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Secondary spontaneous pneumothorax in rapidly progressive forms of silicosis: characterization of pulmonary function measurements and clinical patterns

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Background: A secondary spontaneous pneumothorax is a complication of an underlying pulmonary disease. In recent years, there have been only a few scattered reports of patients with silicosis also having a pneumothorax. Silicosis, a form of disabling pulmonary fibrosis, is a well-known occupational disease resulting from high-level exposure to silica or silica-containing dusts. The objective of the present study was to elucidate any associations between the occurrence of a pneumothorax, and pulmonary function tests and clinical observations performed prior to the pneumothorax; these two factors may be predictors for a pneumothorax among workers exposed primarily to silica-containing respirable dust. **Methods**: A diagnosis of silicosis was made on several factors: silica dust exposure, appropriate interval of time after exposure, clinical findings, pulmonary function tests and chest radiological findings. A checklist was designed for collecting data of occupational history, respiratory signs, and symptoms from onset of dust exposure to the occurrence of a pneumothorax. Spirometery was conducted in accordance to the recommendations of standard protocols and guidelines posited by the American Thoracic Society. Autopsies were performed in three cases where the patient had suffered a pneumothorax due to silicosis. Mann–Whitney *U*-tests and Fisher's exact tests were used to determine any associations between pneumothorax and predictor factors. **Results**: An association between a progressive decrease in pulmonary function test values and a pneumothorax was observed. The occurrence of a pneumothorax was associated with complaints of pleuretic chest pain, resting dyspnea, respiratory distress, paroxysmal nocturnal dyspnea, orthopnea and crackle. **Conclusion**: A characteristic decline in pulmonary function test values and the severity of respiratory impairment may facilitate the occurrence of a pneumothorax in silicosis. *Toxicology and Industrial Health* 2007; **23:** 125–132.

Key words: *pneumothorax; pulmonary function test; silica; silicosis*

Introduction

A pneumothorax is defined as the entry of air into the pleural space (Light, 1995). Combulsier described the pathophysiology of a pneumothorax in 1747, recognizing that the decrease in pulmonary function was a result of lung compression due to air in the pleural space (Sadikot *et al.*, 1997). A spontaneous pneumothorax can be divided into either a primary or secondary class description. A primary spontaneous pneumothorax is the idiopathic variety that can occur in healthy persons. A secondary spontaneous pneumothorax is a complication of an underlying disease (Gupta *et al.*, 2000; Sahn and Heffner, 2000). In recent

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years, there have been only a few scattered reports where patients with silicosis developed a pneumothorax (Kawano *et al.*, 2002; Kobashi *et al.*, 2003; Rao and Rau, 1993). Silicosis is caused by the inhalation of very fine particles of free silica dust, and it is perhaps the oldest occupational disease. It has likely existed since the Paleolithic period, and Hippocrates and Pliny have both referred to this specific disorder (Sherson, 2002; Zenz *et al.*, 1994). Silicosis is a disabling and non-reversible disease that occurs in chronic, accelerated and acute forms (Baxter *et al.*, 2000). Acute and accelerated silicosis, rapidly progressive forms of the disease, are rare in the world (Cohen *et al.*, 1999; Purohit *et al.*, 1992; American Thoracic Society, 1997; Marachiori *et al.*, 2001; Sundaram *et al.*, 2002). Accelerated silicosis takes place after 5–10 years of exposure to high concentrations of crystalline silica whereas the acute form is due to a few weeks to 5 years exposure to very high concentrations of the same dust (NIOSH, 2002). Symptoms of silicosis include shortness of breath, wheezing, chest tightness and cough, although initially there may be no symptoms. In addition to causing silicosis, inhalation of crystalline silica particles has been associated with other diseases such as lung cancer and obstructive pulmonary disease, even in the absence of radiological silicosis (Finkelstein, 2000; Hnizdo and Vallyathan, 2003). Although a precise silicosis diagnosis is difficult, it is usually established on the basis of a medical examination that includes history of silica dust exposure coupled with chest radiological abnormalities, but severity of impairment must also be assessed by a pulmonary function test (PFT) (Harber *et al.*, 1996).

