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Two Asymptomatic Cases with Sarcoidosis Demonstrated Sequential Evolution from Radiographic Stage I to III within Five Years

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ABSTRACT

There are no guidelines regarding the treatment of pulmonary sarcoidosis. Generally, oral corticosteroids are considered the first-line treatment for symptomatic patients with pulmonary sarcoidosis. We report here two Japanese cases with pulmonary sarcoidosis who demonstrated sequential evolution from radiographic stage I to III within five years. Although these two cases had no symptoms, persistent, progressive pulmonary involvements were observed on chest X-ray. Considering the effectiveness of corticosteroids on patients with radiographic type II or III sarcoidosis reported by the British Thoracic Society, corticosteroid therapy might be a choice even in asymptomatic cases, if they demonstrate developing pulmonary involvement.

Key words: *Pulmonary sarcoidosis, Radiographic stage, Corticosteroid treatment*

Sarcoidosis is a chronic granulomatous disease of unknown etiology in which multiple organs are involved. Although the prognosis for most patients with sarcoidosis is considered to be excellent, some have a poor prognosis due to respiratory insufficiency and/or cor pulmonale[6]. However, there are no guidelines regarding the treatment of pulmonary sarcoidosis. Generally, persistent, symptomatic or progressive pulmonary sarcoidosis is accepted to be an indication for a course of systemic corticosteroid therapy.

We report here two Japanese cases with sarcoidosis who demonstrated sequential evolution from radiographic stage I to III within five years. Although persistent, progressive pulmonary involvements were observed on chest X-ray, these two cases had no symptoms. The role of corticosteroid treatment in asymptomatic progressive pulmonary sarcoidosis will be discussed.

CASE REPORT

CASE 1

A 23-year-old man was admitted to Hiroshima University Hospital in 1992, because of radiographic evidence of bilateral hilar lymphadenopathy (BHL) (Fig. 1A). Physical examination revealed no remarkable findings. A tuberculin skin test using 2.5 TU of purified protein derivative (PPD) was negative. A computed tomographic (CT) scan of the chest disclosed enlargement of the mediastinal and hilar lymph nodes. Pulmonary-function studies disclosed that the vital capacity was 5.06 liters (106% of predicted), the first-second vital capacity (FEV1) was 4.04 liters (79.8% of forced vital capacity). The single-breath carbon monoxide diffusing capacity (DLco) was 25.2 ml/min/mm of mercury (75.9% of predicted). The level of angiotensin-converting enzyme was 33.0 U/liter (normal range, 7.0 to 25.0 U/liter). Microscopical examination of biopsied lymph nodes obtained from the right supraclavicular region disclosed the presence of discrete, non-caseating, epithelioid cell granulomas.

The patient was followed-up as an outpatient without any medication. Three years after the first admission, bilateral interstitial infiltrates appeared in addition to the BHL on chest X-ray (Fig. 1 B). Five years after the first admission an X-ray film of the chest showed bilateral reticulonodular shadows in the upper lung fields without evidence of BHL (Fig. 1 C). Although he had no complaints, pulmonary-function studies revealed an impairment of pulmonary function (VC: 3.95 liters; %VC: 84.9%; FEV_1: 2.80 liters; FEV_1%: 70.2%; %DLco: 81.5%).

CASE 2

A 35-year-old woman was admitted to Hiroshima University Hospital in 1998, because of radiographic evidence of pulmonary abnormalities.

