

DIFFERENT COURSE OF SILICOSIS IN FOUR BROTHERS OF ONE FAMILY

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Abstract

Silicosis remains a common occupational respiratory disease. Even in this era of highly sophisticated hygiene in European countries, new occupational cases of silicosis continue to be reported. Four cases of silicosis which developed after a relatively short occupational exposure to respirable silica among the members of one family are described. Four young men worked illegally abroad in mining in one of European countries. All of them were employed together in the same working conditions. One of the brothers died due to the acute form of the disease (lipoproteinosis). Two of the brothers suffered from simple nodular silicosis, and the fourth brother developed very early nodular silicosis and small airway dust disease. A one year follow-up revealed moderate/severe worsening of the disease in all surviving brothers.

Key words:

Bronchoscopy, Pneumoconiosis, Silicosis

INTRODUCTION

Silicosis is the oldest of the pneumoconioses, dating back to the times of Hippocrates and the ancient Egyptians. Despite being recognized for centuries as a preventable disease, both the classical nodular silicosis and the rapidly fatal acute form, silicoproteinosis continue to be diagnosed [1,2].

Respirable silica is a fibrinogenic dust [3]. Occupational exposure to airborne particles of respirable silica occurs in numerous industries and occupations and has been associated with work in mining, quarrying, tunneling, construction, sandblasting, masonry work, foundry operations,

glass manufacture, in the production of ceramics, pottery, cement, concrete etc. [4]. Although silicosis typically occurs after a long exposure to silica, some individuals developed silicosis after a relatively short time [5]. Only a small proportion of workers exposed to silica dust contract this disease [6].

Due to non-specific clinical symptoms and non-recognizable shadows on roentgenogram in the early phase of the disease, silicosis may fail to be recognized and tends to be underestimated [5,7].

We have described four cases of silicosis developed after a relatively short period of occupational exposure to

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respirable silica in the members of one family. One of the four brothers died and the diagnosis of acute silicosis (lipoproteinosis) was established only after autopsy. Three other brothers had features of chronic, accelerated and very early nodular silicosis. They are alive and followed-up.

CASE REPORT

Previously healthy four young men, brothers of one family, worked illegally abroad in one of European countries in mining between 2003 and 2007. Men No. 1, No. 2, No. 3 and No. 4 were 26, 29, 22 and 20 years old, respectively. All of them were employed together in the same working conditions. However, work duration was different: 36 months, 48 months, 24 months, and 3 months, respectively. All of them were smokers with the smoking status of 12, 30, 2.5, and 3 pack years, respectively. They did not take street drugs or medicines.

They reported working in a private mine, which was not provided with effective ventilation, about four hours per day. Due to low level of education and language barrier, they didn't know details of their actual mining job. However, a major part of their occupational activity was tunneling in solid and shelf-like rock layers containing silica. They claimed that no general dust control was provided at the workplace, but relevant reliable data is not

available. They had respirators, but with respirator on the head, it was very difficult to breathe there; for this reason they did not wear the respirators during all of their employment.

One of the brothers (patient No. 1) suddenly experienced breathlessness, he returned home and applied for physician's consultation. However, the patient became worse and he died in other hospital due to progressing respiratory trouble. The final clinical diagnosis was: acute respiratory failure of unknown etiology. Ante mortem chest X-ray indicated multiple large and small nodules, and

Table 1. Results of pulmonary function testing of surviving patients on first admission and one year later

Indices	Patient No. 2		Patient No. 3		Patient No. 4	
	2007	2008	2007	2008	2007	2008
FVC, % pred	104	78	59	53	105	85
FEV ₁ , % pred	74	55	48	42	80	66
FEV ₁ /FVC	62	59	68	67	65	66
VC, % pred	98	78	57	50	100	83
TLC, % pred	NA	99	NA	63	NA	89
RV, % pred	NA	164	NA	105	NA	104
DLCO, % pred	69	54	56	56	84	63

FVC — forced vital capacity, FEV₁ — forced expiratory volume in one second, VC — vital capacity, TLC — total lung capacity, RV — residual volume, DLCO — diffusing capacity of carbon monoxide. Pred — predicted, NA — not available.