Epidemiological reports of acute or accelerated silicosis are rare and only a few cases have been reported (Cohen *et al.*, 1999; Purohit *et al.*, 1992; American Thoracic Society, 1997; Marachiori *et al.*, 2001). The Occupational Medical Center of Urmia Medical Sciences University is the only reference center for occupational and work-related diseases in the West Azerbaijan province that was accredited by the Iranian Ministry of Health in 2000. At this centre, we registered 21 self-admitted cases of acute and accelerated silicosis among baggers of silica powder in unregulated stone grinding facilities between September 2000 and March 2006. During these years, 10 case patients died, seven experiencing a secondary spontaneous pneumothorax. In order to elucidate the role of both PFT and clinical findings as possible predictive factors for secondary spontaneous pneumothorax in rapidly progressive forms of silicosis, we review here the PFT values and clinical and pathological evidence related to the development of a secondary spontaneous pneumothorax in silica dust-exposed workers.

Materials and methods

The current retrospective study was approved by the Urmia Medical Sciences University Occupational Medical Center Review Board. Subjects were retrospectively identified from the pneumoconiosis registry program at the clinic. The clinic is dedicated to keeping records of patients with occupational diseases, mainly those with silica-related pneumoconiosis. The sampling frame was census, and the selection mode of our case and control groups was carried out based on radiological evidence of spontaneous pneumothorax in silicosis patients.

Patient procedures

In each subject's first visit, a diagnosis of silicosis was made on the basis of an unequivocal history of substantial silica dust exposure, an appropriate interval of time after exposure, clinical findings, PFT values and chest X-ray findings, all in accordance with criteria described by the International Labor Organization (ILO) as international standard classifications for radiographs of pneumoconiosis. We designed a checklist, collecting data in accordance with occupational history, complaints, symptoms and clinical findings. Checklist items for occupational history included the precise nature of present and previous occupations and work duration in any dusty environment. Complaints, symptoms and clinical findings were registered on the first visit. Any new respiratory symptoms and signs were recorded during periodic follow-ups that took place within 5 years. In those who experienced a secondary spontaneous pneumothorax, we recorded any clinical observations found in their medical documents from previous follow-ups that took place prior to the occurrence of a pneumothorax. All patients were followed and evaluated uniquely by an occupational medicine specialist with an interest in occupational lung diseases and certified in Reading Thoracic

Radiographs (according to the ILO 2000 International Classification of Radiographs of Pneumoconiosis).

Body mass index (BMI) was calculated by dividing the patient weight in kilograms by the patient height in metres squared, based on the most current data prior to the occurrence of a pneumothorax. Height was measured while the subject stood erect on a flat platform looking straight, in a forward direction. Body weight was measured with light clothing on but without shoes, using a calibrated bathroom scale.

In each periodic subject follow-up, spirometery was performed by means of a ZAN 530 (Messgerate GmbH, Germany). All measurements were conducted in accordance to recommendations for standard protocols and guidelines posited by the American Thoracic Society (ATS). Each subject performed up to eight repeated measurements until three acceptable forced expiration manoeuvres were obtained. The best value was defined as the highest of the three readings. All forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) values were corrected to body temperature and pressure saturated conditions by twice-daily recordings of room temperature and barometric pressure. Each value of FVC, forced expiratory volume in 1 s (FEV1, FEV1/ FVC ratio, peak expiratory flow (PEF) and forced expiratory flow from 25–75% of vital capacity (FEF 25–75%) was calculated using standard reference prediction equations. Then, disability evaluations were performed in accordance to the American Medical Association (AMA) Classes of Respiratory Impairment. Since the PFT performance was contraindicated in patients who experienced a pneumothorax, we selected the most recent PFT from their previous follow-ups.

Finally, we assessed the chest X-ray films of each subject, which were taken annually in previous periodic follow-ups. The assessments included an investigation of criteria that was coded in the ILO scheme. Review of chest radiographs was performed consensually by a B-reader certified in ILO classification of pneumoconiosis and experienced in the national board certification of occupational physicians. The B-reader certification is not required in our country for official assessment of pneumoconiosis. Findings of chest radiographs were confirmed by computed tomography (CT) of the lungs.

An official document was submitted for each patient to the National Committee of Occupational Health for medico-legal confirmation of the diagnosis. Autopsies were carried out in three cases, chosen randomly from the patient study population, 24 h after death.

Occupational exposure

In facilities where patients were employed, 15 workplaces were selected for the assessment of environmental monitoring of silica particles. To measure concentrations of silica particles in the ambient air, an air sampler pump (Model 224–30, SKC) connected to a mini-cyclone (SKC), and glass filters was used. Gravimetric analysis was performed to differentiate respirable dust from non-respirable. X-ray diffraction was then used to determine inorganic compounds and their crystalline structures.

