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*Case Report*

# Pulmonary Sarcoidosis Showing a Solitary Large Nodule with a "Pseudo-alveolar" Pattern

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An abnormal shadow was detected on chest radiograph in a 28-year-old male on a routine medical check. The chest radiograph showed a solitary mass-like opacity in the right upper lung field. The patient attended our hospital for further examination on May 22, 2002. High-resolution computed tomography showed an aggregate of micronodular opacities consistent with the "pseudo-alveolar" pattern described in recent reports. The final diagnosis was pulmonary sarcoidosis as confirmed by the presence of epithelioid granulomas in specimens from transbronchial lung biopsy. Pulmonary sarcoidosis with a pseudo-alveolar pattern is unusual, particularly in the absence of bilateral hilar lymphadenopathy. Therefore, this case might be instructive for the diagnosis of pulmonary sarcoidosis.

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## Introduction

Sarcoidosis is a systemic granulomatous disease of unknown etiology that can affect any organ, but is most common in the lungs, eyes and skin. Although referral to specialist physicians from ophthalmologists or dermatologists is increasing in Japan, one-third of all cases of sarcoidosis are still diagnosed after abnormal chest radiograph findings during routine medical checks.[1] Bilateral hilar lymphadenopathy (BHL) is the hallmark of sarcoidosis on chest radiograph, but the condition can also manifest other patterns on chest radiograph, including nodular opacity (solitary or multiple), diffuse micronodular opacities, cavity formation and a pseudo-alveolar pattern.[2-6] Baughman et al.[7] classified the chest radiograph findings of sarcoidosis and found that BHL alone (type I) was present in 39.7% of cases, whereas a normal chest radiograph (type 0) was found in 8.3%. Abnormal opacity in the lung fields with BHL (type II) were present in 42.2%, in the absence of BHL (type III) were present in 9.8%, and finally, BHL was not detected in 18.1% of all cases.[7]

We encountered a patient with sarcoidosis who presented with a solitary mass-like opacity without BHL on chest radiograph. The mass-like opacity comprised an aggregate of many micronodular opacities on high-resolution computed tomography (HRCT). We report here a case of pulmonary sarcoidosis with a solitary "pseudo-alveolar" pattern and without BHL.

## Case Report

A 28-year-old male who worked in an electrical construction factory visited our hospital. He had a history of smoking 16 cigarettes a day for 12 years, but did not drink alcohol. The family members were all free from any disease, and in particular none had ever had sarcoidosis. He had no contact with animals, had not traveled to any foreign country recently and lived in a modern well-maintained building. He underwent a routine medical check each year at the company's medical center. He had never had an abnormal chest ra-

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diograph previously.

On the most recent routine medical check, he was found to have a solitary mass-like opacity in the right upper lung field that resembled lung cancer or tuberculosis. He was referred to our hospital for further examination on May 22, 2002. At that visit, he was asymptomatic. No systemic lymphadenopathy was detected. Chest auscultation revealed no abnormal lung and cardiac sounds. Levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were slightly increased due to fatty liver, but C-reactive protein (CRP), gamma-globulin and serum calcium levels were not elevated (Table 1). Pulmonary function testing showed a decreased lung perfusion test. No microorganisms were detected by serum antigen testing or antibody testing. The chest radiograph showed a solitary 4-cm diameter mass-like opacity in the right upper lung field (Figure 1). The mass was localized to the right S2 area by HRCT inspection, and comprised an unusual aggregate of several micronodular opacities. In adittion, an air-bronchogram was observed in the mass (Figure 2 A). The opacites were also seen in the right lower lung lobe (RLL) (Figure 2 B). Sputum cytology was negative. The acid-fast strain test was negative, as was polymerase chain reaction. *Haemophilus influenzae* and *Staphylococcus aureus* were detected in sputum

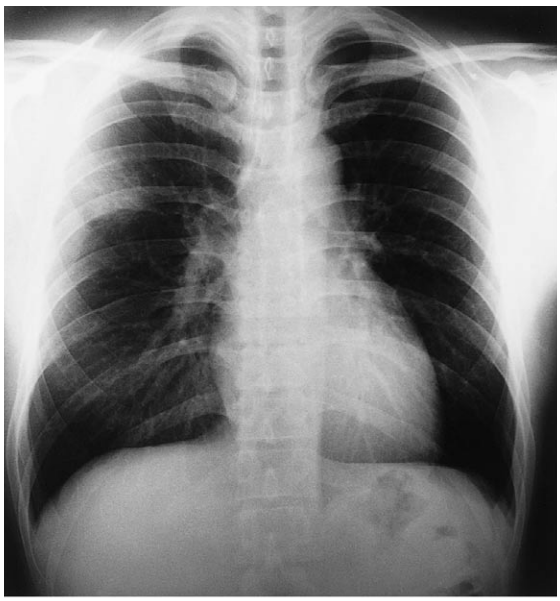

**Figure 1.** Chest radiograph on admission on May 22, 2002 showed a solitary mass-like opacity in the right upper lung field in the absence of bilaterial hilar lymphadenopathy (BHL).

