Spontaneous pneumothorax associated with ankylosing spondylitis

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Objective. To review the incidence and clinical characteristics of spontaneous pneumothorax in patients with ankylosing spondylitis (AS).

Methods. This is a retrospective observational cohort study. Chest radiographs and medical records of patients with a diagnosis of AS from 1993 to 2003 in a tertiary referral centre were reviewed.

Results. A total of 1028 patients with a diagnosis of AS were identified from July 1993 to July 2003. Twenty-two patients had typical apical lung fibrotic changes in the chest radiographs (22/1028, 2.1%). Three of these patients (3/22, 13.6%) with lung disease had pneumothorax. Two patients had recurrences and received video-assisted thoracoscopic surgery (VATS) on the second attack. The third patient received talc pleurodesis on the first attack and did not have a recurrence. The incidence of spontaneous pneumothorax in patients with AS was 0.29% (3/1028) with an incidence density of 64.85/100000 patient-yr (95% confidence interval: 66.17–63.57/100000).

Conclusion. Spontaneous pneumothorax appears to be exceedingly rare in AS unless there is an underlying fibrocystic lung disease, in which case its occurrence is not uncommon. Cigarette smoking may be an important co-factor. Once developed, recurrences are common even after treatment. Prophylactic procedures should thus be considered for the first attack of spontaneous pneumothorax.

Key words: Ankylosing spondylitis, Spontaneous pneumothorax.

Ankylosing spondylitis (AS) is a chronic inflammatory disease that primarily affects the joints of the axial skeleton. It is a multisystem disease and several extra-articular manifestations have been described, including ocular, cardiovascular, renal and neurological complications [1]. Pulmonary involvement consists primarily of upper lobe fibroblastic changes and chest wall restriction [2, 3]. Theoretically, this well-recognized apical fibroblastic lung disease carries a high risk for spontaneous pneumothorax (SP). However, such reports have been rare [2]. We recruited a total of 1028 patients with a confirmed diagnosis of AS at a 2400-bed tertiary centre over a 10-yr period. Of these, three patients were found to have SP. We describe the clinical and imaging characteristics of these three patients and discuss the possible pathogenesis. Since cigarette smoking and recurrences are common characteristics of these patients, we suggested that the cessation of cigarette smoking and the introduction of prophylactic procedures in the management of SP may be important in the prevention of future attacks.

Materials and methods

We identified potential cases of AS between July 1993 and July 2003 from an automated database of the National Taiwan University Hospital, a 2400-bed tertiary medical centre, by ICD-9 codes.

The database was composed of medical records of patients from the hospital, the emergency department and the out-patient clinic. We reviewed all of the diagnoses specific for AS (e.g. ICD-9 720.0, ankylosing spondylitis) and sampled from the other related diagnoses (e.g. ICD-9 720.1, spinal enthesopathy; 720.2, sacroilitis, not elsewhere classified; 720.8, other inflammatory spondylopathies; 720.9, unspecified inflammatory spondylopathy). Medical records meeting the above selection criteria were reviewed by a study physician to confirm the diagnosis of AS by the New York criteria.

Fibroblastic lung diseases of AS were screened by the presence of any upper lung fibrotic lesions in chest radiograph reports given by radiologists. The original chest radiographs of the selected patients with upper lung lesions were further reviewed and confirmed by a pulmonologist who is experienced in the disease. The diagnosis of pneumothorax was based on medical records and chest radiographs. All included patients either received a mailed questionnaire or a telephone interview from two study nurses to confirm the absence of extra episodes of SP that were not recorded in our medical charts.

The medical records of this cohort were analysed for age, age at diagnosis of AS, age at the first pneumothorax, modality of treatment and recurrences. Incidence density for SP was estimated as the number of patients with SP divided by the sum of the
cumulative patient-years between the first diagnosis of AS and the last out-patient clinic visit in the study period. Statistics were calculated with use of SPSS software, version 12.0. Descriptive statistics were presented as 95% confidence intervals (CIs). Comparisons of the continuous variables between the two groups of patients were done using the Student’s t-test; a two-tailed \( P \) value < 0.05 was considered as significant.