Statistical analysis

Differences between the two groups (silicosis with pneumothorax and silicosis without pneumothorax) in both age and silica exposure duration were assessed by the use of the independent *t*-test. The Mann–Whitney *U*-test was used to determine associations between values of FVC, FEV1, FEV1/FVC and FEF 25–75%. The Fisher's exact test was used to determine associations between pneumothorax and clinical predictor factors.

Results

Characteristics of the study population

All study subjects worked at the same stone grinding workplace as seasonal migrant workers; all do not have any prior reported silica exposure. Patients described the working environment as being heavily dusted, with no provision for engineering controls or exhaust ventilation. Total work period was 12–14 h a day for 1–5 consecutive years. All subjects were male and non-smokers with the youngest being 20 and the oldest 79; 18 (86%) of the participants were younger than 40. None of the workers used adequate respiratory protective devices. The mean exposure duration in patients with pneumothorax was 2.14 ± 1 years, and in those without pneumothorax, 2.86 ± 1.2 years. There was a significant difference between the two groups in the

Table 1. Comparison of age, exposure–diagnosis span and exposure duration between the two groups

Variable (per years)	Silicosis with pneumothorax (mean ± SD)	Silicosis without pneumothorax (mean ± SD)	*T*	*P*-value
Age	26.43 ± 5.85	34.50 ± 17.7	1.22	0.073
Exposure duration	2.14 ± 1	2.86 ± 1.2	1.3	0.19

exposure–diagnosis span and no significant differences in age and exposure duration (see Table 1).

Work place characteristics

The characteristics of the workplace where silicosis occurred included: (1) failure to substitute less toxic raw material for the toxic substance; (2) lack of environmental monitoring; (3) inadequate engineering controls and work safety practices; (4) inadequate respiratory protection for the workers; and finally, (5) failure to conduct efficient medical surveillance programmes.

Environmental monitoring of silica particles in the selected workplace showed the following values: total respirable and non-respirable dust ($1725 \pm 217\,mg/m^3$), total respirable dust ($110.34 \pm 25.12\,mg/m^3$) and average of respirable quartz ($35.27 \pm 12.35\,mg/m^3$).

Lung function changes associated with pneumothorax

In predicted values, an association between mean values for FVC, FEV 1, FEV1/ FVC and FEF 25–75% was not seen ($P > 0.05$ for all). Decreases in FVC and FEV1 were associated with a pneumothorax, with *P*-values equal to 0.009 and 0.023, respectively. The reduction observed in the FEV1/ FVC ratio and FEF 25–75% (percent of predicted value) was not statistically significant, with *P*-values equal to 0.78 and 0.126, respectively. The PFT measurements and disability evaluations of the study population, in accordance with AMA Classes of Respiratory Impairment, are given in Table 2.

Respiratory symptoms and signs

Table 3 shows an association of various clinical findings with the occurrence of a pneumothorax. A pneumothorax was strongly associated with a history of pleuretic chest pain, respiratory distress, resting dyspnea, paroxysmal nocturnal dyspnea (PND), orthopnea and crackle.

Autopsy and pathological investigations

Autopsies in three cases, chosen randomly from our study population, revealed a collapsed lung, pleural

Table 2. Results of PFT measures, and theirs interpretation in accordance with AMA classes of respiratory impairment