Table 2. Results of chest X-ray and lung computed tomography scan examination on first admission and one year later

Patient	Chest X-ray		Computed tomography	
	2007	2008	2007	2008
No. 1	Multiple large and small nodules, patchy pulmonary oedema	NA	NA	NA
No. 2	Multiple small nodules	Worsening: more nodules	Multiple small nodules, pleural thickening, lymphadenopathy, some foci of pneumofibrosis	Worsening: more pneumofibrotic lesions
No. 3	Multiple small nodules	Worsening: more nodules	Multiple small nodules, pleural thickening, lymphadenopathy, few foci of pneumofibrosis	Severe worsening: massive fibrosis, left-sided pneumothorax
No. 4	Normal	Normal	Few small nodules, pleural thickening, lymphadenopathy, some foci of pneumofibrosis in the upper lobes	Same as in 2007

NA — not available (patient died).



Fig. 1. No. 1 patient's chest radiograph showing tumoral form of silicosis, massive progressive pneumofibrosis in both lungs.



Fig. 2. No. 3 patient's initial chest radiograph showing multiple small nodules in both lungs.

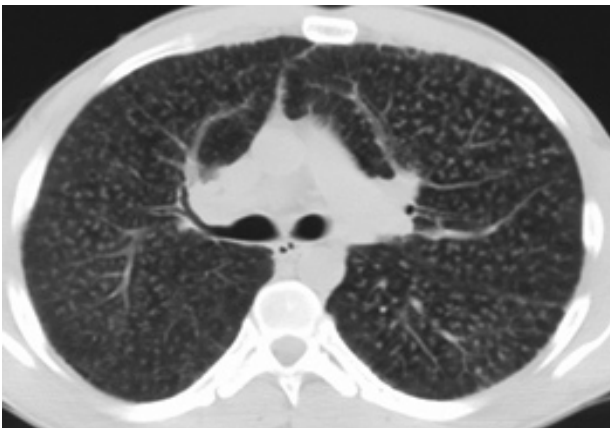


Fig. 3. No. 3 patient's initial chest CT scan showing multiple small nodules.

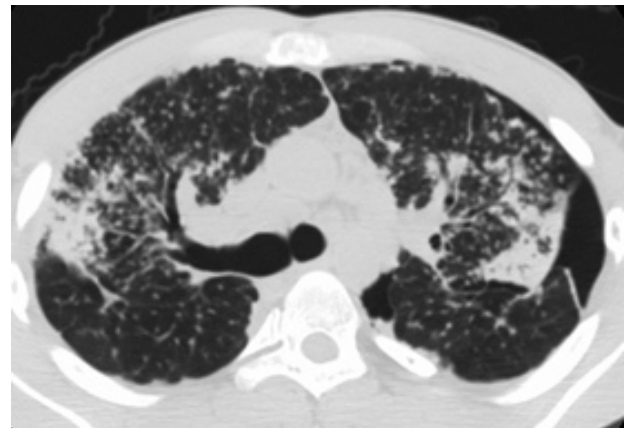


Fig. 4. No. 3 patient's chest CT scan one year later showing multiple small nodules, massive progressive pneumofibrosis, pleural thickening and left-sided pneumothorax.

patchy pulmonary oedema (Fig. 1). Autopsy revealed acute silicosis (lipoproteinosis). Examination of necropsy specimens showed multiple silicotic nodules. Alveoli spaces were dilated and filled with lipoproteinaceous materials. Hyaline membrane was not found. Examination for infectious agents was negative (we are not able to show necropsy photograph because, due to legal considerations, autopsy was performed in hospital of another city).

Three other brothers were feeling quite well, but they stopped working in the mine and also returned home. After their brother had died they were insistently invited to

examine the respiratory function. They were examined in our clinic. All surviving brothers reported cough, sputum production and dyspnoea on moderate exertion. Auscultation of the lung revealed no rales (patient No. 2), fine rales (patient No. 3) and wheeze (patient No. 4). All of them underwent chest X-ray, computed tomography (CT), respiratory function tests, bronchoalveolar lavage (BAL) and bronchoscopic lung biopsy. Data of pulmonary function examination are presented in Table 1. Findings of the chest X-ray and CT examination are shown in Table 2 and Figures 2–4.

