

Hard Metal Lung Disease Diagnosed on a Transbronchial Lung Biopsy Following Recurrent Contact Dermatitis

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Abstract

A 63-year-old man employed in a hard metal manufacturing company for 40 years presented with a chronic dry cough and exertional dyspnea 20 years after the onset of recurrent exanthemas. A chest radiograph revealed bilateral reticular shadows in the upper lung field. Pathological specimens in which tungsten was detected were obtained via a transbronchial lung biopsy. Patch tests were positive for cobalt and other metals. The patient was diagnosed with hard metal lung disease (HMLD) concurrent with contact dermatitis and treated with corticosteroids. This case suggests that allergies to metal may play a role in the onset of HMLD.

Key words: hard metal lung disease, contact dermatitis, patch test

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Introduction

Hard metal lung disease (HMLD) is an occupational lung disease caused by the inhalation of hard metal dust predominantly composed of tungsten carbide and cobalt alloys. These metals are used in the manufacturing of drill tips, tool edges and armament components. HMLD is characterized pathologically by giant cell interstitial pneumonia [GIP (1)]. A surgical lung biopsy is generally required to diagnose GIP.

Exposure to hard metals has been reported to cause other diseases in addition to HMLD, including bronchial asthma and contact dermatitis (2, 3). However, to our knowledge, very few studies have reported that these diseases coexist in patients with HMLD (4). We herein describe the unusual case of a manufacturing worker exposed to hard metal who developed HMLD 20 years after the onset of recurrent contact dermatitis characterized by exanthemas.

Case Report

This report describes the case of a 63-year-old man who worked in the office of a hard metal manufacturing company for 40 years (from 20 to 60 years of age), then became a manufacturing worker (mixing, pressing and sintering metal powder) at 61 years of age. He used a mask only on the production line, and his nasal cavity was dirty and black once he completed his work. He had a history of smoking one pack of cigarettes/day from 18 to 48 years of age and had experienced recurrent exanthemas on his neck, axilla and legs starting at approximately 40 years of age. The characteristics of the exanthemas did not change according to the type of work. He consulted a few dermatologists; however, the cause of the exanthemas remained unclear. A patch test was performed, although the metals were not included.

The patient presented at our hospital with a three-month history of a dry cough and exertional dyspnea that did not

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Figure 1. Chest radiograph at first visit showing the bilateral reticular shadow predominantly distributed in the upper lung field.

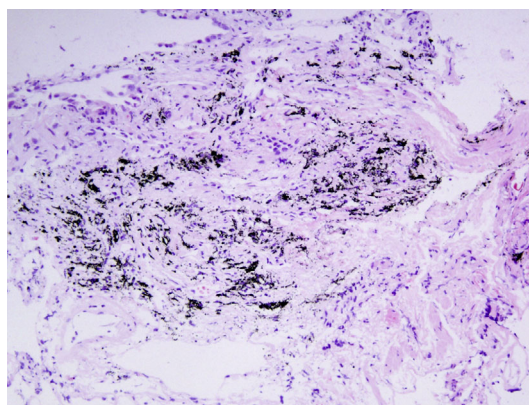


Figure 3. Lung biopsy specimen obtained using TBLB showing fibrotic change of alveolar septum, organization of exudates, and small black deposits, but no findings of GIP (Hematoxylin and Eosin staining $\times 50$).