Case no	Pneumo thorax	FVC/L -value	FVC percent of predicted	FEV1/ L -value	FEV1 percent of predicted	FEV1/ FVC ratio	FEF 25–75% L/S	FEF 25–75% of predicted	Severity of respiratory impairment	PFT pattern	Classes of impairment of whole person
1	Yes	1.49	34	1.27	34	85	1.53	31	Severe	Restrictive	4
2	Yes	1.78	38	1.50	37	84	1.40	30	Severe	Restrictive	4
3	Yes	1.36	30	1.35	35	99	2.40	51	Severe	Restrictive	4
4	Yes	1.56	35	1.07	28	83	0.72	15	Severe	Restrictive	4
5	Yes	1.59	36	1.27	34	80	1.14	25	Severe	Restrictive	4
6	Yes	2.10	48	2.09	56	99	1.92	41	Severe	Restrictive	4
7	Yes	1.62	34	1.56	39	96	2.79	58	Severe	Restrictive	4
8	No	1.51	34	1.07	28	86	0.78	16	Severe	Restrictive	4
9	No	1.29	29	1.28	34	99	2.34	50	Severe	Restrictive	4
10	No	3.36	89	1.97	61	59	1.12	26	Mild	Obstructive	2
11	No	3.71	82	2.69	70	72	1.99	42	Mild	Obstructive	1
12	No	3.57	80	2.42	63	67	1.72	37	Mild	Obstructive	2
13	No	3.62	81	2.10	55	58	1.51	32	Moderate	Obstructive	3
14	No	1.89	47	1.71	50	90	2.01	48	Severe	Restrictive	4
15	No	1.79	65	1.13	54	63	0.63	25	Mild	Mixed	2
16	No	3.18	81	2.63	82	83	2.81	73	Normal	Normal	1
17	No	3.84	88	3.06	82	80	2.83	61	Normal	Normal	1
18	No	3.05	81	2.43	82	80	2.22	68	Normal	Normal	1
19	No	3.25	83	2.69	83	83	2.78	69	Normal	Normal	1
20	No	4.72	96	3.96	95	84	3.73	76	Normal	Normal	1
21	No	3.02	73	2.60	73	86	2.82	62	Mild	Restrictive	2

Table 3. Relationship between pneumothorax and clinical findings

Independent variable		Pneumothorax		Test	*P*-value	Signification
		No	Yes			
BMI ≤18	No	13	6	Fisher's exact test	0.567	Non-significant
	Yes	1	1			
Pleuretic chest pain	No	10	1	Fisher's exact test	0.021	Significant
	Yes	4	6			
Breathlessness	No	3	0	Fisher's exact test	0.274	Non-significant
	Yes	11	7			
Resting dyspnea	No	10	1	Fisher's exact test	0.021	Significant
	Yes	4	6			
Anorexia	No	10	2	Fisher's exact test	0.080	Non-significant
	Yes	4	5			
Dysphagia	No	12	6	Fisher's exact test	0.753	Non-significant
	Yes	2	1			
Orthopnea	No	10	1	Fisher's exact test	0.080	Non-significant
	Yes	4	6			
PND	No	10	1	Fisher's exact test	0.021	Significant
	Yes	4	6			
Crackle	No	7	0	Fisher's exact test	0.030	Significant
	Yes	7	7			
Respiratory distress	No	11	1	Fisher's exact test	0.009	Significant
	Yes	3	6			

thickening and enlargement of hilar lymph nodes in both lungs. Pathological investigation of lungs showed confluent nodules, which included collagen fibres that were laid down in a concentric fashion.

Discussion

To the best of our knowledge, predictor factors for pneumothorax as a complication of silicosis have not been extensively described in the literature (Gupta *et al.*, 2000; Kawano *et al.*, 2002; Kobashi *et al.*, 2003; Light, 1995; Mazziotti *et al.*, 2002; Rao and Rau, 1993; Sahn and Heffner, 2000; Shida *et al.*, 1996; Weill *et al.*, 1994).

The rate of recurrence for secondary spontaneous pneumothorax has been similar to that for primary spontaneous pneumothorax, ranging from 39% to 47% (Sahn and Heffner, 2000). In our case study group, we found refractory recurrent episodes of secondary spontaneous pneumothorax. Overall, all patients who had suffered from a pneumothorax had presented a severe restrictive pattern of PFT before the pneumothorax occurrence. We believe that pneumothorax observed in rapidly progressive forms of silicosis could be related to a progressive decline in lung function.

In another reported case series study, secondary spontaneous pneumothorax due to advanced silicosis were investigated and the conclusion was drawn that there was no correlation between the onset of a secondary spontaneous pneumothorax and the duration of occupational exposure to silica (Kawano *et al.*, 2002). Our findings support this hypothesis, as shown in Table 1.

There is a consistent association between increased pulmonary function abnormalities and estimated measures of cumulative silica exposure within the allowable Occupational Safety and Health Administration (OSHA) regulatory levels (Hertzberg *et al.*, 2002). It is well recognized that severe silicosis can cause significant lung function impairment (Hnizdo and Vallyathan, 2003). In PFT of silicosis patients, those who suffered mixed abnormalities had the maximum risk of death (Mathur, 2005). In the current study, decreases in both FVC and FEV1 were related to the occurrence of pneumothorax.

