

# Hard Metal Lung Disease—The First Case in Singapore

K L Tan,<sup>\*FAMS, MRCP(UK), FCCP</sup>, H S Lee,<sup>\*\*FAMS, MBBS, MSc (Occup Med)</sup>, W T Poh,<sup>\*\*\*FAMS, MBBS, FRCPA</sup>, M Q Ren,<sup>\*\*\*\*MSc</sup>,  
F Watt,<sup>+PhD</sup>, S M Tang,<sup>++PhD</sup>, P Eng,<sup>+++FAMS, M Med (Int Med), FACP</sup>

## Abstract

**Introduction:** We report the first case of hard metal lung disease in Singapore and the occupational investigative work and control measures that were undertaken. **Clinical Picture:** A 38-year-old machinist in the tool manufacturing industry presented with exertional dyspnoea and cough. Chest X-ray revealed bilateral reticulonodular infiltrates with honeycombing. High resolution computed tomography scan of the thorax confirmed the presence of interstitial fibrosis. Open biopsy of the lung showed features of pneumoconiosis. Particle induced X-ray emission (PIXE) analysis, a relatively new elemental analysis technique, performed on the lung biopsy specimen confirmed the presence of tungsten and titanium; and he was diagnosed to have hard metal lung disease. Microbiologic, serologic and histologic investigations excluded an infective cause. Serial pulmonary function tests on follow-up showed no progression. He presented with haemoptysis 10 months later and was diagnosed to have tuberculosis on the basis of positive sputum and bronchoalveolar lavage cultures for *Mycobacterium tuberculosis* complex. **Treatment:** Preventive measures and permanent transfer to non-cobalt work were instituted. **Outcome:** The interstitial fibrosis appears to have stabilised. **Conclusion:** The diagnosis of hard metal lung disease must be considered in a worker exposed to cobalt presenting with interstitial fibrosis.

*Ann Acad Med Singapore* 2000; 29:521-7

**Key words:** Cobalt, Fibrosing alveolitis, Interstitial fibrosis, Tuberculosis

## Case Report

A 38-year-old Chinese man and lifetime non-smoker, who had previously been well, was referred for investigation of bilateral reticulonodular infiltrates noted on his chest roentgenogram. He had experienced progressive dyspnoea on exertion associated with cough productive of whitish sputum for 6 months preceding this evaluation in April 1998. There was no past history or family history of tuberculosis. He did not keep any pets. He worked as a machinist in a machinery manufacturing wood-working tools for the past 10 years. His duties consisted of grinding the cutting surfaces of the cutting tools and welding the cutting parts of the tool.

Clinical examination was unremarkable. He was neither clubbed nor cyanosed. There was no significant lymphadenopathy. Auscultation of the lungs revealed normal

bronchovesicular breath sounds with no added sounds. Chest roentgenogram revealed bilateral reticulonodular infiltrates with honeycombing (Fig. 1). Full blood count, liver function tests, prostatic specific antigen, carcinoembryonic antigen and alphafetoprotein were within normal limits. Mantoux test was negative. Human immunodeficiency virus (HIV) serology was negative. Lung function tests showed disproportionate reduction in forced vital capacity (FVC) as compared to forced expiratory volume in one second (FEV<sub>1</sub>) and no significant reversibility following bronchodilator administration (Table I). The total lung capacity (TLC) was low normal with air trapping. High resolution computed tomography scan (HRCT) of the thorax showed predominantly diffuse interstitial thickening with some traction bronchiectasis (Fig. 2). Bronchoscopy revealed no endobronchial lesion.

---

\* Consultant

+++ Senior Consultant and Head

Department of Respiratory and Critical Care Medicine, Singapore General Hospital

\*\*\* Senior Consultant

Department of Pathology, Singapore General Hospital

\*\* Specialist Medical Advisor

Department of Industrial Health, Ministry of Manpower, Singapore

\*\*\*\* Research Assistant

+ Professor of Physics and Director of Centre for Nuclear Microscopy Research

++ Professor of Physics

Department of Physics, National University of Singapore

Address for Reprints: Dr Tan Keng Leong, Department of Respiratory and Critical Care Medicine, Singapore General Hospital, 1 Hospital Drive, Singapore 169608.