**Table 1.** Laboratory findings on admission[a]

| | | | |
|---|---|---|---|
| <Hematology> | | Globulin fraction | |
| WBC (cells/mL) | 4600 | $\alpha_1$-gl (%) | 2.9 |
| Neutrophils (%) | 52.0 | $\alpha$-gl (%) | 8.8 |
| Lymphocytes (%) | 36.0 | ß-gl (%) | 9.4 |
| Monocytes (%) | 7.0 | $\gamma$-gl (%) | 14.4 |
| Eosinophils (%) | 0.0 | | |
| Basophils (%) | 0.0 | <Serology> | |
| Erythrocytes (cells/mL) | $465\times10^4$ | CRP (mg/dL) | 0.04 |
| Hemoglobin (g/dL) | 14.6 | ACE (IU/mL) | 15.7 |
| Platelets (cells/mL) | $26.5\times10^4$ | Lysozime (μg/dL) | 6.0 |
| | | *Chramydia pneumoniae* | Negative |
| <Blood chemistry> | | *Mycoplasma pneumoniae* | <40 |
| TP (g/dL) | 6.7 | | |
| Total bilirubin (mg/dL) | 0.8 | <Bacterial examination> | |
| AST (IU/L) | 13 | Culture | *H. influenzae* |
| ALT (IU/L) | 8 | | |
| LDH (IU/L) | 155 | <Acid-fast bacterial examination> | |
| ALP (IU/L) | 267 | Acid-fast staining | Negative |
| $\gamma$-GTP (IU/L) | 18 | Culture | Negative |
| BUN (mg/dL) | 13.5 | PCR | Negative |
| Cr (mg/dL) | 0.5 | | |
| Na (mEq/L) | 135 | <PPD Skin Test> | Negative |
| K (mEq/L) | 3.9 | | 0×0/3×5 |
| Cl (mEq/L) | 101 | | |
| Ca (mEq/mL) | 9.7 | ABG | Not tested |
| Glucose (mg/dL) | 107 | $SpO_2$ (%) | 97 |

[a]WBC=White blood cell count ; TP=Total protein; AST=Aspirate aminotransferase; ALT=Alanine aminotransferase; LDH=Lactate dehydrogenase; ALP=Alkaline phosphatase; $\gamma$-GTP=$\gamma$-glutamyl transpeptidase; BUN=Blood urea nitrogen; CRP=C-reactvie protein; ACE=Angiotensin converting enzyme; PCR=Polymerase chain reaction; PPD=Purified protein derivative; ABG=Arterial blood gas; $SpO_2$=Pulse oxygen saturation.