Cumulative exposure to repairable dust is the most important factor in reported respiratory symptoms (Ulvestad *et al.*, 2001). In one cohort study, the risk of silicosis was investigated in 2235 subjects. The researchers concluded that the risk of silicosis was strongly dose-dependent. However, among the study subjects, the latency period appeared to be largely independent of the dose (Hnizdoe and Sluis-Cremer, 1993). In accordance with recommendation from the U.S. National Institute for Occupational Safety and Health

(NIOSH), the maximal permissible exposure level to quartz is 0.05 mg/m^3 (ACGIH, 2000). In this study, gravimetric and X-ray diffraction analysis of its crystalline structure showed that the average of respirable quartz was 25–70 times the recommended NIOSH value. This finding further supports the studies of Hnizdoe and confirms a basic need to decrease ambient air levels of silica dust in stone grinding workplaces.

In a progressive state of silicosis, the following symptoms may be present: shortness of breath following physical exertion, severe cough and fatigue, loss of appetite, chest pain and fever (Baxter *et al.*, 2000). In sandstone quarry workers, mortality rates have been significantly associated with a BMI of $<$17.51, complaints of chronic chest pain and complaints of chronic dyspnea (Mathur, 2005). As shown in Table 2, we found pneumothorax were associated with pleuretic chest pain, respiratory distress, resting dyspnea, paroxysmal nocturnal dyspnea and orthopnea. Odds for a fatal pneumothorax increased more than those who experienced mild respiratory disorder.

Most silicosis-associated deaths occurred among persons $>$65 years old, often following many years of silica dust exposure. However, the previously identified silicosis-related deaths in young adults revealed that relatively recent overexposure had sufficient magnitude to cause severe morbidity and mortality, after even relatively short periods of exposure (CDC, 1998). Our findings show that pneumothorax-associated deaths occur even among persons $<$40 years old, with a history of 1–5 years of high intensive exposure to silica dust. The findings strongly support the hypothesis that overexposure might be a possible predictor factor for the occurrence of fatal pneumothorax in young adults.

Radiographic abnormalities increase among workers with a high exposure to silica, and an association is present between radiographic abnormalities and additive exposure to quartz-containing dust (Tjoe Nij *et al.*, 2003). In accordance to our hypothesis, our findings support an association between variation of chest X-ray abnormalities and the intensity of quartz-containing dust exposure, as shown in Figures 1–3.

The fine particles of silica sand that disperse in the air are small enough to be inhaled deeply into the lungs, and they are known as respirable crystalline silica. Inhaling fine silica particles causes more lung damage than inhaling larger particles (Seaton and Cherrie, 1998). Diagnosis of silicosis usually does not include histopathological confirmation, which is generally utilized to rule out a potentially treatable disease rather than confirming a diagnosis (Silicosis and Silicate Disease Committee, 1988; Weill *et al.*, 1994). Results of autopsies and histopathological investigations of

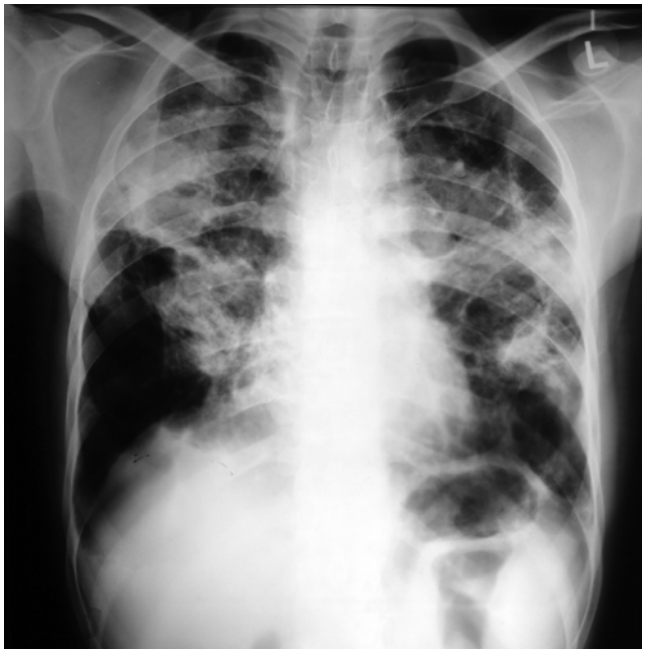

Figure 1. Chest radiograph of a 36-year old man with 4 years of silica dust exposure shows (1) small opacities shape-size (r/r) with radiological profusion category; (2) a large, localized pneumothorax in the right lower pleural space; (3) bullae in the lower zone of the right lung; (4) bullae in the lower zone of the left lung; (5) pleural thickening in the mediastinum and borders of the right lung, and; (6) Severe tenting of both diaphragms [r = rounded opacity; the diameter is $>$3 mm but $<$10 mm.]