TABLE I: SERIAL PULMONARY FUNCTION TESTS

|                           | Initial<br>pre-<br>bronchodilator | Initial<br>post-<br>bronchodilator | 9 months    |
|---------------------------|-----------------------------------|------------------------------------|-------------|
| FEV <sub>1</sub> (L)      | 1.65 (54.3)                       | 1.75 (57.8)                        | 1.80 (59.9) |
| FVC (L)                   | 1.79 (47.4)                       | 1.83 (48.3)                        | 2.09 (55.1) |
| FEV <sub>1</sub> /FVC (%) | 91.8                              | 95.5                               | 86.6        |
| RV (L)                    | 2.19 (168.6)                      | -                                  | 1.84 (139)  |
| TLC                       | 4.10 (81.6)                       | -                                  | 4.08 (81.9) |
| RV/TLC (%)                | 53.5 (216)                        |                                    | 45.1 (220)  |
| KCO (mmol/min/kPa/L)      | -                                 | -                                  | 1.94 (109)  |

Figures in ( ) represent % of predicted normal values.

Bronchoalveolar lavage was negative for bacterial cultures, respiratory viruses, cytomegalovirus, herpes simplex virus, legionella, acid-fast bacilli, mycobacteria cultures, *Pneumocystis carinii*, fungal cultures and malignancy. Bronchoscopic lung biopsy showed chronic inflammation



Fig. 1. Chest roentgenogram showing bilateral reticulonodular infiltrates with honeycombing.



Fig. 3. Lung showing emphysema with focal fibrosis and interstitial pneumonitis (H & E x40).

and was negative for malignancy, fungi, acid-fast bacilli, granulomata and viral inclusion bodies. He underwent open biopsy of the right lung in May 1998. Histology of the lung showed diffuse emphysematous changes with focal fibrosis centred mainly around bronchovascular structures (Fig. 3). The alveolar spaces in the vicinity of these fibrotic foci were destroyed and the thickened inter-alveolar septae showed abundant infiltrates of pigment-laden macrophages, several of which were multinucleated (Fig. 4). Multinucleated giant cells are present within alveolar spaces as well as in the interalveolar septae. Polarising microscopy revealed presence of fine birefringent particles within the macrophages as well as loose within the inter-alveolar septae. The features are those of a patchy giant cell interstitial pneumonitis and non-specific interstitial pneumonia with fibrosis and excess macrophages. Histologically, these features are not diagnostic for a hard metal pneumoconiosis. There was no evidence of granuloma or malignancy and special stains were negative for fungi and acid-fast bacilli. Lung tissue for mycobacteria and fungal cultures were negative.

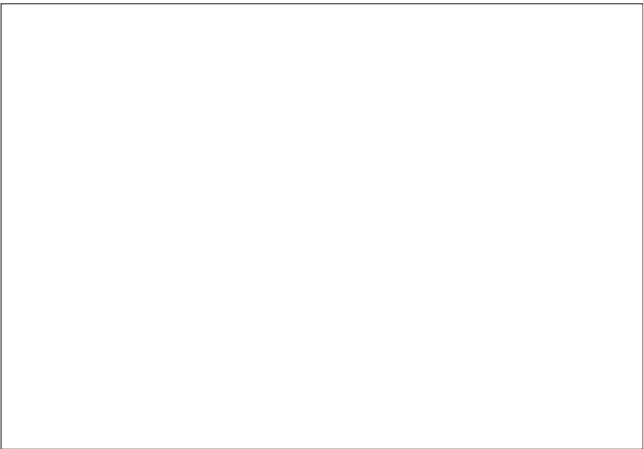


Fig. 2. Diffuse interstitial thickening confirmed on high resolution computed tomography scan of the thorax.



Fig. 4. Thickened inter-alveolar septa showing abundant pigment-laden macrophages. An occasional multinucleated macrophage is present (see arrow head) (H & E x400).