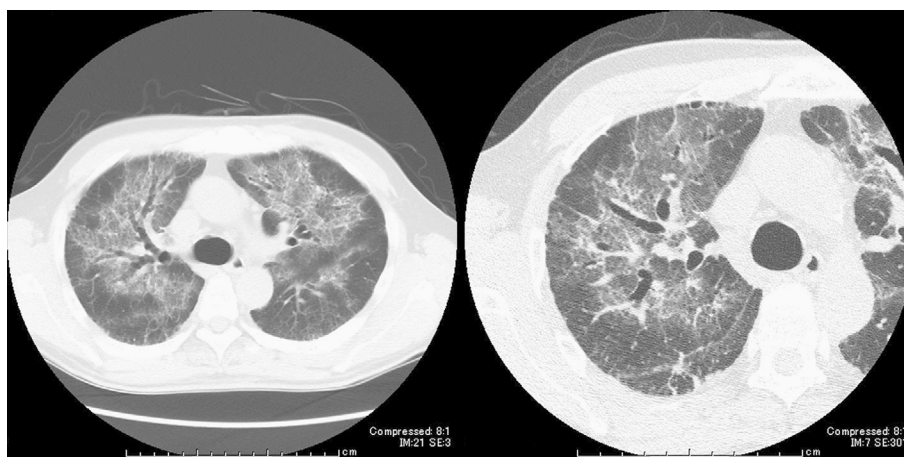


Figure 2. Chest computed tomography showing diffuse ground-glass opacities along the respiratory tract, traction bronchiectasis, and reticular opacities without honeycombing.

change on working days or holidays. At the time, he had slight exanthemas on both legs. A physical examination revealed the following findings: height, 164.8 cm; weight, 58.9 kg; body temperature, 36.7°C ; pulse rate, 88 beats/min; blood pressure, 112/80 mmHg; and respiratory rate, 12 breaths/min. A chest examination disclosed fine crackles in the upper right and left lung areas. The patient's fingers did not exhibit clubbing. There were no findings suggestive of a collagen disease. An arterial blood gas analysis performed on room air demonstrated a pH of 7.44, a PaCO_2 of 39.1 Torr and a PaO_2 of 80.4 Torr. A laboratory analysis indicated a white blood cell count of $9,500/\text{mm}^3$ (79.6% neutrophils, 0.7% eosinophils, 0.2% basophils, 4.4% monocytes, 15.1% lymphocytes), an LDH level of 295 IU/L and an IgE level of 16 U/mL. The serum levels of KL-6 and SP-D were remarkably elevated at 3,090 U/mL and 314 ng/mL, respectively. Tests for collagen disease-related autoantibodies were negative.

A chest radiograph revealed bilateral areas of opacity concentrated in the upper lung fields that were not observed on chest radiography performed 10 months earlier (Fig. 1).

High-resolution computed tomography (HRCT) displayed diffuse ground-glass opacity along the respiratory tract, traction bronchiectasis and reticular opacity without honeycombing (Fig. 2). Pulmonary function tests demonstrated restrictive ventilatory impairment characterized by a low vital capacity of 2.58 L (76.1% of predicted) and a percent forced expiratory volume in one second of 89.1%.

An analysis of bronchoalveolar lavage (BAL) fluid yielded 4.00×10^2 cells/mL (4.5% neutrophils, 25.0% eosinophils, 50.1% lymphocytes and 19.5% macrophages). The CD4/8 lymphocyte ratio in the BAL fluid was 0.5, and the BAL fluid was negative for bacterial infection or multinucleated giant cells (MGC). A lung biopsy specimen obtained via TBLB showed fibrotic remodeling of the alveolar septum, early organization of intra-alveolar exudate and small black deposits without evidence of GIP (Fig. 3). To establish a definitive diagnosis, we recommended a surgical lung biopsy; however, the patient did not consent to this procedure. Therefore, we opted to detect hard metal lung deposition using an electron probe microanalyzer (EPMA). The EPMA detected tungsten and other elements but no cobalt. In con-