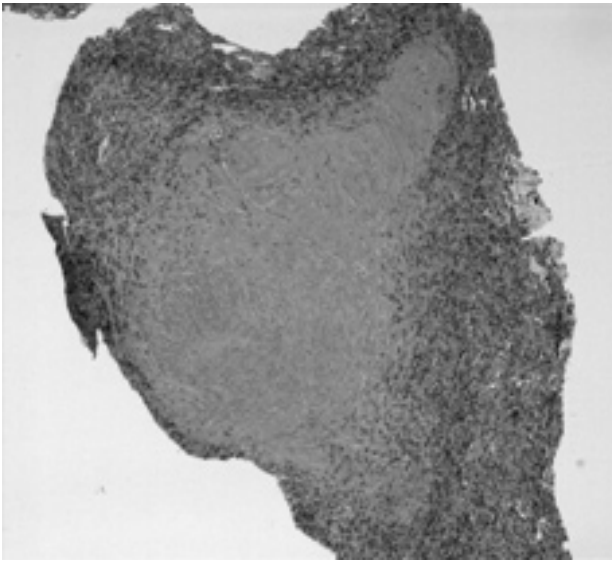


Fig. 5. No. 3 patient's bronchoscopic lung biopsy specimen. Well-demarcated nodule composed of concentrically arranged collagen bundles and rim of histiocytes (HE stain, $\times 40$).

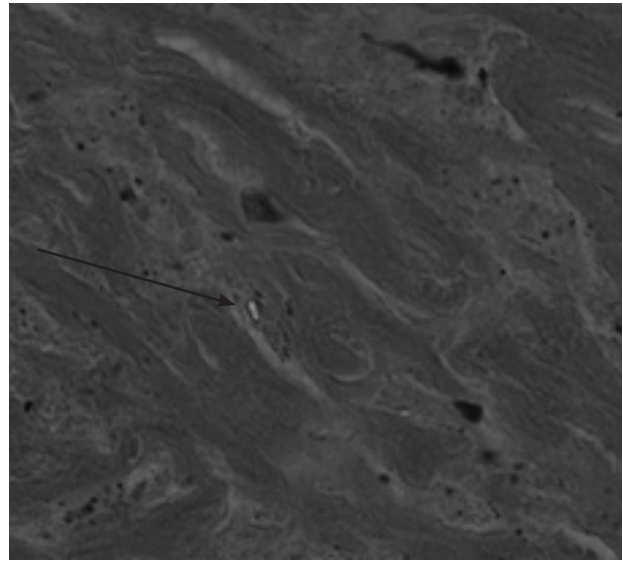


Fig. 6. No. 3 patient's bronchoscopic lung biopsy specimen. Weakly birefringent silica particles (arrow) are seen in polarized light within the silicotic nodule (HE stain, $\times 400$).

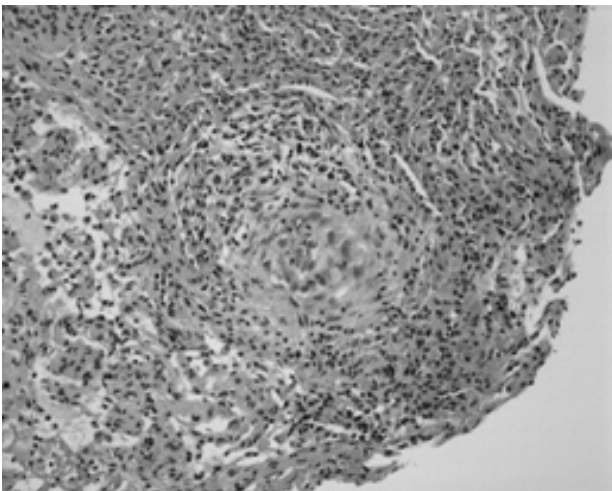


Fig. 7. No. 4 patient's bronchoscopic lung biopsy specimen. Early silicotic nodule composed of fibroblasts and histiocytes (HE stain, $\times 100$).

