharyngeal pain, and wheezing, which were treated at another hospital with short-term intravenous corticosteroids and oral antibiotics, based on a diagnosis of asthma exacerbation due to upper respiratory tract infection. He had never smoked; but was occupationally exposed to silica dust from the fourth to the seventh decades of his life when he worked at a motorcycle manufacturing company, where he handled sand mold casting without the use of any respiratory protection. All members of his family were never-smokers and while some colleagues at the same factory were smokers, they had scarcely smoked in the factory. His medical history included hypertension and diabetes.

A physical examination was unremarkable, and the breath sounds were normal for both lungs. The laboratory findings were not contributory. The serum immunoglobulin E level was 6 IU/mL; radioallergosorbent tests against common inhaled allergens were all negative. Serum autoantibodies, including rheumatoid factor, anti-cyclic citrullinated peptide

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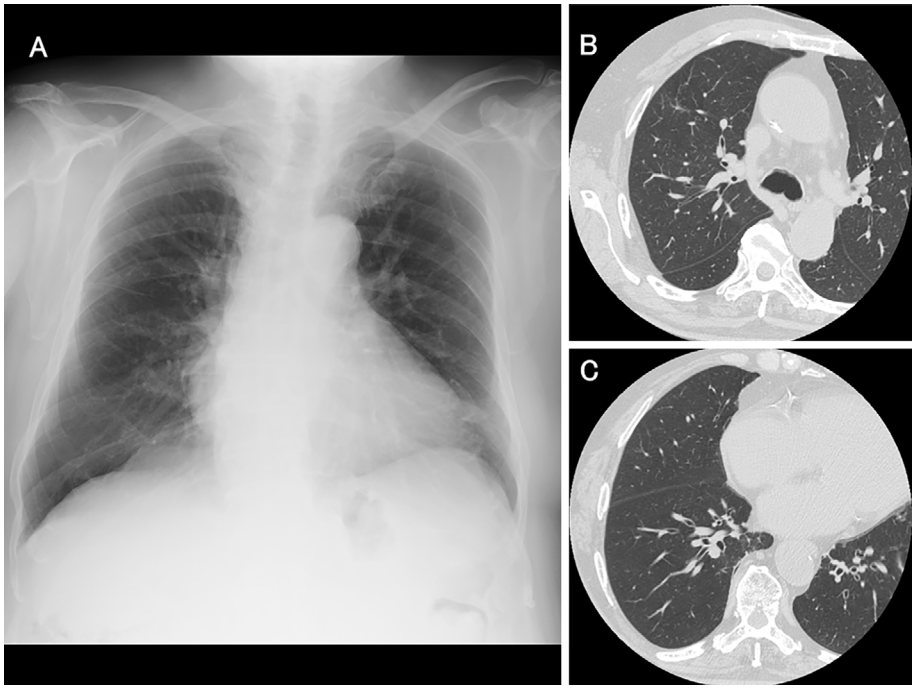

Figure 1. **Chest radiograph taken at initial presentation shows no abnormality (A). Computed tomography of the chest shows thickening of the bronchial wall without emphysema (B, C).**

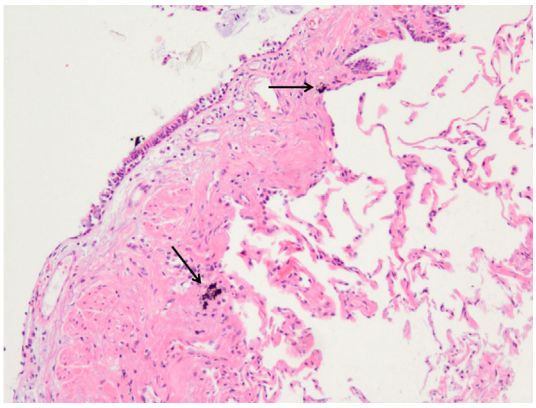

Figure 2. **A transbronchial lung biopsy specimen shows fibrous thickening and slight pigmentation (arrow) of the bronchiole (Hematoxylin and Eosin staining, ×100).**

antibody, and anti-nuclear, anti-SS-A, and SS-B antibodies, were also negative. The fractional exhaled nitric oxide concentration measured by NIOX MINO (Aerocrine, Solna, Sweden) was 15 ppb. The findings on a bronchial provocation test with acetylcholine chloride was negative. The results of a pulmonary function test were as follows: vital capacity 2.70 L (90.6% predicted), forced vital capacity (FVC) 2.69 L (90.3% predicted), forced expiratory volume in 1 second ($FEV_{1.0}$) 1.16 L (62.7% predicted), $FEV_{1.0}$/FVC 43.12%, maximum mid-expiratory flow rate 0.25 L/sec (10.6% predicted), residual volume per total lung capacity 43.98% (110.4% predicted), diffusion capacity of the lung for carbon monoxide (DLco) 13.67 mL/min/mmHg (85.3% predicted), and DLco divided by the alveolar volume 3.57 mL/min/mmHg (90.2% predicted). The bronchial reversibility after ultrasonic nebulization with procaterol hydrochloride was 10.3%. An arterial blood gas analysis on room air showed pH 7.406; arterial oxygen tension 87.3 mmHg; and arterial carbon dioxide tension 40.2 mmHg. On a sputum smear, numerous neutrophils without eosinophils were observed. Chest radiograph showed no abnormalities (Fig. 1A), and high resolution computed tomography (HRCT) of the chest showed thickening of the bronchial walls without emphysema (Fig. 1B and C). The macroscopic findings on fiberoptic bronchoscopy were unremarkable. A transbronchial lung biopsy (TBLB) showed fibrosis and slight pigmentation of the bronchioles (Fig. 2) with small crystals viewed by polarized light microscopy, suggestive of silica exposure (5).

