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【 CASE REPORT 】

Pneumoconiosis Caused by Inhalation of Metallic Titanium Grindings

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Abstract:

A 61-year-old man was referred to our hospital with dyspnea and an abnormal lung shadow. His occupational history, pathological findings, and an elemental analysis led to a definitive diagnosis of pneumoconiosis induced by titanium grindings. The patient experienced gradual improvement solely by avoiding titanium grindings. Titanium-induced lung disease is very rare, and most of these cases are caused by inhalation of titanium dioxide (TiO_2), which is included in a wide range of commercially available products, such as paints, pigments, and cosmetics. However, industrial workers can also develop lung diseases due to the inhalation of metallic titanium materials during metal grinding.

Key words: pneumoconiosis, metallic titanium, titanium dioxide, elemental analysis, NSIP

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Introduction

Inhalation of metal dust and fumes can induce a wide variety of pulmonary diseases, including lung cancer, airway diseases, and pneumoconiosis (1-3). In cases of pneumoconiosis induced by metal inhalation, patients usually show yearly progression of disease, which results in pulmonary fibrosis. Various metals, including aluminum, iron, and hard metals, have been reported to cause pneumoconiosis (4-6); however, there are few reported cases of lung disease caused by titanium, with most such cases caused by titanium dioxide (TiO_2) or titanium dioxide nanoparticles (TNP) (2, 7-11). TiO_2 and TNP are usually included in paints, pigments, or cosmetics; however, titanium exposure can also occur in metal grinding. In general, titanium grindings are recognized as metal titanium and are distinguished from TiO_2 or TNP.

We herein present a case of subacute pneumoconiosis caused by the inhalation of metallic titanium grindings. The diagnosis was made based on a pathological examination and was confirmed by an elemental analysis. Lung infiltration gradually diminished without any medication after avoidance of titanium exposure.

Case Report

A 61-year-old man was referred to our hospital for the examination of an abnormal lung shadow. He had been engaged in the metalworking industry for 40 years. Four months prior to his admission, he had started a new task of cutting metal pipe and processing it into screws. Although the task involved heavy exposure to titanium grindings, he did not wear a dust protective mask during the work. Subsequently, he gradually developed a dry cough and dyspnea on exertion. One month prior to his admission, he went to a clinic because of these symptoms. Chest radiography showed consolidation on both sides of the upper lung fields. Despite treatment with antibiotics and diuretics, the lung consolidation gradually worsened. He was referred to our hospital for further investigation and treatment. His past medical history included chronic heart failure and paroxysmal atrial fibrillation. His medications included metildigoxin, candesartan cilexetil, carvedilol, and bepridil. He had a 20 pack/year smoking history but had stopped smoking for 20 years.