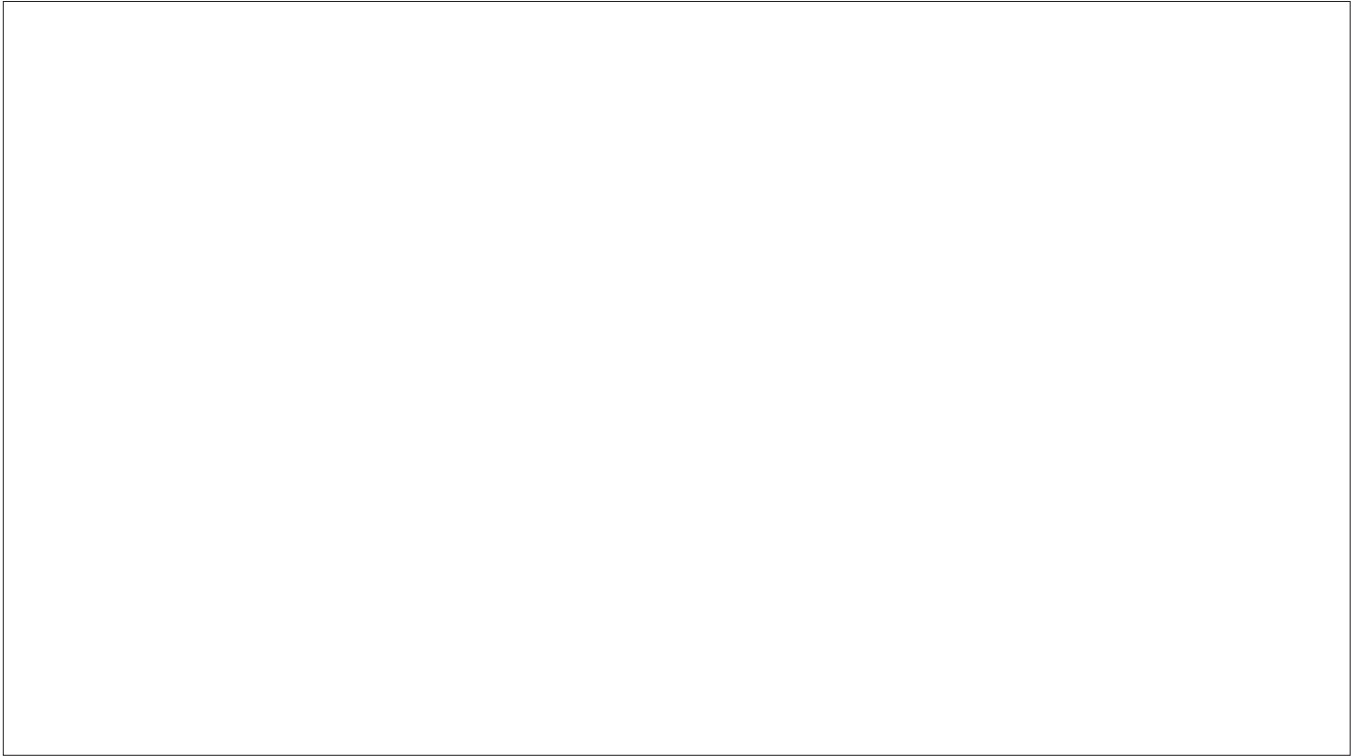


Fig. 5a. PIXE elemental maps from a 4 mm x 4 mm scan over a section of the patient's lung tissue.  
P: phosphorus; S: sulphur; Ca: Calcium; Ti: Titanium; Fe: Iron; W: Tungsten