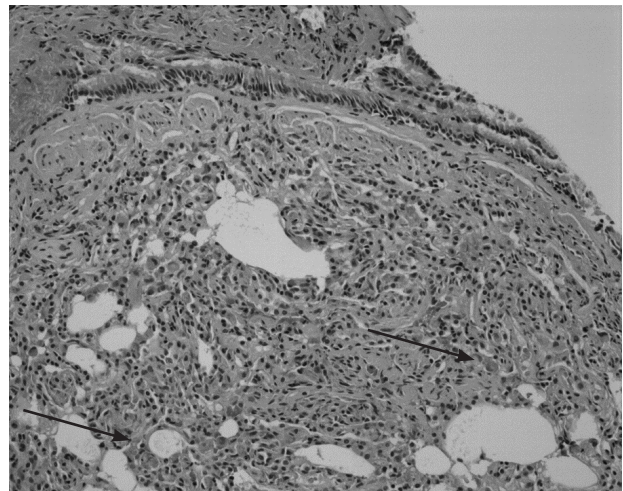


Fig. 8. No. 4 patient's bronchoscopic lung biopsy specimen. Respiratory bronchiolitis: pigmented macrophages (arrows) and respiratory bronchiole (HE stain, $\times 100$).

Examination of the material of the bronchoscopic lung biopsy revealed typical nodular silicosis (Patients No. 2 and No. 3, Figures 5 and 6), very early nodular silicosis and dust small airways disease (Patient No. 4, Fig. 7 and 8). Mycobacterium tuberculosis and fungi were not found in biopsy specimens or BAL fluid.

Treatment with bronchodilators was prescribed to all of the brothers. We hesitated to prescribe corticosteroids due to the high risk of reactivation of tuberculosis (the prevalence of latent and active tuberculosis in our country

is high). The patients were advised to stop smoking, but they refused to do that.

During the follow-up visit one year later all of these patients underwent computed tomography (CT) and pulmonary function testing (PFT). All three brothers felt quite well, but PFT revealed severe worsening of respiratory function in No. 2 and No. 4 patients, as well as moderate worsening in patient No. 3. CT scan of patient No. 3 showed massive progressive pneumofibrosis and he suffered two episodes of spontaneous pneumothorax

in recent year (Fig. 4). For this patient, surgical pleurectomy was recommended to prevent recurrence of pneumothorax.

DISCUSSION

Silicosis is usually classified into acute, subacute/accelerated and chronic simple silicosis [8]. However, different authors vary considerably in their description of each form of silicosis [1,3,4,6–9]. Thus, it was not easy to assign each of the brothers to a specific form of silicosis. There is no doubt that the young man who had died had acute silicosis. It is interesting to note that he worked and smoked not longer than his brother (patient No. 2). Probably he was overexposed to respirable silica. Death cases among young adults are likely to reflect more intense and recent exposure [4]. In acute disease, silica induces severe inflammation, extensive apoptosis and formation of protein-rich oedematous fluid in the lung, which severely impair the respiratory function [3,10–12]. Acute silicosis is usually fatal [9].

On the first admission, all of three surviving brothers had symptoms of simple (chronic non-complicated) disease — small nodules in the lung [13], small foci of fibrosis, mediastinal lymphadenopathy [14] without calcifications (yet). However, significantly decreased indices of respiratory function (patients No. 2 and No. 4) in the absence of exposure to silica dust for 1.5 years and two episodes of spontaneous pneumothorax (No. 3 patient) are features of accelerated silicosis. Patient No. 3 progressed from simple to complicated silicosis with progressive massive fibrosis. Large conglomeration of the numerous micro nodules into masses greater than 1 cm was seen at the follow-up examination. Spontaneous pneumothorax, which is observed in rapidly progressive forms of silicosis, may be related to progressive decline in the lung function [15].