On examination, his vital signs were normal with a pe-

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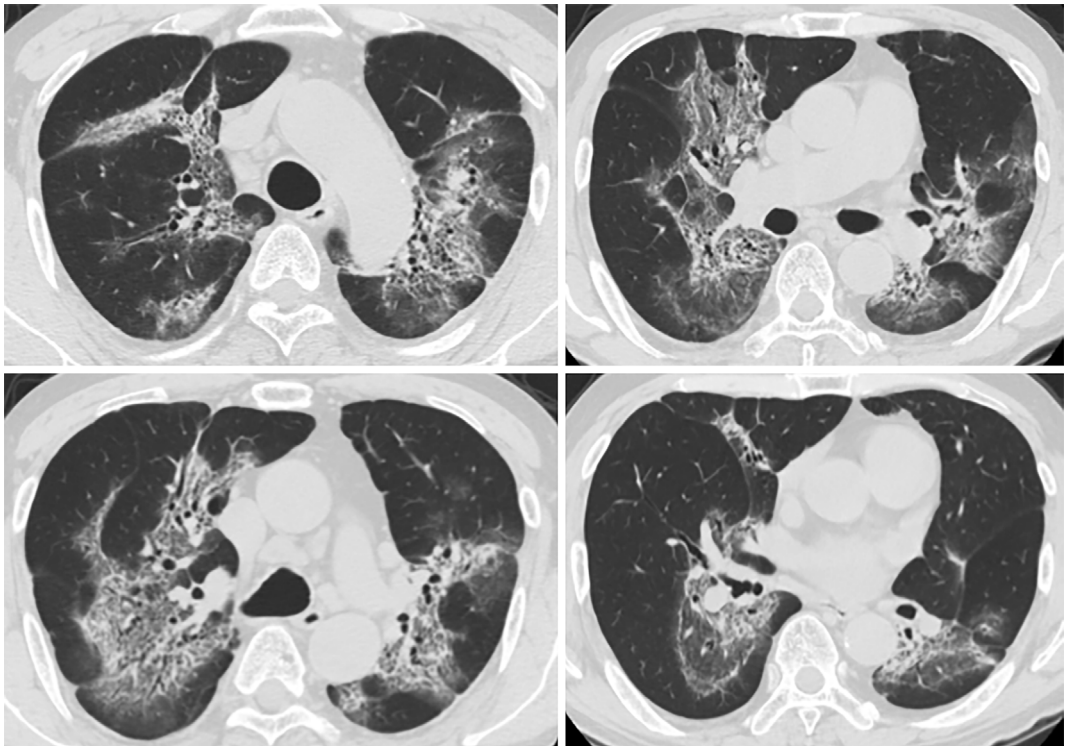

Figure 1. **CT findings at the first visit to our hospital. Ground-glass opacities (GGOs) with a peribronchial distribution were predominantly observed in the upper lung.**

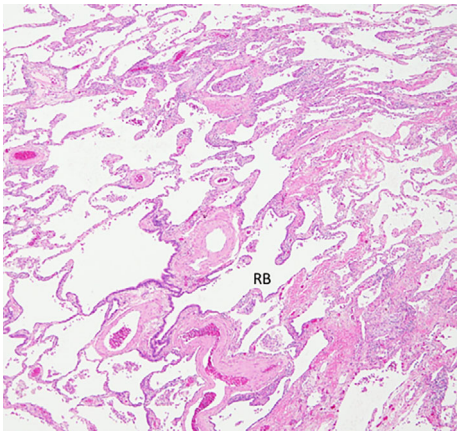

Figure 2. **Histopathological findings of the lung. A video-assisted thoracoscopic biopsy (VATS) specimen obtained from the left S1+2 showed infiltration of lymphocytes around the respiratory bronchiole (hematoxylin-eosin, ×4). RB: respiratory bronchiole**

ripheral oxygen saturation of 95%. Finger clubbing was observed and rhonchi were detected at the right middle lung field on auscultation. A laboratory analysis revealed elevated levels of Krebs von den Lungen-6 (KL-6; 1,910 U/mL) and surfactant protein D (SP-D; 340 ng/mL). A chest X-ray showed consolidation and reticular shadow on the right middle, right lower, left upper, and left lower lung fields. High-resolution CT (HRCT) showed ground-glass opacities with traction bronchiectasis, which was dominant in the upper lungs, where it showed a central distribution (Fig. 1). Bronchoalveolar lavage (BAL) indicated mild lymphocytosis with 33% lymphocytes and 66% macrophages. The ratio of CD4 to CD8 T lymphocytes in the BAL fluid was 0.61.