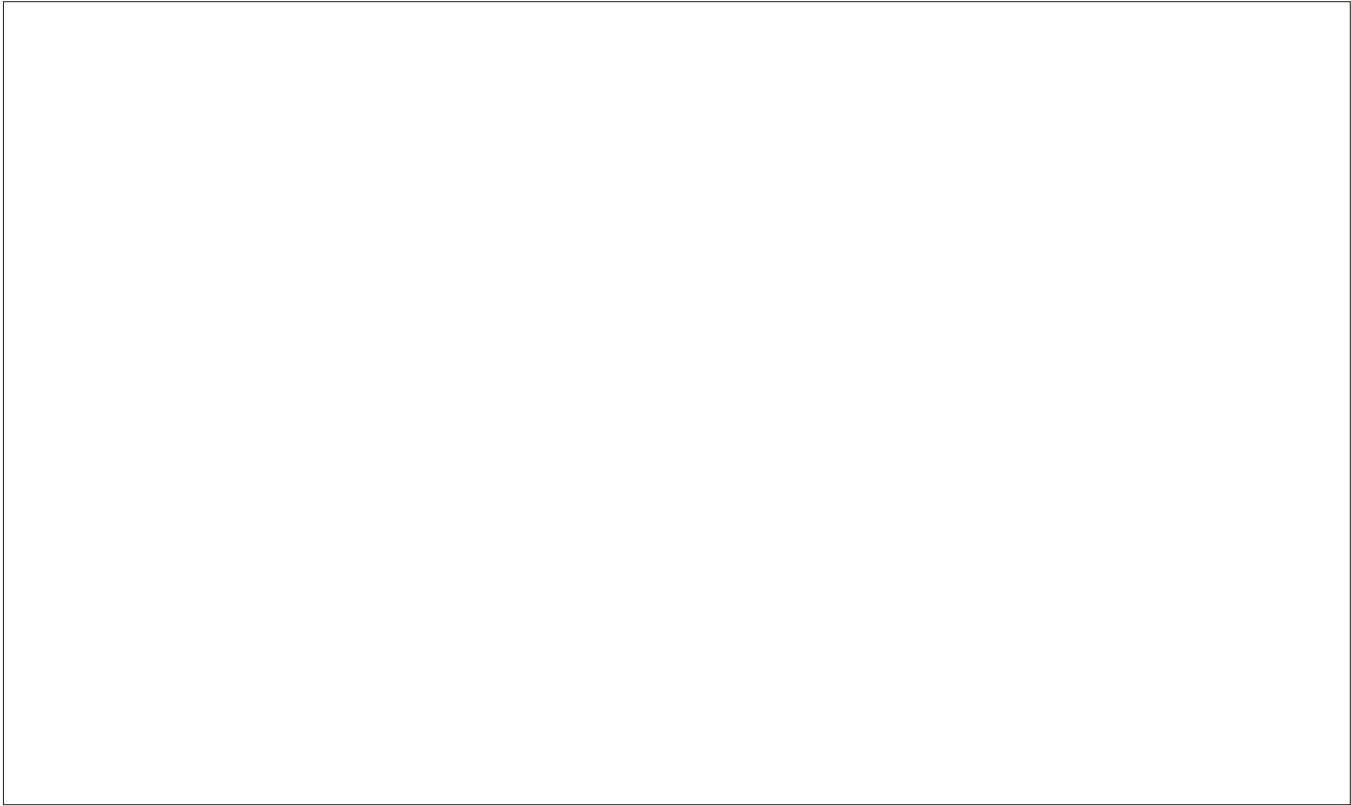


Fig. 7a. PIXE elemental maps from 400 µm x 400 µm scan over the tungsten rich area of the big scan. P: phosphorus; S: sulphur; Ca: Calcium; Ti: Titanium; Fe: Iron; W: Tungsten

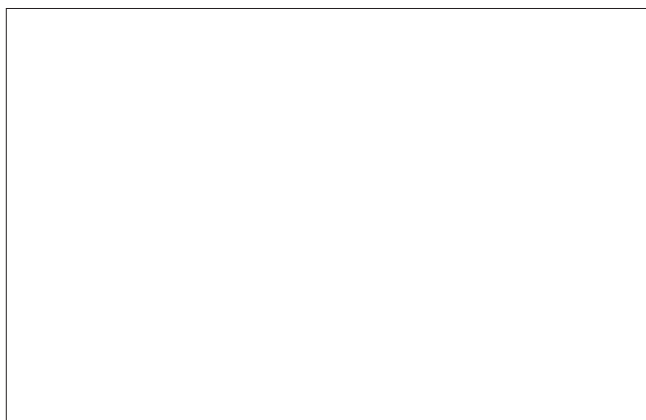


Fig. 5b. PIXE spectrum of the region referred to in Figure 5a. P: phosphorus; S: sulphur; Cl: Chlorine; K: Potassium; Ca: Calcium; Fe: Iron; W: Tungsten

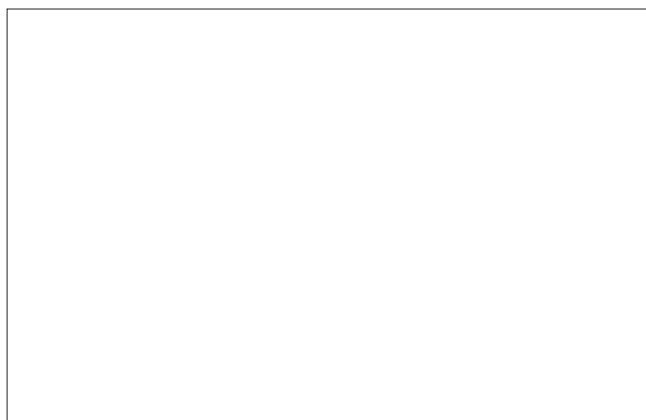


Fig. 7b. PIXE spectrum of the area referred to in Figure 7a. P: phosphorus; S: sulphur; Cl: Chlorine; K: Potassium; Ca: Calcium; Ti: Titanium; Fe: Iron; W: Tungsten

### Elemental Analysis

Particle induced X-ray emission (PIXE) analysis on the lung biopsy specimen confirmed the presence of tungsten and titanium. The elemental maps and corresponding PIXE spectrum (Fig. 5) indicate that there are several heavy metal elements present in the tissue at concentrations that are not found in normal lung tissue (Fig. 6). These include iron, tungsten and a small amount of titanium. In the higher magnification maps of Figure 7 (the area depicted by the squared region on Figure 5), the tungsten, iron and titanium profiles are similar, implying that these contaminant heavy metal elements are co-localised. Although the presence of cobalt was investigated, its concentration was found to be below the detection limit (approximately 100 ppm) under the experimental conditions employed in the measurements. The ratio of cobalt to tungsten in this region was estimated to be less than 1 part in 500.