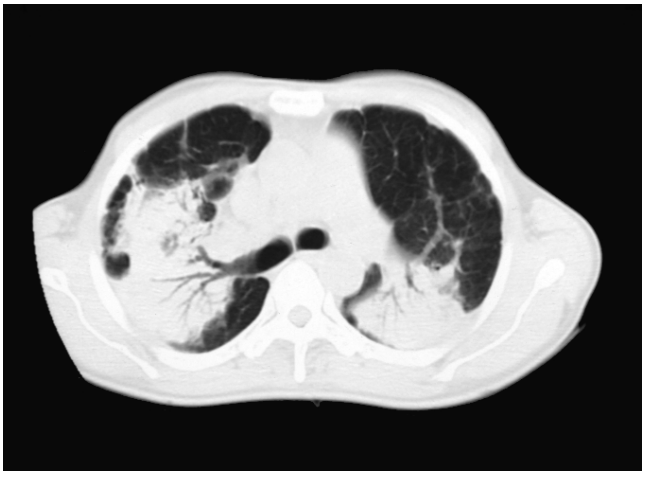

Figure 2. The lung CT of a 36-year old man with 4 years of silica dust exposure shows (1) a ground glass pattern in the upper segment of the lower lobes; (2) mixed density in the reticular and airacinus space, and; (3) few bullae in the peripheral zones.

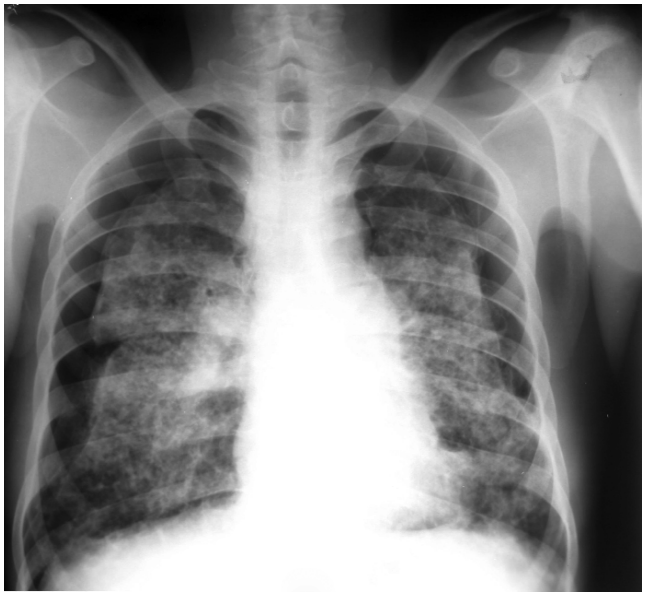

Figure 3. Chest radiograph of a 21-year old man with <2 years of silica dust exposure shows (1) p/r shape size of small opacities; (2) 3/3 scale of small opacities profusion in upper, middle and lower zones of both lungs, and; (3) bilateral sever pneumothorax [p = rounded opacity with diameter <1.5 mm and r = rounded opacity, where diameter >3 mm but <10 mm].

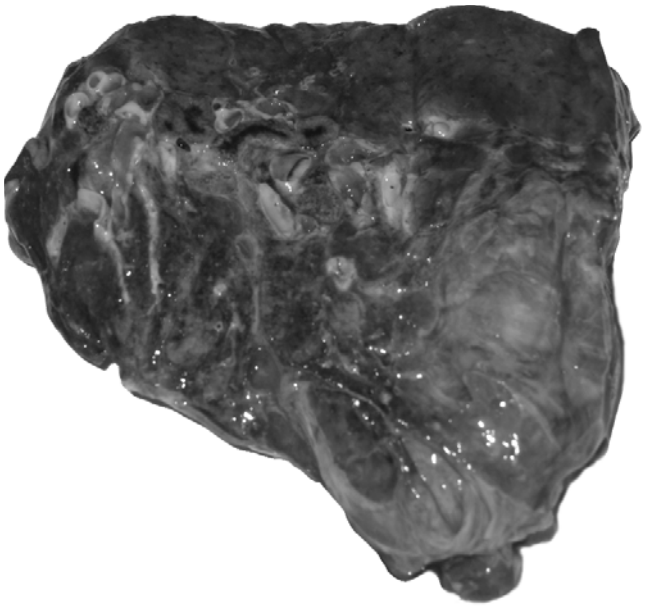

Figure 4. An autopsy of a 22-year old man with 2 years of silica dust exposure revealed pigmented masses and progressive massive fibrosis.