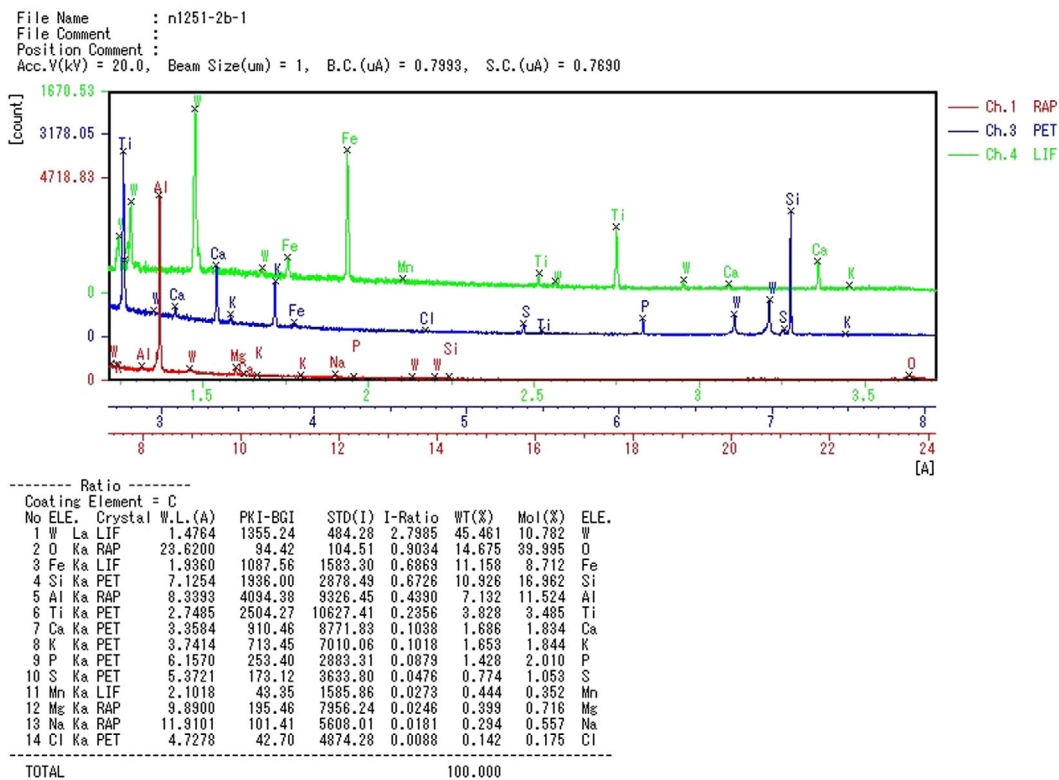


Figure 4. Tungsten was detected in a TBLB specimen by an electron probe microanalyzer. Other elements such as oxygen (O), silicon (Si), iron (Fe), and aluminum (Al) were also detected, but cobalt was not detected.

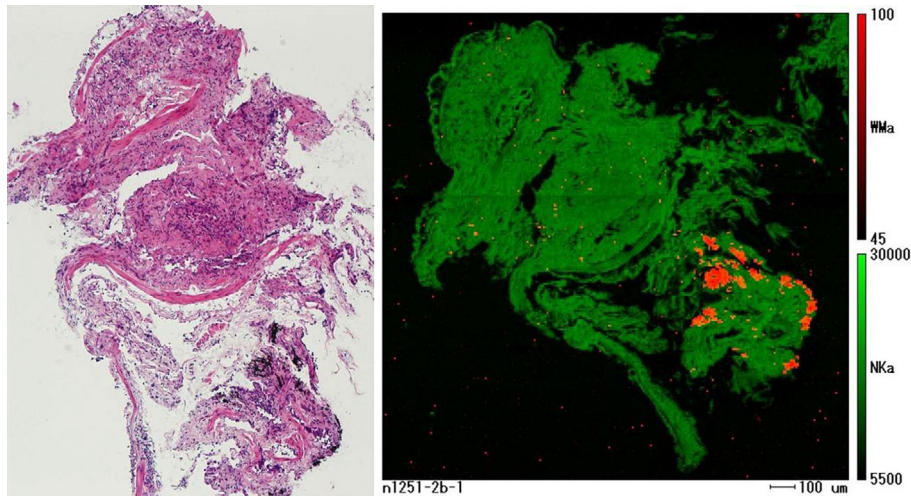


Figure 5. Distribution map of elements shows tungsten as red and nitrogen as green. Tungsten detection was consistent with small black deposit observed in Hematoxylin and Eosin staining.

trast, patch tests were positive for cobalt and other metals (Figs. 4, 5). These findings led to a diagnosis of HMLD and contact dermatitis.

