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Case Report

A case of acute tuberculous pneumonia in a patient with asthma

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Abstract

A 49-year-old Japanese man with bronchial asthma was admitted to hospital because of acute lobar pneumonia. A diagnosis of acute tuberculous pneumonia was made based on the pathologic findings of lung biopsy specimens and bacteriologic examination. For the 5 years before the onset of pneumonia, the patient had been treated with inhaled beclomethasone dipropionate (600 μg/day) and was well controlled. Laboratory findings revealed no immunosuppressive conditions, nor had the patient used oral corticosteroids for the treatment of his asthma. A tuberculin skin test had been negative approximately 30 years ago and annual chest X-ray examination had shown no evidence of tuberculosis over the past 5 years. Fiberoptic broncoscopic examination showed no evidence of bronchial tuberculosis or perforated lymph nodes. Because acute tuberculous lobar pneumonia in the lower lung field is rare, except in patients receiving oral corticosteroids or with immunodeficiency conditions, in this patient the inhalation of corticosteroids may have predisposed him to the onset of this condition.

Key words: asthma, beclomethasone dipropionate, inhalation therapy, lower lung field tuberculosis, oral corticosteroid, tuberculous pneumonia.

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Introduction

Inhalation of corticosteroids has been used as first-line treatment of bronchial asthma worldwide for the past 20 years.[1] This treatment modality has not been thought to predispose patients to infectious diseases of the airway and lungs, with the exception of the development oropharyngeal candidiasis as a local side effect.[2–4] In the present study, we report on a case of acute tuberculous pneumonia (ATBP) confined to the lower lung field in a patient with asthma that was treated with inhaled beclomethasone dipropionate (BDP).

Case Report

A 49-year-old Japanese man with asthma was admitted to hospital with fever (37.8°C), productive cough and general fatigue for 2 days. On admission, the patient's weight was 66 kg, his height was 169 cm and his state of nutrition was good. No abnormal physical signs were observed, except coarse rales on the left anterior chest wall. Chest X-ray films showed consolidation in the lingular segment without hilar lymph node enlargement (Fig. 1). The chest X-ray film obtained the previous year was normal. Asthmatic symptoms had been well controlled in the patient using inhaled BDP (600 μg/day) for the past 5 years and daily peak expiratory flow values had been within the normal range. Abnormal laboratory findings on admission were an increased erythrocyte sedimentation rate, C-reactive protein and neutrophilia (Table 1). No immunologic abnormalities were found and human immunodeficiency virus (HIV) titers were negative. Results of bacteriologic examination of the sputum for 3 consecutive days were unremarkable. Based on these findings, the patient was tentatively treated with minocycline, clindamycine and cefoperazone–sulbactam, in that

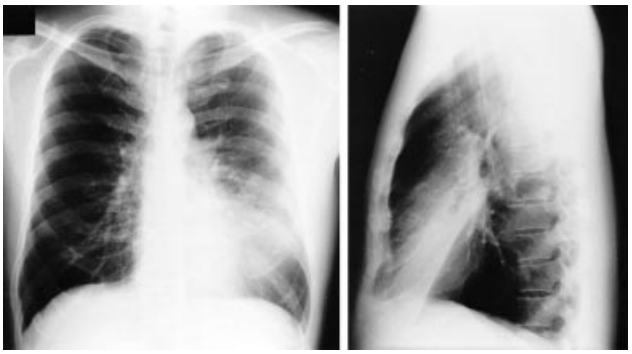

Fig. 1 Chest X-ray films on admission show hazy opacities in the lingular segment of the left lung.

order, over a 14 day period. However, his infectious symptoms deteriorated and consolidation on chest X-ray film expanded into the left lower lobe. A high-resolution computed tomographic scan showed a high-density area occupying the entire lingular segment with air bronchograms and acinar high-density patterns in the lower lung field (Fig. 2). Because the tuberculin skin test was strongly positive on the 10th day of admission, even though the patient had had a Bacillus Calmette–Guérin vaccination in childhood and had never been in contact with any person who had been diagnosed with tuberculosis, fiberoptic bronchoscopic examination was performed to confirm the pathogenesis. There were no remarkable abnormalities in the bronchial epithelial surface nor perforated lymph nodes into the lumen. Histologic examination using the specimens obtained by transbronchial lung biopsy showed multiple immature epithelioid granulomas without central necrosis (Fig. 3). Based on these histologic findings, a diagnosis of tuberculous pneumonia was made. Treatment with common antibiotics was discontinued and the patient was then treated using a combination of the following drugs: isoniazid (0.3 g/day), rifampicin (0.45 g/day) and ethambutol (0.75 g/day). Culture of the specimen obtained from bronchial lavage showed 11 colonies of *Mycobacterium tuberculosis* at the 4th week and culture of sputum also showed 15 colonies of *M. tuberculosis* at the 6th week. Both were not drug-resistant *in vitro*. Symptoms and abnormal shadows on chest X-ray film completely resolved in 2 months (Fig. 4).