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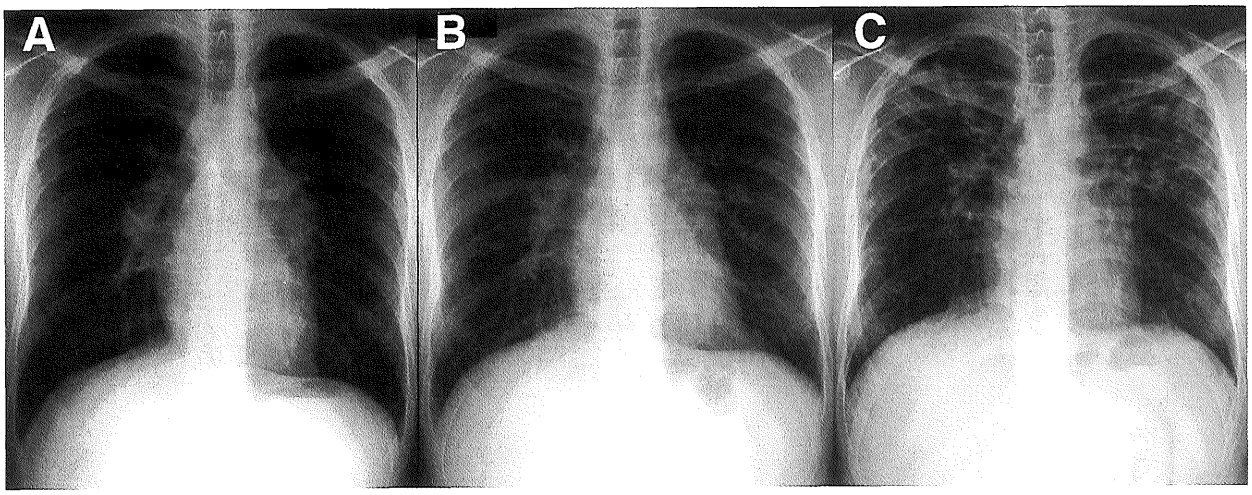

Fig. 1. Chest X-ray films in case 1 on admission with bilateral hilar lymphadenopathy (BHL) (A), three years after the first admission with bilateral interstitial infiltrates in addition to BHL (B), and five years after the first admission with bilateral reticulonodular shadows in the upper lung fields without evidence of BHL (C).

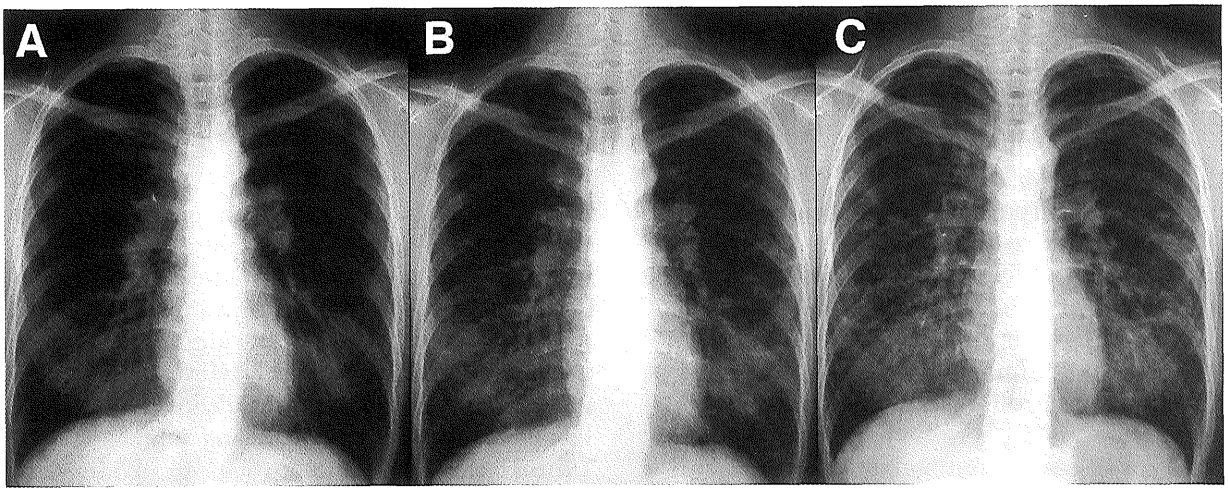

Fig. 2. Chest X-ray films in case 2 taken two years before admission with bilateral hilar lymphadenopathy (BHL) without evidence of lung involvement (A), three months before admission with bilateral fluffy consolidations and BHL (B), and on admission with bilateral fluffy consolidations (C).