Because the symptoms of dry cough and exertional dyspnea did not improve, even after the patient quit his job approximately four weeks earlier, he was treated with corticosteroids (30 mg/day). After receiving the medication, his symptoms and the findings of an HRCT scan obtained two months later gradually improved; however, they did not dis-

appear. Similarly, the serum levels of KL-6 and SP-D decreased, although they remained high (1,950 U/mL and 142 ng/mL, respectively). The exanthemas on the patient's legs disappeared; however, a slight exanthema recurred on his neck when the corticosteroid dose was 5 mg/day. Therefore, the dose of corticosteroids was tapered (5 mg/day), and the patient has continued to receive this treatment to date.

Discussion

Hard metals are produced using the powder metallurgy method because tungsten has an extremely high melting point, which makes fusion difficult. The average particle diameter of raw materials is approximately 0.5-15 μm . These particles enter the alveoli and cause occupational lung disease. Animal experiments suggest that cobalt is toxic to the lungs and that the combination of cobalt and tungsten carbide may be worse than cobalt alone (5, 6). The prevalence of HMLD is reported to be approximately 0.13-3.8% in hard metal-related workers (1).

The most reliable histopathological characteristic of HMLD is GIP, identified according to a large number of MGC with cannibalistic features accumulating in the alveoli (7). A centrilobular distribution of the lesions is another characteristic (8). We performed TBLB, which was negative for both characteristics. Abraham et al. reported that TBLB was used to diagnose three of their six cases of GIP (9). Making a diagnosis of GIP is difficult using TBLB because the size of the specimen is not adequate for a pathological diagnosis. It has been reported that the results of BAL fluid analyses are equivalent to those of tissue biopsies for diagnosing of GIP (10). However, not all confirmed cases of HMLD present with BAL fluid positive for MGC, as in the case of our patient. In addition, the pathologic findings of HMLD are similar to those of not only GIP, but also UIP and DIP (7), and it is considered that HMLD can present with the pathologic findings of various interstitial lung diseases. When HMLD is suspected based on hard metal exposure, even if characteristic histopathological findings are not observed in small TBLB specimens, it is important to ultimately conduct an analysis using an EPMA. In the present case, tungsten and other metals were detected, while cobalt was not. The high solubility of cobalt in plasma prevents it from accumulating in tissues, which explains why the metal is not detected in many biopsy specimens of lung tissue (11).

Large variability in individual sensitivity to hard metals is expected, since no other workers at this manufacturer had HMLD. Interestingly, cobalt exposure also causes allergic diseases, such as a contact dermatitis and bronchial asthma. As such, an allergy to cobalt may constitute a susceptibility marker for HMLD (12). In the present report, we found the patient to be positive for cobalt sensitivity according to a patch test. This diagnosis was not made earlier, despite the 20-year history of exanthemas because hard metals are not included in patch tests. Because the patient did not exhibit other specific skin reactions indicative of skin diseases, we considered that his exanthemas were reflective of systemic contact dermatitis caused by cobalt exposure.

Systemic contact dermatitis describes a skin reaction that occurs in response to systemic exposure to an allergen, although the first sensitizing exposure to the allergen may have been via topical application (13). Five types of clinical

manifestations of systemic contact dermatitis have been identified: 1) pompholyx dyshidrotic eczema; 2) flare-ups earlier patch test reactions; 3) a generalized maculopapular-vesicular rash; 4) erythema multiforme and vasculitis; and 5) urticaria and anaphylaxis (13, 14). Our patient presented with the characteristics of a type 3 rash characterized by bilateral eruptions on the elbow flexors, axilla, eyelids, side of the neck and genital area.