He was diagnosed to have hard metal lung disease. Skin patch test for cobalt sensitivity was negative.

In March 1999, 10 months after the diagnosis of hard

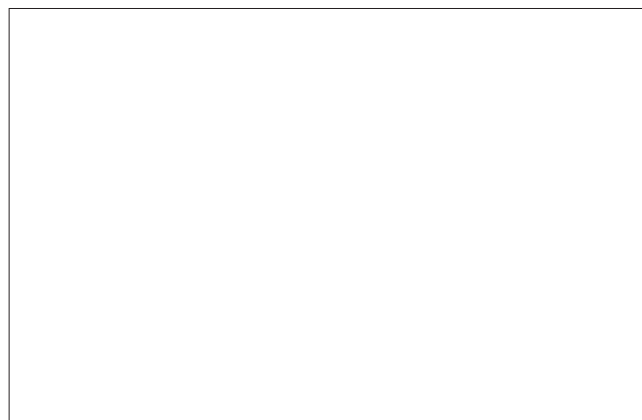


Fig. 6. PIXE spectrum of a 4 mm x 4 mm scan over normal lung tissue section. Zn: Zinc; Br: Bromine

metal lung disease, he presented with haemoptysis. His chest roentgenogram showed new patchy opacities over the right apical region. Bronchoscopy revealed haemorrhage in the right upper lobe. There were no endobronchial lesions. Bronchoalveolar lavage showed an acute inflammatory yield. Sputum and bronchoalveolar lavage were negative for bacterial cultures and acid-fast bacilli. He was started on antituberculous treatment comprising isoniazid, rifampicin and pyrazinamide based on the presumptive clinical diagnosis of tuberculosis. Sputum and bronchoalveolar lavage subsequently grew *Mycobacterium tuberculosis* complex resistant to streptomycin but sensitive to rifampicin, isoniazid and ethambutol. He completed 6 months of antituberculous treatment and repeat chest roentgenogram upon completion of treatment showed clearing of the right apical opacities and persistence of bilateral reticulonodular opacities.

### Occupational History and Exposure

He worked as a machinist in a factory which manufactures saw blades and cutters for woodworking machines for the past 10 years. He has no past or current exposure to silica or asbestos. There was no other significant exposure to dust or fumes in his previous jobs.

In his present workplace, tungsten carbide alloy is welded onto the cutting edges of the blades and cutters. His job is to grind the tungsten carbide edges. He does this for about 8 hours a day and his job has been the same for the past 10 years. The grinding is done with coolant being sprayed (wet machining). This serves as a lubricant but also helps to reduce the dust. However, mist containing tungsten carbide is generated in this process. The material safety data sheet of the alloy confirmed that it contained about 10% cobalt and 90% tungsten. We analysed two specimens of tungsten carbide alloy taken from the factory for the cobalt to tungsten (Co:W) ratio using the PIXE technique and found the ratios to be 6:100 and 34:100.

There is no local exhaust ventilation provided, as the process is not visibly very dusty. He started to use a dust respirator during grinding operations about one year ago after he started to have symptoms of cough and shortness of breath.

Personal cobalt-in-air monitoring over a full work shift showed that he was exposed to  $0.003 \text{ mg/m}^3$  of cobalt. The current occupational permissible exposure level (PEL) for cobalt is  $0.02 \text{ mg/m}^3$ .<sup>1</sup> End-of-shift urine cobalt was  $1.95 \text{ ug/L}$ . The current occupational biological threshold limit value is  $15 \text{ ug/L}$ .<sup>1</sup> His personal exposure to cobalt was about 15% of the current occupational exposure limits for cobalt. However, it is possible that exposures may have been higher in the past prior to the regular usage of dust respirator, when the volume of grinding work was higher and he had more overtime work to do.