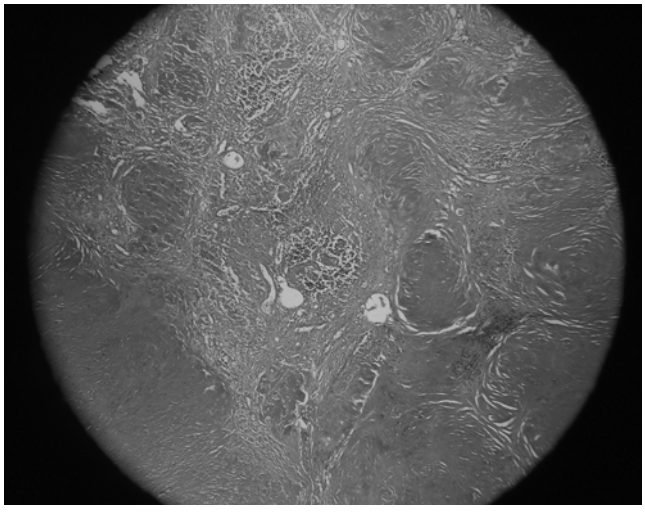

Figure 5. Autopsy lung specimen of a 28-year old man with <2 years of silica dust exposure shows confluent nodules, with central necrosis and hyalinization surrounded by many concentrically-arranged fibroblasts.

three cases support this hypothesis, as shown in Figures 4 and 5.

Our work here emphasizes several important issues related to silicosis among our study participants. First, there was a latent period between exposure and the occurrence of initial clinical symptoms, and diagnosis of silicosis in most cases was missed during this period. This shows a confounding issue that silicosis may be misdiagnosed, and its treatment may then be delayed. Thus, preventive specialized medical surveillance is especially important in implementing effective hygiene and ensuring the health of these workers. In cases where this is not possible, occupational hygiene programmes, environmental monitoring, filtering systems and proper ventilation must be implemented and enforced. Secondly, persons exposed to silica in the workplace were from low-income families and low educational backgrounds. This demographic knowledge indicates that the educational and economical needs of the work staff might be considered more thoughtfully through a structured, integrated support services programme.

Early detection of disease outbreaks enables public health officials to implement immediate control as well as put in place preventative measures (Kulldorf *et al.*, 2004). Therefore, mortality of workers due to unmanaged but preventable diseases, such as the rapidly progressive form of silicosis, is unacceptable.

Conclusion

Although this study has more cases of pneumothorax than any other previous studies performed on rapidly

progressive forms of silicosis, it was difficult to confirm a strong correlation between silicosis and a subsequent pneumothorax. We therefore conclude that a characteristic decline in PFT measures, along with the severity of respiratory impairment, may facilitate the occurrence of a pneumothorax secondary to the rapidly progressive silicosis.

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References

ACGIH. 2000. *Threshold limit value for chemical substances and physical agents and biological exposure indices.* American Conference Governmental Industrial Hygiene.

American Thoracic Society. 1997. Adverse effects of crystalline silica exposure. *Am J Respir Crit Care Med* 155, 761–65.

Baxter, P.J., Adams, P.H. and Aw, T.C. *et al.* 2000. *Hunter's diseases of occupations,* 9th edition. Arnold, 35, 673.

CDC. 1998. Silicosis deaths among young adults. United States, 1968–1994. *JAMA* 280, 13–14.

Cohen, C., Fireman, E. and Ganor, E. *et al.* 1999. Accelerated silicosis with mixed-dust pneumoconiosis in a hard-metal grinder. *J Occup & Environ Med* 41, 480–85.

Finkelstein, M.M. 2000. Silica, silicosis, and lung cancer: a risk assessment. *Am J Ind Med* 38, 8–18.

Gupta, D., Hansell, A. and Nichols, T. *et al.* 2000. Epidemiology of pneumothorax in England. *Thorax* 55, 666–71.

Harber, P., Schenker, M.B. and Balmes, J.R. (eds). 1996. *Occupational and environmental respiratory disease*. Mosby, 24, 373–95.