The authors declare that the design of their work was approved by the Ethical Committee of the National Taiwan University Hospital (NTUH 9461700709).

Results

One thousand eight hundred and thirty-two patients were selected by the broad ICD-9 code screening criteria, of whom 1229 (67.1%) met the New York criteria for idiopathic AS. Two hundred and one patients were further excluded because of incomplete medical records or loss of contact either by mail or telephone. A total of 1028 patients were included in the study. Of these confirmed patients, 22 (2.14%) had typical apical lung fibroblastic changes on chest radiographs. Three (3/1028, 0.29%) developed SP, all cases of which demonstrated apical fibroblastic lung changes in chest radiographs before SP (Figs 1A and 1B), and the area of apical pulmonary densities in the chest radiographs enlarged after SP. The three patients were also included with the 22 patients with fibroblastic disease (3/22, 13.6%). Post-bullectomy computed tomography of patient 1 showed right upper lung collapse, emphysematous changes and numerous blebs or bullae in bilateral upper lungs (Fig. 1C). The mean follow-up duration of the AS patients in the study period was 4.5 ± 3.1 yr. The incidence density

FIG. 1. Posteroanterior (A) and lateral (B) chest radiographs demonstrate bilateral apical fibrotic cap. Note the bamboo spine and increased lung height. (C) High resolution chest CT performed after thoracoscopic bullectomy of the right apical lung. Multiple bullae and interstitial fibrosis were noted at the apex of the left lung.
of SP among AS patients was 64.9/100000 patient-yr (95% CI: 201.3–38.7/100000).

AS was first diagnosed at 18, 19 and 53 yr of age in the three patients, and the first attack of SP occurred at 22, 44 and 63 yr of age, respectively. The mean duration from the diagnosis of AS to the development of SP was 13.0 ± 6.2 yr, but varied widely from 4 to 25 yr. All of the patients had a history of smoking and had a slender build, with a mean body height of 170.3 ± 9.1 cm and a mean body mass index of 18.5 ± 1.6 kg/m².

All three patients received tube thoracotomy on the first episode of SP. Two had recurrences and received video-assisted thoracoscopic surgery (VATS). One of them had a further attack after VATS and received a second treatment. The third patient received talc pleurodesis on the first attack without recurrence of further attacks. Pulmonary function tests were performed in the two older patients, and both showed a restrictive ventilation pattern. Pathological examination of the excised apical lung tissue from VATS of the first two patients showed some blebs with a fibrous wall and mesothelial cell hyperplasia. The adjacent lung tissue revealed interstitial fibrosis, without evidence of vasculitis.

Common respiratory symptoms were chronic productive cough and chronic episodic chest pain. One patient had recurrent haemoptysis. Repeated sputum culture obtained in the three patients did not yield any pathogenic Mycobacterium tuberculosis or fungus. The clinical characteristics of the three patients are summarized in Table 1.

Discussion

Pleur-pulmonary manifestations of AS were first reported in 1941 by Durham and Kautz [2]. The development of apical pulmonary fibrosis and bullous disease is a rare but well-recognized extra-articular manifestation of AS [2]. Most cases are diagnosed 6–35 yr after the onset of arthritic manifestations [3]. Typical abnormalities on chest radiographs include nodules, cyst formation, cavitation and fibrosis of the apical lungs, which in theory pose great risks for the development of SP. However, such occurrences have rarely been reported. In a previous large series of 2080 patients with AS, two were incidentally found to have SP [2]. However, the author did not determine the association between SP and AS, and the actual incidence.

Our results document that the incidence of clinical and radiographic evidence of SP is low (64.9/100000) but higher than the population incidence (24/100000) [4].