Table 1 Laboratory findings on admission

Hematology	
Red blood cells (/mm^3)	541×10^4
Hemoglobin (g/dL)	15.8
Hematocrit (%)	47.8
Platelets (/mm^3)	35.6×10^4
White blood cells (/mm^3)	9800
Neutrophils (%)	73
Eosinophils (%)	5
Monocytes (%)	8
Basophils (%)	1
Lymphocytes (%)	12
Biochemistry	
Total protein (g/dL)	7.1
Albumin (g/dL)	4.1
Total bilirubin (mg/dL)	0.4
Glutamic oxaloacetic transaminase (mU/mL)	13
Glutamic pyruvic transaminase (mU/mL)	11
Lactate dehydrogenase (mU/mL)	182
Blood urea nitrogen (mg/dL)	9
Creatinine (mg/dL)	0.8
Na (mEq/L)	141
K (mEq/L)	4.2
Cl (mEq/L)	101
Serology and immunology	
Erythrocyte sedimentation rate (mm/h)	41
C-Reactive protein (mg/dL)	7.2
IgG (mg/dL)	1177
IgM (mg/dL)	257
IgA (mg/dL)	333
Lymphocytes	
T cell (%)	66.8
B cell (%)	10.6
T cell subsets	
$CD4^+$	44.7
$CD8^+$	22.1
Anti-*Mycoplasma pneumoniae* antibodies (IHA)	< 40
Anti-HIV (ELISA)	Negative
Blood gas analysis (room air)	
pH	7.420
P_aO_2 (mmHg)	79.5
P_aCO_2 (mmHg)	32.8
Sputum	
Bacteriology	Negative
Cytology	Class I
Tuberculin skin test*	37 mm redness and 13 mm induration

*Performed on the 10th day of admission. IHA, indirect hemagglutination.

Discussion

Unlike typical pulmonary tuberculosis, ATBP resembles acute bacterial pneumonia and is diagnosed on the basis of the clinical course and chest X-ray findings.[5,6] It is thought that ATBP is initiated by hypersensitivity to massive inhalation of tubercle bacillus protein[7,8] originating from

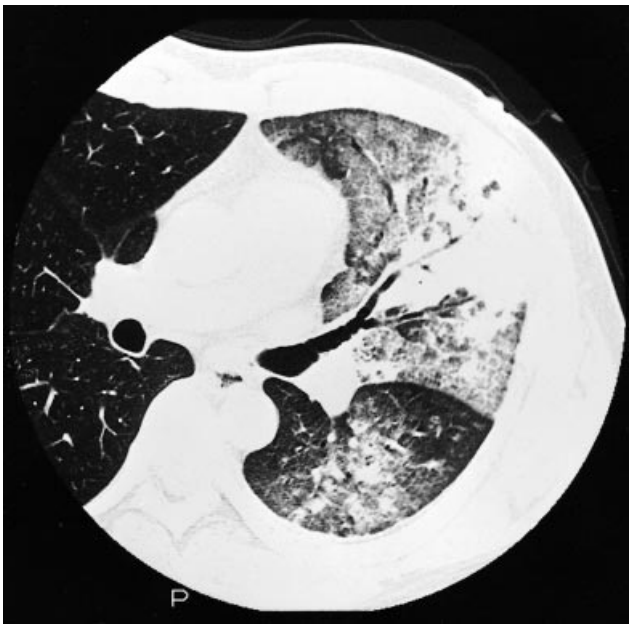

Fig. 2 High-resolution computed tomography of the chest shows a high-density area in the entire lingular segment and lower lobe with air bronchograms.

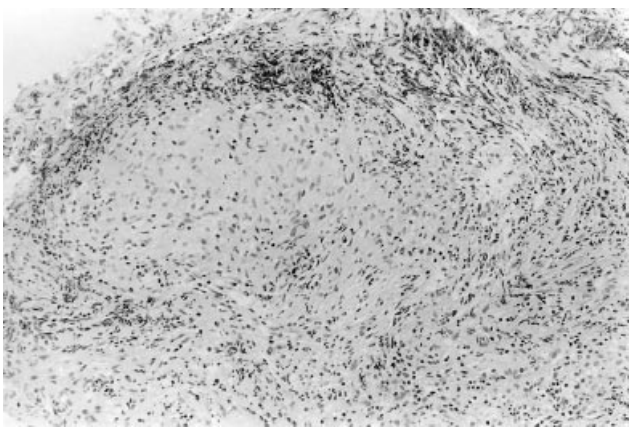

Fig. 3 Histologic features of the specimen obtained by transbronchial lung biopsy show multiple immature epithelioid granulomas without central necrosis. (Hematoxylin–eosin stain; original magnification ×40.)

tubercle bacillus inhaled into peripheral lung tissue through perforated bronchial epithelium from infected lymph nodes or by primary infection.[9] Because the lung lesion is caused by a hypersensitivity reaction to the tubercle bacillus protein, the bacilli are not necessarily detected in specimens.[8,10] The present case of ATBP was classified as 'lower lung field tuberculosis' on the basis of findings of chest X-ray films,[11] in which the development of the lesion is mostly caused by the perforation of

