Treatment of Secondary Spontaneous Pneumothorax Complicating Silicosis and Progressive Massive Fibrosis

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Summary: To clarify the management and treatment for the refractory cases of secondary spontaneous pneumothorax (SSP), we analyzed the clinical features in SSP complicating three cases of advanced silicosis, and discussed the available treatment. All three cases were males of age ranging from 60 to 70 years, and had silicosis with massive progressive fibrosis (PMF), classified as type 4 (PR4) according to the ILO guidelines. There was no correlation between the onset of SSP and the smoking habit, or the duration of the occupational exposure to silica. In a total of ten episodes of SSP, a refractory episode occurred in each of the three patients. No surgical treatment was possible because of some complications. Therefore, we administered conservative treatments under mechanical ventilation. The conservative treatments used were tube drainage with suction in each episode and pleurodesis by the combination of minocycline and OK-432 in one case. Approximately one month was the average time required for the air leak cessation. A significant decline in arterial oxygen tension (PaO₂) was observed after the treatment of one case, suggesting further respiratory deterioration. These results imply that the more aggressive treatments for refractory SSP should be limited because of the patient status and progression. More information might be required before performing these options safely and effectively.

Key words refractory secondary spontaneous pneumothorax, silicosis, pleurodesis

INTRODUCTION

Spontaneous pneumothorax is classified into primary (PSP) and secondary (SSP) [1]. The former occurs in a person without an obvious underlying lung disease, the latter occurs as a complication of an underlying disease, such as COPD [2,3]. Silicosis is classified as a fibrotic lung disease caused by prolonged exposure to silica [4,5]. Pneumothorax is one of the complications of silicosis [1,2]. In most of the patients with PMF, marked emphysema is observed, often followed by refractory SSP [2,3]. In previous reports [2,6] on the complications of silicosis, SSP is considered as life-threatening and resistant to treatment. The present consensus about the treatment for refractory SSP cases is that it should be aggressive [6-8].

In the present report we analyze the clinical course of refractory SSP complicating three cases of advanced silicosis, and discuss the options available in the treatment of these cases.

PATIENTS AND METHODS

The present study is based on three cases of advanced silicosis. The grade of silicosis was determined according to the ILO guidelines [9]. The general profiles were collected from the medical records. All were male, ranging in age from 60 to 70 years and had an occupation history of tunnel working. Also, the clinical course and the treatment were analyzed and compared for possible relations to the outcome and complications. To assess respiratory func-
tion after recovery, arterial blood O₂ and CO₂ tensions were analyzed during several weeks before the onset of, and after the recovery from refractory SSP. The data collected were compared using Student's t-test of significance. A P value less than 0.05 was considered statistically significant.

Case 1

A 66-year-old male patient was admitted in January 2000, because of sudden chest pain and dyspnea. He had a history of 6 years of work-related exposure to silica, and moderate smoking habit (Brinkmann Index; 400). According to the legal compensation scheme, he had been receiving medication for silicosis, classified as type 4 (PR4B), since 20 years ago. Radiological examination revealed an approximately 24% collapse of the right lung with a remarkable emphysematic bulla. Tube drainage with suction was performed on the same day. Although the lung expanded after 7 days, ipsilateral SSP with approximately 44% collapse reoccurred on the 22nd hospital day. The presence of a marked hypoxemia (arterial oxygen tension; 54 Torr) and of subcutaneous emphysema suggested that surgical treatment was not indicated. Chemical pleurodesis with minocycline and OK-432 and double tubes drainage were performed quickly under mechanical ventilation (Table 1 and Fig. 1a). Forty days were required for recovery.

**Fig. 1a.** Case 1: The radiographic examination revealed the progressive massive fibrosis, classified in the category PR 4B, 3/3+r. On the 22nd hospital day, the double tube drainages with suction and the mechanical ventilation were performed for the right recurrent SSP (ipsilateral), and the chemical pleurodesis (Minocycline 100 mg+OK-432 0.5 KE+Saline 100 ml+Lidocaine Hydrochloride 10 ml) was performed three days later.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Grade of Silicosis</th>
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<tr>
<td>1</td>
<td>66/M</td>
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<td>24% collapse of right lung</td>
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<td></td>
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<td>44% collapse of right lung</td>
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<td></td>
<td>+ Pleurodesis x three trials</td>
<td>+ Mechanical ventilation</td>
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<td>16% collapse of right lung</td>
<td>Rest and observation</td>
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<td>30% collapse of right lung</td>
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<td>+ Pleurodesis x one trial</td>
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<td>The regimen of pleurodesis was as follows; Minocycline 100 mg+OK-432 0.5 KE+Saline 100 ml+Lidocaine Hydrochloride 10 ml</td>
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<td>2</td>
<td>65/M</td>
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<td>Death from pyothorax and sepsis</td>
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<td>3</td>
<td>61/M</td>
<td>4C, 3/3 q</td>
<td>17% collapse of left lung</td>
<td>Tube drainage with suction</td>
<td>Recovery after 10 days</td>
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<td>34% collapse of right lung</td>
<td>Tube drainage with suction</td>
<td>Recovery after 20 days</td>
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<td></td>
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<td></td>
<td>33% collapse of right lung</td>
<td>+ Mechanical ventilation</td>
<td>Recovery after 20 days</td>
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</tbody>
</table>

Grade of silicosis was determined according to the ILO guidelines. (Ref. 9)
the air leak cessation after a total of three trials of pleurodesis. After two months of recovery, the same treatment was again performed because of approximately 30% collapse of the same lung. The patient recovered and had no recurrence after four months.