Video-assisted thoracoscopic biopsy (VATS) was performed to obtain specimens of the S1+2 and S6 lesions of the left lung for further investigation. Pathologically, mild infiltration of lymphocytes accompanied with alveolar collapse and fibrosis was observed with a centrilobular distribution, demonstrating a cellular to fibrotic nonspecific interstitial pneumonia (NSIP)-like pattern (Fig. 2). Giant cells were not detected. No obvious metal deposits were seen. Because of the distribution of the lesions, some type of inhalation was suspected as the etiology of the disease. An elemental analysis of the lung tissue was conducted by scanning electron microscopy, which indicated significant deposition of titanium in the lung (Fig. 3). Based on the results of the elemental analysis and the fact that the patient was involved in grinding titanium when the respiratory symptoms occurred, it was suspected that his pulmonary manifestation was caused by titanium exposure. We advised him to avoid exposure to titanium grindings. After the avoidance of titanium exposure, his symptoms and radiological abnormalities gradually diminished without any medication (Fig. 4).

Discussion

We presented a rare case of pneumoconiosis demonstrating an NSIP-like pattern induced by the inhalation of metallic titanium grindings. This case contains two interesting findings. First, metallic titanium grindings were identified as

an additional (in addition to TiO_2 and TNP) cause of lung disease. Second, the progression of lung infiltration in this case was rapid in comparison to other diseases induced by metal inhalation.

Titanium is classified into metallic titanium and TiO_2. These products are refined from titanium ore (ilmenite and rutile) by different processes. Metallic titanium is used for various industrial applications, including applications in the aircraft industry, because of its low specific gravity. On the other hand, TiO_2 is used for wide range of commercially available products, such as paints, pigments, and cosmetics. Among TiO_2 materials, TNP has a minute particle size of < 20 nm. More than 90% of the world's titanium ore production is turned into TiO_2 or TNP, and approximately 5% is used for metallic titanium. Thus, most previous reports about lung toxicity have included cases caused by TiO_2 or TNP exposure. For example, Yamadori et al. reported a case of lung fibrosis and lung adenocarcinoma with TiO_2 deposition in the lung (2). In the case presentation, the patient had been engaged in TiO_2 packing for 13 years. Cheng et al. reported a case of bronchiolitis obliterans organizing pneumonia (BOOP) induced by exposure to TNP included in paints (7). Keller et al. also reported a case of titanium lung in a painter who developed pulmonary alveolar proteinosis (11). Titanium-induced lung diseases are rare and have tended to be reported in nonindustrial workers. Only one case of metallic titanium-associated lung disease has been reported. That report by Redline et al., described a case of granulomatous lung disease with titanium deposition due to daily exposure to various metallic fumes (12). In our case, which was caused by metallic titanium grindings, the pulmonary lesion did not demonstrate granulomas-instead we observed NSIP with peribronchial distribution. Thus, we should be aware that exposure to metallic titanium grindings in metal processing can also cause lung disease.

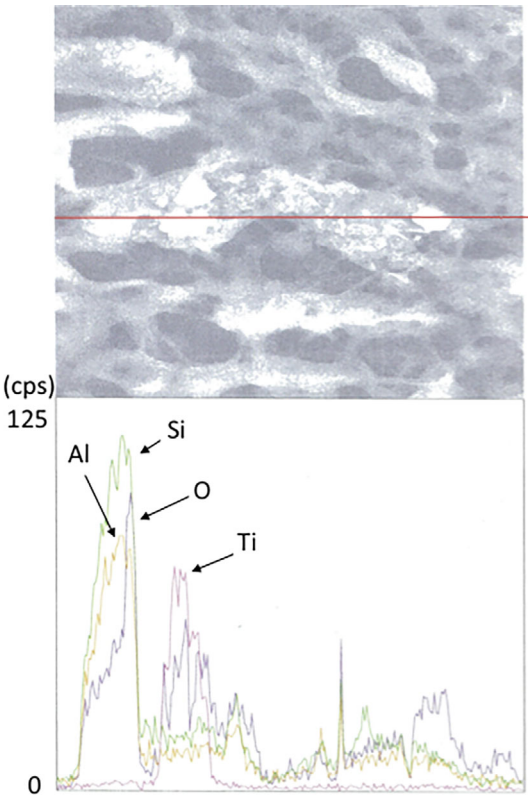

Figure 3. Elemental analysis of the lung. In an elemental analysis by scanning electron microscopy (SEM), the X-rays provided by irradiation of an electron beam are counted along a red line in the specimen. As a result, significant deposition of titanium with aluminum, silicon, and oxygen was indicated.