#### *Screening of Other Exposed Workers*

There were another 5 workers potentially exposed to tungsten carbide from grinding or welding operations in the factory. The longest exposed was 15 years, followed by 8 years and then 2 years. The other two were exposed for less than 2 years. All the grinding operations were using coolant.

All 5 workers were interviewed, examined and had a chest X-ray examination and full lung function testing. None had any symptoms, signs or radiological evidence of hard metal lung disease. Their lung function tests were all within normal limits.

Personal cobalt-in-air levels measured on 3 of these workers ranged from  $0.004$  to  $0.008 \text{ mg/m}^3$  (20% to 40% of the PEL). The end-of-shift urinary cobalt levels ranged from not detected to  $20 \text{ ug/L}$ . Two of these workers had urinary cobalt levels which exceeded the biological threshold limit value (BTLV) of  $15 \text{ ug/dL}$ . However, this was likely to be due to skin contamination and ingestion of cobalt as there was a lot of direct skin contact with the coolant (contaminated with the tungsten carbide) and the cobalt-in-air levels were within the PEL.

#### *Implementation of Control Measures*

Although the cobalt-in-air levels were below the PEL, control measures were recommended to the factory for the protection of their workers. The factory installed local exhaust ventilation systems to reduce exposure to coolant mist. Dust respirators were issued to all workers involved in the grinding operations. Workers were to be educated on the hazards of tungsten carbide and the importance of good personal hygiene such as washing hands before meals and keeping their fingernails clean and short to minimise cobalt ingestion. The patient was transferred out permanently to another job which did not involve exposure to tungsten

cobalt dust. A medical surveillance programme was introduced for all the exposed workers. They were required to undergo an annual chest X-ray (full size) and urinary cobalt examination.

Other factories where workers may be exposed are currently being identified from the suppliers of tungsten carbide. A survey would be conducted to assess the hazard in these factories.

#### **Discussion**

To our knowledge, this is the first case of hard metal lung disease in Singapore. There have been no previous reports of hard metal lung disease locally and previous notification of the disease to the Department of Industrial Health. The manufacture of hard metal alloys began in Germany shortly after the first world war with the discovery of a metallurgical process for the production of hard metals. Hard metals, characterised by extreme hardness which is 90% to 95% to that of diamond, are typically alloys of tungsten carbide, titanium carbide and cobalt, to which small amounts of nickel, chromium, niobium, vanadium or molybdenum may be added.<sup>2</sup> The earliest report of pneumoconiosis due to hard metal was first described in Germany in 1940.<sup>3</sup> The initial observation described a diffuse, progressive pulmonary fibrosis associated with occupational exposure in the cemented tungsten carbide industry. Hard metal disease has subsequently been characterised in detail. Respiratory diseases occur in susceptible workers exposed to airborne dusts and aerosols containing cobalt. Occupations at risk include tungsten carbide producers, diamond polishers, grinders and sharpeners of tungsten carbide tools and metal coaters utilising powdered hard metal.<sup>4</sup>

The disease affects only susceptible subjects, and has varied clinical manifestation: (a) acute – rhinitis, asthma, acute pneumonitis (b) subacute – fibrosing alveolitis and (c) chronic – diffuse and progressive interstitial fibrosis.<sup>5,6</sup> While the disease may appear 6 months to 2 years after exposure, it is not uncommon to observe disease only after 20 to 25 years. It is notable that, as in this patient, the long latency period between the onset of exposure and clinical manifestation of disease that is typical of pneumoconioses such as silicosis and asbestosis, may not apply to hard metal disease.<sup>7</sup> Diffuse interstitial pulmonary fibrosis may progress to respiratory failure and death.<sup>8</sup> The fibrosis observed may regress after removal from exposure.

The diagnosis of hard metal lung disease is made on the basis of the occupational history, radiologic evidence of interstitial lung disease and where present, a bronchoalveolar lavage showing the typical giant cell alveolitis, comprising of up to 15% in the differential count.<sup>9</sup> The finding of giant cell interstitial pneumonia is considered almost

pathognomonic of hard metal disease. Similar multinucleated giant cells can be seen in viral, tuberculous and fungal infections and in foreign body reactions.<sup>10</sup> Hard metal lung disease may sometimes mimic the features of stage II sarcoidosis, when the hilar lymph nodes are enlarged secondary to the drainage of hard metals from the lung tissue via the lymphatics.<sup>11</sup> Although giant cells may be present as high as 13% in the bronchoalveolar lavage fluid of patients with sarcoidosis, the giant cells are typically of the Langhan's type and not foreign body type.<sup>12</sup> Hard metal pneumoconiosis can be present without giant cells being present.<sup>13</sup> Infective causes were ruled out by bacteriologic, serological and histological studies. X-ray microanalysis of the deposited dust particles in the fibrotic regions typically shows the presence of hard metal elements (tungsten, titanium, cobalt, nickel).<sup>14</sup>