Case 2
A 65-year-old male patient was admitted in February 2000, because of gradual dyspnea. He had a history of 22 years of work-related exposure to silica and no smoking habit. According to the legal compensation scheme, he had been receiving medication for silicosis, classified as type 4 (PR4C), since 25 years ago. Radiological examination revealed an approximately 5% collapse of the left lung. He was treated with rest only. On the 7th hospital day, tube drainage with suction was performed because of the deterioration of the pneumothorax size. After two weeks of suction, however, he became suddenly unconscious. Radiological examination revealed a bilateral SSP of 15 to 20%. Bilateral tube drainage with suction and mechanical ventilation were instituted quickly (Table 1 and Fig. 1b). Because of the respiratory deterioration and of repeated obstruction of the drainage tube, pleurodesis or bronchial embolization were not performed in spite of the continuous air leak. Although the air leak ceased after 3 months of hospitalization, the patient died of pyothorax and sepsis several months later.

Case 3
A 61-year-old male in-patient had a remarkable dyspnea with stridor and hypoxemia (arterial oxygen tension; 48 Torr) in January 2001. He had a history of two prior episodes of SSP, a 17% collapse of the left lung in 1993 and a 34% collapse of the right lung in 1996. Tube drainages with suction were performed in both instances. Also, he had a history of 22 years of work-related exposure to silica, and moderate smoking habit (Brinkmann Index; 400). According to the legal compensation scheme, he had been receiving medication for silicosis, classified as type 4 (PR4C), since 25 years ago. Radiological examination revealed that the emphysematic bullae of the right upper lobe had enlarged since the prior examination performed several years ago. On the last SSP recurrence, radiological examination revealed an approximately 33% collapse of the right lung. Tube drainage with suction was performed under mechanical ventilation (Table 1 and Fig. 1c). Pleurodesis

Fig. 1b. Case 2: The radiographic examination revealed the progressive massive fibrosis, classified in the category PR 4C, 3/3q. On the 30th hospital day, the bilateral tube drainages with suction and the mechanical ventilation were performed for the bilateral recurrent SSP. The pleurodesis, however, was not performed because of some complications.

Fig. 1c. Case 3: The radiographic examination revealed the progressive massive fibrosis, classified in the category PR 4C, 3/3q. On the 7th hospital day, the tube drainages with suction and the mechanical ventilation were performed for the right recurrent SSP (ipsilateral). The re-expansion pulmonary edema, however, occurred on the next day, and the optional treatments were not performed.
was not performed because of re-expansion lung edema. After three weeks of tube drainage, the air leak ceased and the patient recovered under supplemental oxygen therapy.

RESULTS AND DISCUSSION

As shown in Table 1, we are reporting ten episodes of SSP, including four episodes in Case 1, three episodes in Case 2, and three episodes in Case 3. The etiology of SSP is attributed to the rupture of bulla associated with pulmonary emphysema and peripheral airway inflammation [1,4,10]. Although enlargement of emphysematic bullae and marked stridor preceded the last SSP episode of Case 3 (Table 1), it was generally difficult to predict the onset of SSP. Recently, Mishima et al. [11] demonstrated that monitoring of the emphysematic change on LAA count by the helical CT scan, and CT would be a useful parameter for the early detection of the deterioration of emphysematic bullae [9,12]. Also, smoking or silica inhalation could contribute not only to the pathogenesis of emphysematic change but also to the onset of SSP [5,10,12-14]. However, the smoking habit and the duration of occupational exposure in the present cases were various, suggesting the participation of other factor [14]. Most episodes occurred within the first several months following the first episode (range 10 days to 5 years in the present report (Table 1)) [3,14]. There seems to be a relationship between onset of an episode and weather changes (the beginning of the winter season in most of the present episodes (Table 1)) [15].

In the first episode of these three cases, pneumothorax size (average collapse size: 15%) and clinical course (average time to recovery: 15 days) did not give cause for concern. However, in the recurrent episodes (the second episode in Case 1, and the third episodes in Case 2 and 3), especially the ipsilateral recurrent SSPs, the general conditions deteriorated and mechanical ventilation was performed to treat the acute respiratory failure (Table 1). In these cases, the time to air leak cessation was longer and the respiratory function failed to recover (Fig. 2). The average time to recovery was approximately one month, significantly longer than in the first episode (Table 1). Also, arterial oxygen pressure (PaO$_2$: Torr) after recovery in Case 2 and 3 was lower than before the episode, decreasing from 76.5±3.8 to 50.0±10.4 (p<0.05) in Case 2 and from 70.3±5.9 to 59.6±10.3 (p<0.10) in Case 3. No significant decline in PaO$_2$ occurred in Case 1. On the other hand, there was no

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**Fig. 2.** Comparison of the respiratory function during several weeks before the onset and after the recovery in each refractory episode.