In the elemental analysis, deposition of aluminum and silicon was also observed. Based on the medical records provided by the patient, who was a reliable skilled worker, he was involved in grinding titanium. Thus, it can be stated that-to some extent-titanium exposure directly or indirectly induced pneumoconiosis as the patient became subacutely symptomatic after he started performing metal titanium processing in the course of his daily work. It is also possible that aluminum and silicon had accumulated in the lung asymptomatically during metalworking processes that he was involved in before his work in titanium processing. It is un-

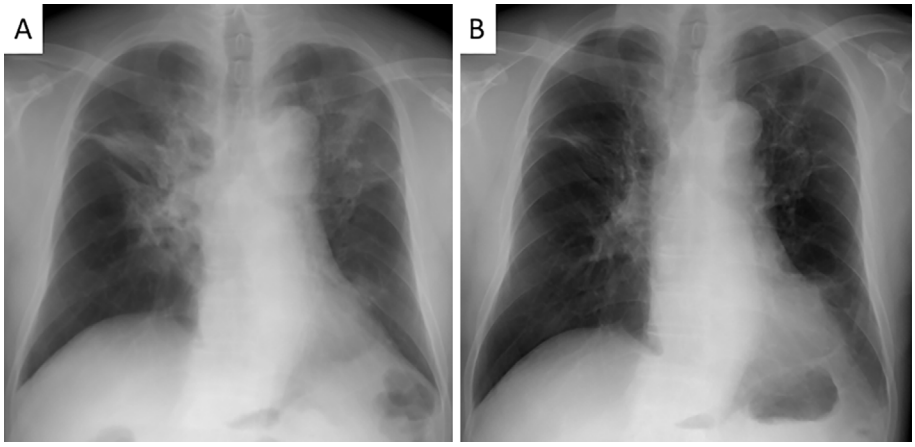

Figure 4. The changes in the chest X-ray findings during the clinical course. (A) At the time of the diagnosis, bilateral consolidation, predominantly in the upper lung field, was indicated. (B) The consolidation gradually resolved after avoiding exposure to titanium for four years.

clear whether titanium was the sole cause of pneumoconiosis or whether there was a synergistic effect between titanium and aluminum or silicon. Thus, there is a limitation in our ability to speculate on the etiology of this case.

Interestingly, the subacute progression of disease was seen in our case. This clinical course resembled that of the case reported by Cheng et al., in which the patient demonstrated BOOP after only 3 months of exposure to inhaled TNP in a paint factory (7). Other than these cases, a few cases of pulmonary silicosis and arc welder's lung have been reported in which patients presented subacute progressive pneumoconiosis (13, 14). In general, however, pneumoconiosis has a chronic course, demonstrating centrilobular granular shadow and a slow progression of fibrosis. Pulmonary silicosis typically occurs after 10-20 years of work while the individuals usually remain asymptomatic (1). Moriyama et al. suggested that the exposure period of hard metal lung diseases was at least 2.5 years, and more than two-thirds of the patients in their study were exposed to hard metal for longer than 5 years (15). From this viewpoint, the clinical course of our case was quite different from a typical case of pneumoconiosis and may present an atypical etiology, such as metal fume fever or a hypersensitivity reaction. The size of the metal particles produced in the working process of metal grinding is between 4 μm and several 100 μm. Small amounts of fumes can also be produced. In this case, no obvious metal deposit was seen in the optical microscope analysis. Thus, we assume that small-sized particles and metal fumes are pathogenic.

In conclusion, we presented a case of pneumoconiosis induced by the inhalation of metallic titanium grindings. The clinical course showed subacute disease progression, indicating that the disease etiology was different from that of typical pneumoconiosis.

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

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