In this patient, we primarily employed the PIXE technique to extract elemental information from sections of lung tissue. Nuclear microscopy is a relatively new, highly sensitive and quantitatively accurate analytical method, based around the interaction between a high-energy proton beam and the sample. Nuclear microscopy utilises a variety of ion beam techniques at sub-micron spatial resolutions to provide structural and quantitative elemental analysis of biological tissue down to the parts per million level of analytical sensitivity.<sup>15</sup> The elemental analysis was carried out using 2 MeV protons at the nuclear microscope facility of the Centre for Nuclear Microscopy Research, National University of Singapore.<sup>16,17</sup>

Cobalt, rather than other components of hard metal, is the causative agent of hard metal lung disease.<sup>18,19</sup> Individual susceptibility to cobalt is variable. Some exposed workers will develop hard metal disease after brief, low cobalt exposures, whilst others develop the disease after higher cobalt exposures of longer duration.<sup>4,11,20</sup> Our patient developed hard metal lung disease even though his current exposure to cobalt was only about 15% of the PEL. He was not the highest or longest exposed worker in the factory, although he was exposed for 10 years. The other workers did not show any evidence of the disease. Cobalt concentrations in biological samples are not significantly different in those who have the pathology and those who do not have and there is no correlation of dose and response at the tissue level.<sup>21</sup> Concentrations of cobalt in lung tissue have been reported as being low to absent in some patients and increased in others.<sup>10</sup> The variable results of the tissue concentrations of cobalt may be due not only to the different analytical methods employed, but also to the latent period between the last exposure and the time when tissue samples are obtained for analysis. Studies of incubated labelled metals and human lung homogenates have shown that cobalt is highly soluble, particularly in lung cytosol

and plasma, in comparison with tungsten. Tungsten is very insoluble and once present in tissue, usually remains.<sup>22</sup> An association of susceptibility to hard metal lung disease and the presence of glutamate 69 in HLA-DP beta chain was reported recently.<sup>23</sup>

The interstitial fibrosis may regress by removal from exposure at an early stage.<sup>24</sup> In some cases, the disease progresses despite discontinuation of exposure.<sup>7</sup> Treatment with corticosteroid may control the progression of fibrosis in some patients, but not in others.<sup>8,10,11</sup> Urinary cobalt serves as an index of exposure to hard metal dust and cobalt.<sup>25</sup> Cobalt patch test may be positive in patients with alveolitis or fibrosis.

In patients with chronic interstitial lung disease, there is a 4.5 times higher incidence of pulmonary tuberculosis.<sup>26</sup> Diffusely damaged lung increases the susceptibility to tuberculosis. We believe this predisposition underlies the association of hard metal lung disease with tuberculosis present in our patient.

## Conclusion

This case illustrates the importance of taking the occupational history in a worker who presents with chronic respiratory symptoms or a chest X-ray showing diffuse reticulo-nodular shadowing. In an older worker, one would have suspected silicosis or asbestosis and looked for past occupational exposure to silica or asbestos. In a younger worker presenting with chronic cough and shortness of breath, a diagnosis of hard metal lung disease should be excluded. A chest X-ray examination should be done and a detailed occupational history to look for work involving grinding or machining. Early confirmation of the diagnosis and removal from further exposure may prevent or delay the progression to respiratory failure and death. It would also result in the protection of other exposed workers.

## REFERENCES

1. TLVs and BEIs Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices. American Conference of Governmental Industrial Hygienists 1999. Cincinnati: American Conference of Governmental Industrial Hygienists, 1999.
2. Payne L R. Manufacturing processes: Hard metal. *J Soc Occup Med* 1976; 26:141-2.
3. Jobs H, Ballhausen C. Powder metallurgy as a source of dust from the medical and technical standpoint. *Vertrauenarzt Krankenkasse* 1940; 5:142-8.
4. Sprince N L, Oliver L C, Chamberlin R I, Eisen E A, Greene R E. Etiology and pathogenesis of hard metal disease. *Sci Total Environ* 1994; 150:187-96.
5. Bruckner H C. Extrinsic asthma in a tungsten carbide worker. *J Occup Med* 1967; 9:518-9.