Non-smoking COPD caused by silica dust was diagnosed, and he was treated with olodaterol and tiotropium bromide. Eight weeks after the initiation of treatment, his exertional dyspnea improved from mMRC grade 1 to 0, and the COPD assessment test score decreased from 7 to 2. Although his airflow obstruction did not improve, his inspiratory capacity increased from 1.86 to 2.01 L on the pulmonary function test.

Discussion

In this case, the patient was observed to have airflow limitation that was not fully reversible. Despite the fact that the patient had been occupationally exposed to silica dust, causality with COPD could not be established because quantification of silica in lung tissue and in the factory environment where he had been working was not performed. Nevertheless, exposure to silica was certain in this patient because he had used sand mold casting and a TBLB specimen

demonstrated findings suggestive of silica exposure, although the pathological findings in our case were slighter than those noted in cases of typical mineral dust airways disease (MDAD) (5). In addition, other diseases that can cause airflow obstruction, such as connective tissue disease (CTD) and bronchial asthma, were excluded based on the absence of clinical findings of CTD, the negative results of serum autoantibodies, and the normal airway hyperresponsiveness. Therefore, although the possible involvement of passive smoking in the development of COPD could not be completely excluded, non-smoking COPD caused by occupational exposure to silica dust was considered in this case.

Epidemiological studies have shown that various occupational and environmental agents, including mineral dusts, such as silica and asbestos, can cause COPD (1). Silica exists in crystalline and amorphous forms. The latter is less toxic and a less common form of exposure than the former. Respirable crystalline silica refers to particles with a diameter of less than 10 μm and these particles are more likely than larger one to reach the bronchioles and alveoli, leading to development of silicosis (6, 7). It has also been reported that chronic levels of silica dust that do not cause disabling silicosis may cause the development of chronic bronchitis, emphysema, and small airways disease which can lead to airflow obstruction (8). However, the clinical features of COPD caused by these agents other than cigarette smoking have not been fully clarified. Several studies have shown that biomass smoke-associated COPD differs from cigarette smoke-associated COPD in several clinical, radiologic, and pathologic aspects. Compared with cigarette smoke-associated COPD, biomass smoke-associated COPD has a greater self-reported impact on health status (9), slower decline in $FEV_{1.0}$ (10), less emphysema, but more air trapping, which may be related to more extensive small airway disease, as seen on chest HRCT (11). However, the mortality was reported to be similar between the two etiologies of COPD (12). In biomass smoke-associated COPD, a strong Th2 inflammatory response similar to bronchial asthma was observed, whereas in cigarette smoke-associated COPD, a Th17 inflammatory response was observed (13).

Although silica dust exposure has been reported to lead to airflow obstruction in the absence of radiologic signs of silicosis even in non-smokers (6), information about the clinical features of silica dust exposure-associated COPD is scarce. As mentioned above, a previous study using lung tissue obtained by pulmonary resection for lung cancer demonstrated that mineral dusts, including silica, can cause small airway lesions that consist of fibrous tissue deposits and are often accompanied by pigmentation. This condition, defined as MDAD, is morphologically distinguishable from small airway disease caused by cigarette smoke (5). In contrast, another study showed that only an insignificant degree of predominantly panacinar emphysema was found in lung tissue obtained by necropsy from lifelong non-smokers who were exposed to silica dust; it is important to note, however, that this study had a small sample size and the pathologic findings of the small airways were not available (14). Other studies have shown that cigarette smoking exacerbated the effect of silica dust on emphysema- like functional changes (15, 16). Similarly, in our case, the findings of emphysema were not evident on HRCT of the chest, and gas transfer was not impaired on pulmonary function testing. Based on these observations, more extensive small airway disease and less extensive emphysema may be the characteristic features of silica dust exposure-associated non-smoking COPD, in contrast to the findings in cigarette smoke-associated COPD. In our case, the HRCT findings of bronchiolar lesions such as centrilobular nodules, were not evident. Although we were unable to find any reports concerning the HRCT findings of MDAD, we believe that the degree of MDAD was too slight to show centrilobular nodules on HRCT in our case. Furthermore, the bronchial wall thickening observed on HRCT in our case might have been due to chronic bronchitis caused by silica, as it has been reported that silica might cause chronic bronchitis, although no reports have been published concerning the radiological, or pathological findings of silica-induced chronic bronchitis.

Eventually, the exertional dyspnea in our present case improved with an inhaled long-acting bronchodilator. We were unable to find studies describing the efficacy of long-acting bronchodilators in patients with non-smoking COPD. Nevertheless, inhaled long-acting bronchodilators seemed less capable of dilating the fibrinous thickened small airways in silica exposure-associated COPD, than in cigarette smoke-associated COPD. Whether or not patients with non-smoking COPD can be successfully treated with inhaled long-acting bronchodilators, similar to patients with smoking COPD, is unclear. Further investigations are necessary to examine the long-term efficacy of inhaled bronchodilators for non-smoking COPD.

In conclusion, we reported a case of non-smoking COPD caused by occupational exposure to silica dust. Physicians should be aware of non-smoking COPD caused by occupational and environmental agents other than cigarette smoke. To clarify the clinical, radiologic, and pathologic characteristics of non-smoking COPD, further investigations involving a large number of patients will be needed.

The authors state that they have no Conflict of Interest (COI).

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