Most HMLD case reports that enforced the use of a patch test reported cobalt-positive results. Accordingly, it is important to conduct a patch test when allergic symptoms, such as exanthema, are detected in workers exposed to hard metals. This proactive measure could potentially prevent the onset of HMLD by stopping hard metal exposure before the establishment of irreversible damage to the lungs. Once lung disease is detected, the patient must refrain from any further exposure to hard metals and may require corticosteroids. In our patient, ongoing treatment partially improved the symptoms of HMLD. On the other hand, HMLD patients who have been exposed to both cobalt and tungsten are at high risk of death from lung cancer (15). Therefore, these patients require long-term follow-up to monitor for any signs of complications.

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

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References

1. Moriyama H, Suzuki E. Diagnostic criteria of hard metal lung disease. *Nihon Kyobu Rinsyou (Jpn J Chest Dis)* **70**: 1206-1218, 2011 (in Japanese, Abstract in English).
2. Davison AG, Haslam PL, Corrin B, et al. Interstitial lung disease and asthma in hard-metal workers: bronchoalveolar lavage, ultrastructural, and analytical findings and results of bronchial provocation tests. *Thorax* **38**: 119-128, 1983.
3. Ficher T, Rystedt I. Cobalt allergy in hard metal workers. *Contact Dermatitis* **2**: 115-121, 1983.
4. Sjögren I, Hillerdal G, Andersson A, Zetterström O. Hard metal lung disease: importance of cobalt in coolants. *Thorax* **35**: 653-659, 1980.
5. Delahant AB. An experimental study of the effects of rare metals on animal lungs. *AMA Arch Ind Health* **12**: 116-120, 1955.
6. Lasfargues G, Lison D, Maldague P, Lauwerys R. Comparative study of the acute lung toxicity of pure cobalt powder and cobalt-tungsten carbide mixture in the rat. *Toxicol Appl Pharmacol* **112**: 41-50, 1992.
7. Ohori NP, Sciurba FC, Owens GR, Hodgson MJ, Yousem SA. Giant-cell interstitial pneumonia and hard-metal pneumoconiosis. A clinicopathologic study of four cases and review of the literature. *Am J Surg Pathol* **13**: 581-587, 1989.
8. Cugell DW. The hard metal lung diseases. *Clin Chest Med* **13**: 269-279, 1992.
9. Abraham JL. Lung pathology in 22 cases of giant cell interstitial pneumonia (GIP) suggests GIP is pathognomonic of cobalt (hard metal) disease. *Chest* **91**: 312, 1987.
10. Kinoshita M, Sueyasu Y, Watanabe H, et al. Giant cell interstitial pneumonia in two hard metal workers: the role of bronchoalveolar

- lavage in diagnosis. *Respirology* **4**: 263-266, 1999.
11. Moriyama H, Kobayashi M, Takada T, et al. Two-dimensional analysis of elements and mononuclear cells in hard metal lung disease. *Am J Respir Crit Care Med* **176**: 70-77, 2007.
12. Kusaka Y, Sugimoto K, Seki Y, et al. Bronchopulmonary diseases due to the hard metal dust. *Sangyo Igaku* **24**: 636-648, 1982 (in Japanese, Abstract in English).
13. Fisher AA. Allergic dermatitis medicamentosa: the "systemic contact-type variety". *Cutis* **18**: 637-642, 1976.
14. Rietschel RL, Fowler JF. Systemic contact-type dermatitis. In: *Fischer's Contact Dermatitis*. 5th ed. Lippincott, Williams and Wilkins, Philadelphia, 2000: 89-100.
15. Moulin JJ, Wild P, Romazini S, et al. Lung cancer risk in hard-metal workers. *Am J Epidemiol* **148**: 241-248, 1998.