Hard Metal Lung Disease Successfully Treated with Inhaled Corticosteroids

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Abstract

We herein report a case of hard metal lung disease that was successfully treated with inhaled corticosteroids. A 46-year-old man was admitted to our hospital due to coughing and an abnormal shadow on a chest radiograph. He had worked as a hard metal tool sharpener for five years. Chest computed tomography scans showed centrilobular micronodules and areas of ground-glass opacity in the bilateral lung fields. Video-associated lung biopsy specimens revealed bronchocentric interstitial pneumonia and cellular bronchiolitis. A high-energy dispersion X-ray microanalysis detected tungsten. The patient was diagnosed with hard metal lung disease. Inhaled corticosteroid therapy (800 μg of ciclesonide hydrofluoroalkane daily) resolved the patient’s symptoms, elevated KL-6 level, abnormal areas of chest opacity and obstructive, restrictive and diffusion impairments.

Key words: hard metal lung disease, inhaled corticosteroid therapy, tungsten, video-associated lung biopsy


Introduction

Hard metal lung disease (HMLD) occurs in workers exposed to hard metals containing tungsten (W), cobalt and other metals. The prevalence of HMLD ranges from 0.13% to 3.8% among tungsten carbide workers (1-3). Although systemic corticosteroid or immunosuppressant therapy is effective in some cases of HMLD (4-6), the efficacy of inhaled corticosteroids (ICSs) has not yet been established. We herein report a case of hard metal lung disease successfully treated with ICSs.

Case Report

In September 2010, a 46-year-old man complaining of a cough visited a nearby hospital. A chest X-ray examination detected reticular shadows in the right lower lung fields. Chest computed tomography scans showed centrilobular nodules and areas of ground-glass opacity throughout the entire lungs, predominately in the lower lung fields. The patient was admitted to our hospital for a further investigation in April 2011. He was a nonsmoker and had no past history of any particular diseases. He had worked as a hard metal tool sharpener for five years. On admission, his temperature was 36.5°C, his pulse rate was 72 beats/min and his respiratory rate was 16 breaths/min. No crackles were heard over the lung fields. No finger clubbing was observed. The laboratory data revealed elevated serum levels of KL-6 (1,017 U/mL, cutoff level: 500 IU/mL), SP-A (53.0 μg/mL, cutoff level: 43.8 μg/mL) and SP-D (121.0 μg/mL, cutoff level: 110 μg/mL). Pulmonary function tests showed a decreased % peak flow (%PEFR: 62.0%) and % forced expiratory flow between 25% and 75% of the vital capacity (%FEF25-75: 39.5%). Meanwhile, the %vital capacity (%VC: 106.7%), % diffusing capacity for carbon monoxide (%DLco: 90.3%), % forced expiratory volume in 1 second (%FEV1: 84.6%) and forced expiratory volume after 1 second (71.8%) were within the normal ranges. Bronchoalveolar lavage fluid (BALF) obtained from the middle lobe (right B5a) showed an increased total cell concentration (7.14×10³/mL), an increased lymphocyte ratio (74.3%) and a decreased CD4/CD8

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Received for publication January 9, 2013; Accepted for publication April 26, 2013

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A high-energy dispersion X-ray microanalysis detected a small amount of W (Fig. 3). The patient fulfilled the diagnostic criteria for HMLD (2, 7-9). He declined our recommendation to quit his job because he needed to make a living. Although he continued to work wearing a dust mask to prevent dust exposure, his symptoms persisted, and the abnormal chest CT shadows decreased but continued (Fig. 1C, D). The serum KL-6 level once gradually decreased; however, it gradually became elevated again (Fig. 4). The FEV1, VC and DLco values also decreased (Fig. 4). We therefore administered ICS therapy (800 μg of ciclesonide hydrofluoroalkane-[CIC-HFA] inhaled daily) in March 2012 because the patient did not consent to systemic steroid therapy. One month after the initiation of ICS therapy, the patient’s cough gradually began to improve. Seven months of ICS therapy resulted in a diminished cough, improved obstructive and restrictive parameters and diffusion capacity on spirometry, resolved centrilobular shadows and areas of ground-glass opacity (Fig. 1E, F) and normalized serum levels of KL-6 (210 IU/mL), SP-A (27.0 μg/mL) and SP-D (80.3 μg/mL).