Case 1; ---, Case 2; ---, Case 3; --. There were the significant declines of PaO$_2$ (Torr) in Case 2 (*p<0.05) and 3 (**p<0.10), suggesting the respiratory distress after recovery. On the other hand, there were no significant changes of PaCO$_2$ (Torr) in all cases.
significant change in arterial carbon dioxide pressure (PaCO₂; Torr) (Fig. 2).

Previous reports [6-8] speculate that more aggressive treatment should be instituted in episodes of so-called refractory pneumothorax, in which the air leak persists for over 20 days and the respiratory function deteriorates. In the cases presented in this report, chemical pleurodesis with suction was performed in Case 1 (Fig. 1a). Tube drainage with suction, without pleurodesis, was performed in the remaining cases (Figs 1b and c), because of the respiratory deterioration and suction trouble in one case, and re-expansion lung edema in the other. The purpose of the treatment of SSP is to eliminate the intrapleural air collection and to prevent a recurrence [1,6]. To this end, treatments, such as Tube drainage (Tube thoracostomy), Pleurodesis and Thoracotomy were performed previously [1-3,6,8]. Recently, video-associated thoracoscopic surgery [6,8,13,16], and bronchial embolization [1,2] were introduced as additional aggressive treatments in SSP. However, these novel treatments may be questionable in cases of refractory SSP complicating advanced silicosis, in which marked emphysematous changes due to PMF, classified as type 4 (PR4) were observed. In advanced silicosis, in addition to marked emphysematus changes, there are also pleural swelling or adhesion, and several cardio-pulmonary dysfunctions including pulmonary hypertension and myocardial ischemia [2,9]. Given the present data, the serial surgical options would seem undesirable and the conservative ones also limited [2,3,13,16,17].

On the available agents for pleurodesis, we first considered the conventional ones, including autologous blood [17] and fibrin glue [16]. However, from our previous experiences that fibrin coagulation after instillation of autologous blood resulted in the repeated obstruction of the drainage tube and afterward in the incomplete expansion and bacterial infection of the lung [16,17], we preferred chemical pleurodesis by the combination of OK-432 and minocycline diluted in saline solution. Chemical pleurodesis is a conservative treatment in which some chemical agents are instilled into the pleural space, and the acute inflammation and the scarring produce the pleural symphysis and the patch of leak site [1,6]. The agents used for chemical pleurodesis are Talc [18], tetracycline derivatives (minocycline) [19-21], pisibanil (OK-432) [22], bron casama berna [1], and TNF-β [23]. Based on efficacy [6,18,19,22] and secondary effects [19-22], the combination of OK-432 and minocycline was the best choice for chemical pleurodesis in Case 1 (Table 1). The instillation of a low dose of each agent (OK-432 (0.5 KE) and minocycline (100 mg)) and the addition of local anesthesia [Lidocaine hydrochloride (10 ml)] minimizes the serial complications, such as chest pain, fever, and acute respiratory distress syndrome. No marked respiratory distress, fortunately, was observed after recovery (Fig. 2). In our limited experience, chemical pleurodesis with the combination of OK-432 and minocycline is one of effective and aggressive treatments for refractory SSP. However, further studies are required to establish the mechanism of pleurodesis [19] and the course of the disease after this treatment [2,20,21]. In particular, the case of ipsilateral recurrence after two months of recovery suggests the possibility of inaccuracy in targeting the leak by blind instillation of these chemical agents as well as of ineffectiveness of pleurodesis by low dosage agents (Table 1) [3,16].

On the other hand, no reliable options were devised in Case 2 and 3 because of the existing clinical problems. In these cases, only tube drainage with suction was performed to treat the persistent air leak (Table 1). If the air leak persists after the solution of the obstruction of tube drainage or the re-expansion lung edema, we would consider a more aggressive option, such as pleurodesis with thoracoscopy [6,8,21]. More care, however, is necessary because of the limited experience with such treatments, according to the Delphi consensus statement by Baumann et al. [5]. In short, the more aggressive treatments for the refractory cases should be performed under reasonable considerations of risk factors between the patient and treatment [2,6,8].

In conclusion, Silicosis is known to progress despite ceasing silica exposure. More research is needed on the treatment, outcomes and mortality of SSP complicated with silicosis, especially advanced silicosis with PMF [2,4,5]. The present report suggests that although chemical pleurodesis could be effective for treating refractory SSP complicating silicosis and PMF, its indication may be limited because of the patient clinical state and progression. Safer and more effective techniques would be desirable. The results of research in this area will be useful for the legal compensation scheme in the future [2,4].

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REFERENCES