6. Coates E O Jr, Watson J H. Diffuse interstitial lung disease in tungsten carbide workers. *Ann Intern Med* 1971; 75:709-16.
7. Fischbein A, Luo J C, Solomon S J, Horowitz S, Hailoo W, Miller A. Clinical findings among hard metal workers. *Br J Ind Med* 1992; 49: 17-24.
8. Ruokonen E L, Linnainmaa M, Seuri M, Juhakoski P, Soderstrom K O. A fatal case of hard metal disease. *Scand J Work Environ Health* 1996; 22:62-5.
9. Davidson A G, Haslam P L, Corrin B, Coutts II, Dewar A, Riding W D, et al. Interstitial lung disease and asthma in hard-metal workers: bronchoalveolar lavage, ultrastructural, and analytical findings and results of bronchial provocation test. *Thorax* 1983; 38:119-28.
10. Cugell D W. The hard metal diseases. *Clin Chest Med* 1992; 13:269-79.
11. Sjogren I, Hillerdal G, Andersson A, Zetterstrom O. Hard metal lung disease: importance of cobalt in coolants. *Thorax* 1980; 35:653-9.
12. Constabel U, Matthys H, Guzman J, Freudenberg N. Multinucleated cells in bronchoalveolar lavage. *Acta Cytol* 1985; 29:189-90.
13. Ohori N P, Sciurba F C, Owens G R, Hodgson M J, Yousem S A. Giant cell interstitial pneumonia and hard metal pneumoconiosis. *Am J Surg Pathol* 1989; 13:581-7.
14. Rizzato G, Lo Cicero S, Barberis M, Torre M, Pietra R, Sabbioni E. Trace of metal exposure in hard metal lung disease. *Chest* 1986; 90:101-6.
15. Watt F, Grime G W. The high energy ion microprobe. In: Johansson S A E, Campbell J L, Malmqvist K G, editors. *Particle Induced X-Ray Emission Spectrometry*. New York: Wiley, 1995:101-65.
16. Watt F, Orlic I, Loh K K, Sow C H, Thong P, Liew S C, et al. The National University of Singapore nuclear microprobe facility. *Nucl Instr Meths B* 1994; 85:708-15.
17. Watt F, Osipowicz T, Choo TF, Orlic I, Tang SM. Nuclear microprobe analysis and imaging: current state of the art performance. *Nucl Instr Meths B* 1998; 136:313-7.
18. Miller C W, Davis M W, Goldman A, Wyatt J P. Pneumoconiosis in the tungsten carbide tool industry. *Arch Ind Hyg Occup Med* 1953; 8: 453-65.
19. Demedts N, Gheysens B, Nagels J, Verbeken E, Lauweryns J, Van den Eeckhout A, et al. Cobalt lung in diamond polishers. *Am Rev Respir Dis* 1984; 130:130-5.
20. Kitamura H, Kitamura H, Tozawa T, Kimula Y. Cemented tungsten carbide pneumoconiosis. *Acta Pathol Jpn* 1978; 28:921-35.
21. Chiappino G. Hard metal lung disease. In: Stellman J M, editor. *Encyclopaedia of Occupational Health and Safety*. 4<sup>th</sup> ed. Vol I. Geneva. International Labour Office, 1998:10.63-10.66.
22. Edel J, Sabbioni E, Pietra R, Rossi A, Torre M, Rizzato G, et al. Trace metal lung disease: *In vitro* interaction of hard metals with human lung and plasma components. *Sci Total Environ* 1990; 95:107-17.
23. Potolicchio I, Mosconi G, Forni A, Nemery B, Sequhizzi P, Sorrentino R. Susceptibility to hard metal lung disease is strongly associated with the presence of glutamate 69 in HLA-DP beta chain. *Eur J Immunol* 1997; 27:2741-3.
24. Hartung M, Schaller K H, Brand E. On the question of the pathogenic importance of cobalt for hard metal fibrosis of the lung. *Int Arch Occup Environ Health* 1982; 50:53-7.
25. Linnainmaa M, Kiilunen M. Urinary cobalt as a measure of exposure in the wet sharpening of hard metal and stellite blades. *Int Arch Occup Environ Health* 1997; 69:193-200.
26. Shachor Y, Schindler D, Siegal A, Lieberman D, Mikulski Y, Bruderman I. Increased incidence of pulmonary tuberculosis in chronic interstitial lung disease. *Thorax* 1989; 44:151-3.