**Discussion**

In the present case, a small amount of W deposition was detected on an X-ray microanalysis. With respect to HMLD, qualitative analyses can detect Al, Si, Ti and Fe in both HMLD patients and control subjects; however, W is detected only in patients with HMLD, not in control subjects (9). Different from silicosis, collier’s lung and asbestosis, a cumulative dose of hard metal is not correlated with the occurrence of HMLD (10). On the other hand, the pathologic patterns depend on the amount of W deposition. Non-giant interstitial pneumonia (GIP) is observed in 60% of HMLD patients, with less W deposition than that observed in patients with GIP (10). Our patients demonstrated a non-GIP pattern with centrilobular interstitial pneumonia and cellular bronchiolitis in the absence of apparent giant-cell infiltration and severe fibrosis. We speculate that a small amount of W exposure would result in relatively mild lesions. The typical BALF features of HMLD include mild to moderate T lymphocytosis with an inverted CD4/CD8 ratio (11-13). Moriyama et al. suggested that CD8⁺ lymphocytes are found predominantly in centrilobular fibrosing lesions and HMLD may result from chronic hypersensitivity reactions (9). In our case, the number of lymphocytes in the BALF was increased and the CD4/CD8 ratio was below 1.0. In addition, infiltration of lymphocytes and macrophages was observed in the alveolar space. Restrictive or mixed obstructive and restrictive impairment of the pulmonary function is observed in patients with HMLD (14-16). In the present case, obstructive parameters were impaired with decreased values of %PEFR and %FEF25-75 on the first admission. Although the values of %VC, %FEV1.0 and %DLco were within the normal limits on the first admission, the levels of VC, FEV1.0 and DLco decreased during the clinical time course and recovered following the administration of ICS therapy. We ex-
included the possibility of bronchial asthma based on the negative results of a bronchial hypersensitivity test (FEV_{1.0} before β2-stimulant inhalation: 2,790 mL, FEV_{1.0} after β2-stimulant inhalation: 3,020 mL, improvement rate of FEV_{1.0}: 8.9%, improvement volume of FEV_{1.0}: 230 mL) and the absence of apparent eosinophilic inflammation in the BALF and biopsy specimens. We also excluded the possibility of hypersensitivity pneumonia based on the negative results of a precipitation antibody test for various fungi and the absence of granuloma formation in the biopsy specimen.

To our knowledge, there are no case-controlled studies regarding the treatment of HMLD. The most important point is to prevent disease progression by avoiding further exposure to the hard metal. Although several authors have reported improvement with systemic steroid or immunosuppressant therapy (4-6), such therapies are often associated with a variety of side effects. The diameter of CIC-HFA is approximately 1.1 μm, similar to that of metallic dust particles, and is an optimal size for maximal alveolar dust deposition (17). In a previously reported case of hypersensitivity pneumonia, treatment with chlorofluorocarbon-beclomethasone dipropionate with a diameter of 3.5 μm was ineffective, while therapy with hydrofluoroalkane-134a-beclomethasone dipropionate with a diameter of 1.1 μm was effective (17). In our case, CIC-HFA was effective in treating the bronchocentric and alveolar lesions. Indeed, following the administration of ICS therapy, the obstructive, restrictive and diffusion parameters on spirometry improved,
the serum KL-6, SP-A and SP-D levels, which reflect alveolar epithelial cell injury (17, 18), normalized and the areas of ground-glass opacity, which reflect airspace macrophage infiltration (19), resolved.

We herein demonstrated a case of hard metal lung disease successfully treated with ICSs. ICS therapy is effective for treating mild lesions of HMLD. Further observation is needed to determine the long-term effects of ICS in patients with HMLD.

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

Acknowledgement

We thank Dr. Yasuo Morimoto for analyzing the metal elements using a high-energy dispersion X-ray microanalysis, Dr. Jun-ichi Fukuoka for the pathological diagnosis of the lung specimen and Ms. Mariko Ono and Kaori Hirano for their valuable technical assistance.

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