In determining the association between SP and fibroblous pulmonary disease of AS in our patients other causes of secondary SP should be excluded. Chronic obstructive pulmonary disease (COPD) and pulmonary tuberculosis are the leading causes of secondary SP [4–6]. Evidence of such co-morbidity in our patients did not exist. The older two patients both had a restrictive pattern rather than an obstructive pattern on pulmonary function tests and repeated cultures for Mycobacterium were negative. In younger patients, the age and stature were more compatible with the clinical and epidemiological characteristics of primary idiopathic SP. Such a possibility has not been supported by pathological findings of the resected bullae, which showed the diffuse interstitial fibrosis seen in pulmonary fibroblous diseases of AS but rarely found in idiopathic SP [4–6].

The mechanism of recurrent pneumothorax in our patients is not clear. The multiple bleb-like lesions associated with AS and smoking might play some role. Fibroblous changes have been ascribed to recurrent mycobacterial or fungal infection, or the autoimmune activity of AS [7–10]. However, none of our patients yielded positive results for Mycobacterium or fungus culture. Pathological examination of the pulmonary lesions also showed no findings of autoimmune-related pulmonary disease, such as inflammatory cell aggregation, vasculitis, venous thromboembolism or infarction [11].

Smoking has been recognized as a risk factor in both primary and secondary SP, and has probably added to the risk of pneumothorax in these three patients [12]. Common pathological findings in chronic smokers, like respiratory bronchiolitis, were not noted in our patients because the excised peripheral lung tissue from the VATS bullectomy was insufficient to evaluate the condition of the bronchioles.

The three patients were slender, with a mean body mass index significantly lower than that of the AS patients in other reported series (18.5 ± 1.6 vs 25.6 ± 3.4 kg/m², P < 0.05) [13]. Slenderness has been implicated as a risk factor for SP, and may also have contributed to the development of SP in these three patients [14].

Patients with secondary SP are at an increased risk for recurrence, as was the case in patients 1 and 2. As regards to management, a trend towards initiating prevention of recurrence after the first, rather than after the second, occurrence was noted. Pleural abrasion and bullectomy stood out as the most favoured operative procedures [15].

The results of this investigation should be interpreted in the light of some limitations. The study was carried out in the setting of a tertiary centre and did not allow for the accurate estimation of the incidence, recurrence rate or risk factors among the general population. Moreover, we could not exclude the possibility that episodes of occult pneumothorax may present as vague chest pain and mild dyspnoea, in which case the incidence of SP was underestimated.

In conclusion, we have shown that SP should be included as a pleuro-pulmonary manifestation of AS. The incidence is low, estimated at 0.29%. Smoking may possibly contribute to its pathogenesis. Once pneumothorax develops, recurrence is likely, and a prophylactic procedure is suggested after the first attack.

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
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<tbody>
<tr>
<td>Age (yr)</td>
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</tr>
<tr>
<td>Sex</td>
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<tr>
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<td>17.87</td>
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<td>Duration of smoking before SP (yr)</td>
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<td>5</td>
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<tr>
<td>Spontaneous pneumothorax (yr)</td>
<td>44</td>
<td>22</td>
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<td>Age of first pneumothorax attack (yr)</td>
<td>25</td>
<td>4</td>
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<tr>
<td>Duration from AS diagnosed to pneumothorax (yr)</td>
<td>30</td>
<td>5</td>
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</table>

**Rheumatology**

- Spontaneous pneumothorax (SP) is rare in patients with ankylosing spondylitis (AS) (0.29%), but is not uncommon in patients with AS-associated fibrocystic lung disease (13.6%).
- Prophylactic procedures should be considered for the first attack of SP in patients with AS, because recurrence is common.

**Key messages**

**Acknowledgement**

The authors are indebted to Dr Yih-Leong Chang for her critical review of the manuscript.

The authors have declared no conflicts of interest.
References