Physical examination revealed no abnormalities. An X-ray film of the chest showed bilateral areas of fluffy consolidation (Fig. 2 C). A tuberculin skin test with 2.5 TU of PPD was negative. A CT scan of the chest disclosed bilateral mottling without enlargement of the mediastinal lymph nodes. A gallium scan of the thorax, performed after intravenous injection of ^{67}Ga, revealed an increase in uptake of the radionucleotide in the bilateral lower and middle lung fields. The level of angiotensin-converting enzyme was 26.6 U/liter. A lung biopsy from the right lung under video-associated thoracoscopic surgery was performed. Microscopical examination of the biopsy specimen disclosed the presence of noncaseating, epithelioid cell granulomas.

An X-ray film of the chest taken three months before admission showed bilateral areas of fluffy consolidation and BHL (Fig. 2 B). A careful retrospective review of chest X-ray films taken at her annual medical checkup revealed that a chest X-ray film taken two years before admission showed BHL without the evidence of lung involvement (Fig. 2 A). There was no evidence of BHL or lung involvement on a chest X-ray taken three years before admission.

DISCUSSION

The chest radiograph is important in the initial evaluation of patients with sarcoidosis, because it reveals abnormalities in more than 90% of known cases and carries prognostic information[6]. The disease is divided into three stages according to chest X-ray findings: stage I is characterized by BHL without evidence of interstitial infiltrates; stage II, BHL with pulmonary infiltrates; and stage III shows interstitial infiltrates without evidence of hilar lymphadenopathy[3]. Patients with stage I have the best overall prognosis, while patients with stage III have a relatively poor prognosis,

and a few patients are known to demonstrate sequential evolution in radiographic stage during the course of their disease[3,7].

The optimal treatment for pulmonary sarcoidosis remains unclear. Generally, oral corticosteroids are considered the first-line treatment for symptomatic patients with pulmonary sarcoidosis. There is general agreement on the effect of corticosteroids in suppressing the acute consequences of widespread pulmonary granulomas, but their effects on the overall natural history and any long term benefits are much less certain. Indeed, corticosteroids are effective agents for most symptomatic patients with pulmonary sarcoidosis in the short term. However, corticosteroids are not curative for the disease and have significant side effects. Once steroid therapy has been started, a significant percentage of patients will require long term treatment. After therapy is discontinued, relapse is likely to occur in some patients.

In 1996, the British Thoracic Society reported the effects of long term corticosteroid treatment in sarcoidosis[2]. In that study, asymptomatic patients with persistent radiographic infiltrates, as in our cases, randomly received either prednisolone for at least 18 months or no therapy. Both groups were followed-up for 5 years, with the steroid treatment group showing a 9% higher vital capacity, a lower rate of symptoms and improved chest radiographic findings[2]. This suggests that corticosteroids attenuate or even avert loss of pulmonary function in patients with radiographic types II or III, even in asymptomatic patients like our cases. On the other hand, Hunninghake et al proposed that the use of corticosteroids should be limited to those patients who had objective evidence of recent deterioration in lung function or serious extrapulmonary disease[4].

A study by Gottlieb et al failed to demonstrate any long term benefit for patients beyond the period of treatment[1]. It was reported that relapse occurred frequently in patients with sarcoidosis who had been treated with corticosteroids, and rarely occurred in patients who had not been treated with corticosteroids[1]. Since corticosteroids were administered to sufficiently symptomatic patients in that study[1], it was suggested that severe presenting symptoms portend a protracted and recurrent course. Alternatively, the authors suggested that corticosteroids contributed to the prolongation of the disease by delaying resolution.

Severity in Japanese pulmonary sarcoidosis is generally mild, and the prognosis for patients with pulmonary sarcoidosis in Japan is considered to be better than those in North America or Europe[5]. In patients with a favorable prognosis, the corticosteroid therapy may deteriorate the quality of life because of side effects. Izumi reported that the percentage of patients with persistent X-ray shadows was higher in patients administered steroids among patients with BHL alone in whom the disease was detected by health screening, and proposed that use of steroids should be limited to temporarily controlling the symptoms[5]. However, our asymptomatic cases developed pulmonary fibrosis without administration of corticosteroids. Considering the effectiveness of corticosteroids on patients with radiographic type II or III sarcoidosis reported by the British Thoracic Society, corticosteroid therapy might be a choice even in asymptomatic cases, if they demonstrate developing pulmonary involvement.

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