Hertzberg, V.S., Rosenman, K.D. and Reilly, M.J. *et al.* 2002. Effect of occupational silica exposure on pulmonary function. *Chest* 122, 721–28.

Hnizdoe, E. and Sluis-Cremer, G. 1993. Risk of silicosis in a cohort of white South African gold miners. *Am J Ind Med* 24, 447–57.

Hnizdo, E. and Vallyathan, V. 2003. Chronic obstructive pulmonary disease due to occupational exposure to silica dust: a review of epidemiological and pathological evidence. *Occupational and Environmental Medicine* 60, 237–44.

Kawano, M., Miura, H. and Anan, H. *et al*. 2002. Treatment of secondary spontaneous pneumothorax complicating silicosis and progressive massive fibrosis. *Kurume Med J* 49, 35–40.

Kobashi, Y., Manabe, T. and Hara, H. *et al.* 2003. A case of silicoproteinosis with pneumothorax. *Nihon Kokyuki Gakkai Zasshi* 41(2), 117–22.

Kulldorf, M., Zhang, Z. and Hartman, J. *et al.* 2004. Benchmark data and power calculations for evaluating disease outbreak detection methods. In *Syndromic surveillance: reports from a national conference, 2003. MMWR* 53, 144–51.

Light, R.W. 1995. Pneumothorax. *Pleural diseases*, 3rd edition. Williams & Wilkins, 242–77.

Marachiori, E., Ferrira, A. and Muller, N. 2001. Silicoproteinosis: High resolution CT and histologic findings. *J Thoracic Imaging* 16(2), 127–29.

Mathur, M.L. 2005. Pattern and predictors of mortality in sandstone quarry workers. *Indian Journal of Occupational and Environmental Medicine* 9, 80–85.

Mazziotti, S., Costa, C. and Ascenti, G. *et al.* 2002. Unusual pleural involvement after exposure to amorphous silicates (liparitosis): report of two cases. *Eur Radiol* 12, 1058–60.

NIOSH. 2002. *Case study in occupational epidemiology, silicosis in sandblasters, dhhs* (NIOSH) publication-number June 2002; 105.

Purohit, S.D., Gupta, P.R. and Gupta, M.L. *et al.* 1992. Acute silicosis in handlers of silica powder bags. *Lung India* 10(4), 145–48.

Rao, S. and Rau, P.V. 1993. Bilateral spontaneous pneumothorax in silicosis. *Indian J Chest Dis Allied Sci* 35(1), 47–49.

Sadikot, R.T., Greene, T. and Meadows, K. *et al.* 1997. Recurrence of primary spontaneous pneumothorax. *Thorax* 52, 805–809.

Sahn, S.A. and Heffner, J.E. 2000. Spontaneous pneumothorax. *NEJM* 342, 868–74.

Seaton, A. and Cherrie, J. 1998. Quartz exposures and severe silicosis: A role for the hilar. *Occupational and Environmental Medicine* 55, 383–86.

Sherson, D. 2002. Silicosis in the twenty first century. *Occupational and Environmental Medicine* 59, 721–22.

Shida, H., Chiyotani, K. and Honma, K. *et al.* 1996. Radiologic and pathologic characteristics of mixed dust pneumoconiosis. *RadioGraphics* 16, 483–98.

Silicosis and Silicate Disease Committee. 1998. Diseases associated with exposure to silicate minerals. *Arch Pathol Lab Med* 112, 673–720.

Sundaram, P., Kamat, R. and Joshi, J.M. 2002. Flour mill lung: pneumoconiosis of mixed etiology. *Indian J Chest Dis Allied Sci* 44, 117–20.

Tjoe Nij, E., Burdorf, A. and Parker, J. *et al.* 2003. Radiographic abnormalities among construction workers exposed to quartz containing dust. *Occup Environ Med* 60, 410.

Ulvestad, B., Bakke, B. and Eduad, W. *et al.* 2001. Cumulative exposure to dust causes accelerated decline in lung function in tunnel workers. *Occup Environ Med* 58, 663–69.

Weill, H., Jones, R.N. and Parkes, W.R. 1994. Silicosis and related diseases. In Parks W.R ed. *Occupational lung disorders*, 3rd edition. Butterwoorth-Heinemann, 285–339.

Zenz, C., Dickerson, O.B. and Horvath, E.P. 1994. *Occupational medicine*. Mosby, 13, 172–76.