It is not easy to explain the difference in the course of the disease between the four brothers. It is likely that different amount of silica was inhaled. The brothers consistently refused to wear respirators in the mining tunnel (because the respirators made breathing even more difficult). It is not possible now to calculate actual

individual working time without respirator. It is not realistic to estimate real amount of inhaled silica from the samples collected during bronchoscopic lung biopsy. However, it is unlikely that smoking status might significantly influence the course of the disease because, of all surviving brothers, Patient No. 3, who had the most severe progression of the disease, had had the shortest history of smoking. Thus, a reasonable explanation is that the brothers inhaled different amounts of mixed dust.

There are two distinct types of silica found in nature, crystalline and amorphous. The differential ability of amorphous and crystalline silica to induce fibrosis is probably related to the physical and inflammatory properties of the silicas [16]. Several possibilities exist how silica induces fibrotic changes in the lungs. Silica incites pulmonary inflammation. When inhaled crystalline silica particles are ingested by alveolar macrophages, the macrophages are activated and damaged, resulting in ongoing injury and ultimately leading to the development of fibrosis. However, silica dust may evoke the production of mediators which potentially cause fibroblast proliferation and increased matrix production even in the absence of inflammatory cells. Fibrosis leads to distortion of the normal lung architecture and disruption of the normal physiological processes of the lung [16,17].

Amorphous silica is more soluble and is more easily cleared from the lungs. Crystalline silica particles are far larger and less easily removed from the lung, the epithelial damage they cause is more persistent, whereas macrophages that ingest crystalline silica are activated and damaged. This persistent irritation could allow the establishment of a profibrogenic milieu [16]. Usually, accumulation and deposition of respirable silica mineral containing particles within the lung produce a chronic lung disease characterized by granulomatous and fibrotic lesions [18]. However, co-existing chronic interstitial pneumonia with honeycombing has been reported [19,20]. Crystalline but not amorphous silica may cause genotoxic effects in alveolar epithelial cells, despite a high degree of inflammatory-cell response after subchronic exposure to both types of silica [21].

We had no chance to evaluate the situation in the workplace of our patients as they had been working illegally abroad. However, all the brothers worked under the same conditions. Although they have had different exposure period, their „resistance“ and „susceptibility“ [6] to dust was similar. The risk of silicosis is strongly related to cumulative exposure to silica dust [22]. However, progression of the disease may depend on the activity of individual antioxidative, antiapoptotic, and anti-inflammatory enzymes [23].

Silica exposure is associated with restrictive or mixed obstructive-restrictive features [2,9,24]. Obstructive changes are found in smokers [25]. We have found mixed obstructive-restrictive features in our patients. Mineral dust airway diseases lead to progressive airway obstruction and restrictive functional deficit. The obstructive functional impairment is caused by the synergetic effect of chronic dust inhalation and cigarette smoking. However, no correlation between the profusion of nodules and functional parameter was found [26].

The complicating effects of cigarette smoking, exposure to mixed dust and other harmful agents in the workplace, and presence of other lung diseases, such as chronic bronchitis, emphysema and tuberculosis lead to a wide variation of clinical and functional responses [9].

All our reported patients are low educated and come from a low-income family. These factors, in conjunction with latent period between exposure and the occurrence of initial clinical symptoms, led to delayed diagnosis of silicosis and more severe disease [15]. Our patients are additionally handicapped in the sense that they are not authorized to receive any indemnity.

There is no specific treatment for silicosis. Management of the disease involves prevention of progression and reducing the risk of complications [8]. Only partial [24] and transient [27] improvement of acute silicosis may be achieved by corticosteroid therapy.

Silicosis may highly increase the risk of lung cancer [28,29] and tuberculosis [30], especially in resource-limited countries [31]. Patients should be carefully followed-up. A recently published study [32] indicates that the exposure

limit for crystalline silica valid currently in many countries is not sufficiently protective against silicosis mortality.

In conclusion, it must be stated that nowadays silicosis continues to cause death and disability. Work in similar polluted workplace air conditions may lead to different course of silicosis. Even a very short duration of the exposure to silica dust may cause typical changes in the lungs and result in rapid deterioration of the respiratory function, even though silica exposure is stopped. There is still a great need for effective tools of disease prevention and for increasing the awareness of the problem among concerned people.

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