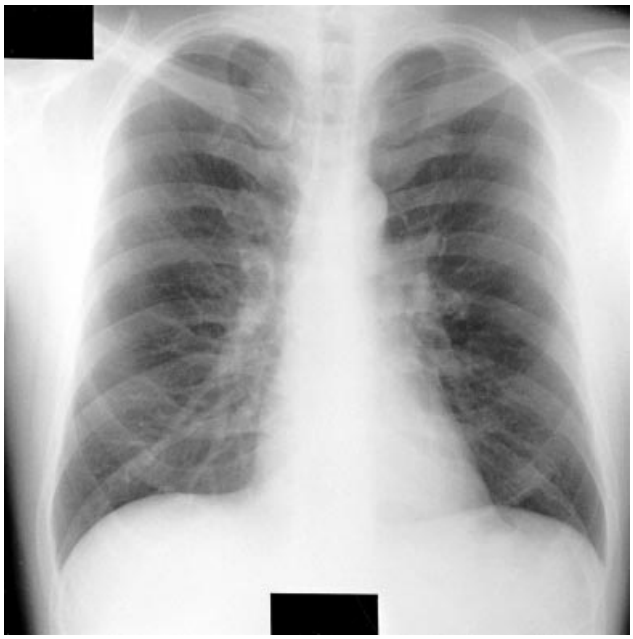

Fig. 4 A chest X-ray film 2 months after antitubercular treatment shows complete improvement.

infected hilar lymph nodes and spread of bacilli to the lung parenchyma.[11,12] However, because the present case did not show any evidence of perforated lymph nodes by fiberoptic bronchoscopic examination and the previous tuberculin skin test was negative, the 'lower lung field tuberculosis' could have been due to primary infection rather than reactivation or secondary infection. Previous studies[11,13–15] have shown that 'lower lung field tuberculosis' occurs only in 1–7% of patients with pulmonary tuberculosis and that it is rarely caused by primary infection. Therefore, patients tend to be misdiagnosed initially and treatment is delayed.[8,15] In fact, we had administered common antibiotics to this patient under the tentative diagnosis of mycoplasma or other bacterial pneumonia before ATBP was confirmed.

Inhaled corticosteroids for the treatment of asthma have been used throughout the world since 1972[1] and are recognized as very effective in controlling asthma symptoms.[16] Although these agents have not been shown to increase the risk of lung infection,[2–4] there are two reports that have shown a relationship between the incidence of pulmonary tuberculosis and inhaled corticosteroids in patients with asthma. Horton and Spector reported a case of pulmonary tuberculosis in a 43-year-old patient with asthma who had been treated using inhaled BDP at 800 μg/day and oral corticosteroids.[17] In another report, Shaikh described eight cases of

pulmonary tuberculosis of 548 patients with asthma who were using inhaled BDP (400–800 μg/day).[18] All eight cases had typical pulmonary tuberculosis associated with a cavity in the apical–posterior segment. Although there is no evidence to suggest that inhaled corticosteroids, even in high doses, increase the risk of pulmonary tuberculosis,[19] the incidence (1.48%) of pulmonary tuberculosis in patients who used inhaled corticosteroids, as reported by Shaikh,[18] was much higher than that in the general population, which, for example, is approximately 0.035% in Japan.[20] It is widely known that systemic corticosteroid therapy can reactivate latent tuberculosis or increase the risk of primary tuberculosis.[21–25] Immunocompromised individuals, such as those that are HIV positive, also have a high incidence of pulmonary tuberculosis, including 'lower lung field tuberculosis'.[26,27] The present patient was HIV negative and had no evidence of immunologic abnormalities. Therefore, it is possible that inhaled corticosteroids could have predisposed this patient to the development of tuberculosis because they have higher topical activity than oral corticosteroids and decrease T lymphocyte activity in the epithelium.

More than 200 patients have been diagnosed with active tuberculosis in the past 10 years in our institute and more than 2000 patients with asthma have been treated with inhaled BDP during the same period. However, the current case of tuberculosis was the first at our institute of a patient who had been treated with inhaled corticosteroids for asthma. Therefore, inhaled corticosteroids do not appear to increase the risk of tuberculosis and the circumstances of development of tuberculosis in our patient may be coincidental. However, Sahn and Lakshminarayan reported on six patients with 'lower lung field tuberculosis' on chest X-ray films of a total of 13 patients in whom tuberculosis had developed after oral corticosteroid treatment[28] and this type of tuberculosis is uncommon in patients not using corticosteroids. Because the present case had primary 'lower lung field tuberculosis', which is very rare, the effect of inhaled corticosteroids cannot be ruled out. Moreover, because inhaled corticosteroids have a dose-dependent systemic effect, although less than oral corticosteroid treatment,[29] careful follow up should be undertaken for patients with asthma who are treated with inhaled corticosteroids. When acute pneumonia develops in these patients, atypical pulmonary tuberculosis should be taken into account as a differential diagnosis.

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