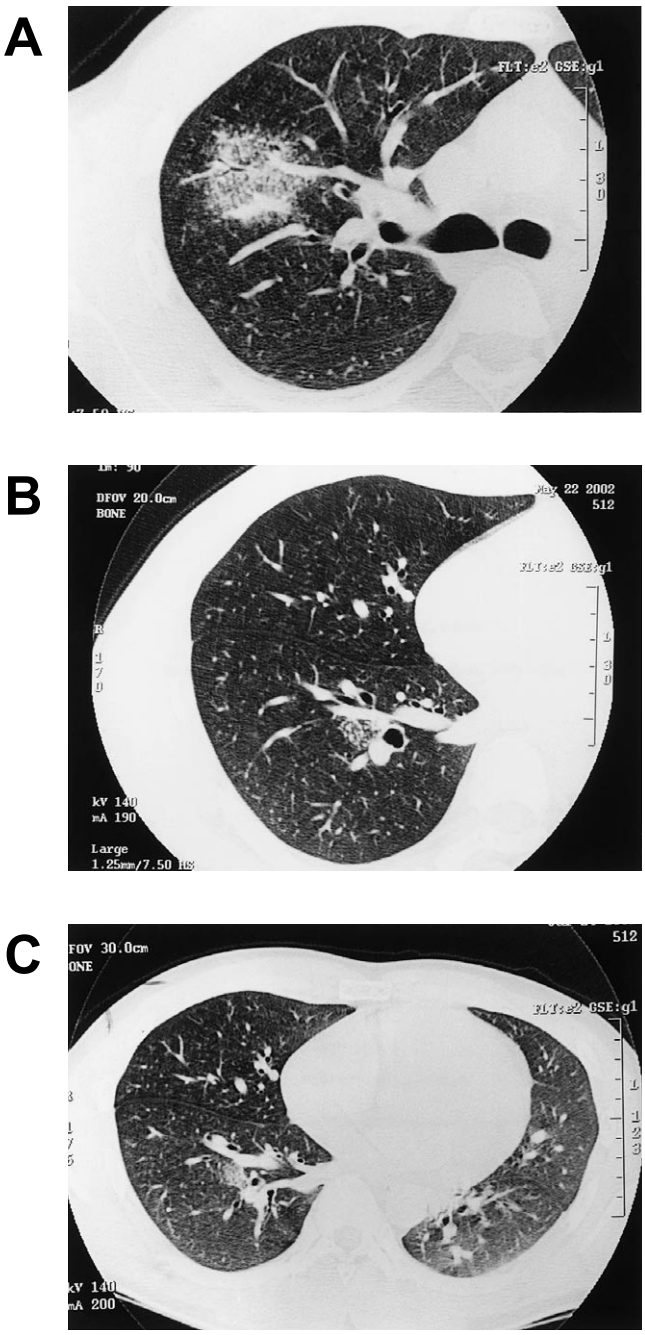


**Figure 2. A.** A "pseudo-alveolar" pattern was seen in the right S2 segment at the first visit. The shadow comprised numerous micronodular opacities by high resolution computed tomography. An air-bronchogram was observed in the mass. **B.** Focal opacities were seen in the right lower lung lobe at the same time. **C.** Opacities in the right lower lung lobe were increased on July 24, 2002.

bacterial examination, but the bacterial concentrations were too low to reflect bacterial pneumonia.

The patient was young, sputum was scant, no abnormal breath sounds were audible, and multiple opacities were detected on HRCT. Based on these features, the provisional diagnosis was atypical pneumonia. The patient was treated with levofloxacin at 300 mg/day for one week; however, no change was observed on chest radiograph on June 12, 2002.

At the time of the fourth visit, cardiac examination was normal. Auscultation of the lungs revealed no wheeze or no fine crackles. The abdomen was normal with no organomegaly. The eyes and skin were normal, as inspected by an ophthalmologist and dermatologist, respectively. Laboratory tests revealed that the low level liver dysfunction was still evident. Otherwise, all blood tests were normal. HRCT demonstrated that the mass-like lesion did not change in size. However, new patchy focal opacities were appeared in the right middle lobe (RML).

At that stage, we considered the possibility of sarcoidosis. Serum angiotensin converting enzyme and lysozyme were examined, but were not elevated. The purified protein derivative (PPD) skin test was negative, which is one of the most important signs of sarcoidosis. To establish a firm diagnosis, examination using a flexible fiberscope, such as bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB), was considered necessary. The patient however, declined to undergo fiberscope examination at that time as he was asymptomatic, so we agreed to continue observation of the clinical course.

The solitary mass-like opacity had not changed by July 24 2002, but the focal patchy opacities at the RML and RLL were increased on HRCT (Figure 2 C), suggesting disease progression. He consented to fiberscope examination at that stage and underwent BAL and TBLB on August 2, 2002. The BAL fluid showed lymphocytosis (43%) and a decreased ratio of lymphocyte expression markers (0.73) (Table 2). The specimen obtained from TBLB contained a granuloma containing giant cells, confirming the diagnosis of sarcoidosis. Although cardiac muscle scintigraphy and gallium scintigraphy were later performed, no abnormal findings were observed.

Since he remained asymptomatic, and it was a relatively short time from disease onset, the likelihood of natural improvement was considered strong, so we decided to observe the patient without any treatment. At the latest follow-up visit to the outpatient clinic on February 15, 2003, the patient was free of symptoms and the ab-

**Table 2.** Analysis of bronchoalveolar lavage fluid[a]

| BAL (rt. B4a) | |
|---|---|
| Cell count | $1.04\times10^7$ |
| Alveolar macrophages (%) | 57.4 |
| Lymphocytes (%) | 39.4 |
| Neutrophils (%) | 3.2 |
| Eosinophils (%) | 0.0 |
| CD4/CD8 | 0.73 |
| Cytology | Class II |
| Bacterial examination | Normal flora |
| Acid fast staining | Negative |
| TBC PCR | Negative |

[a]BAL=Bronchoalveolar lavage; TBC=Tuberculosis.

normal opacity had disappeared on both the chest radiograph and HRCT.

## Discussion

Mathieson et al.[8] reported that chest CT improved the diagnosis rate of sarcoidosis by 28% compared with chest radiograph, and Grenier et al.[9] also reported the usefulness of chest CT inspection. The typical sign of sarcoidosis on HRCT is considered to be small nodular opacities spreading peri-lobularly, with patchy focal increased interlobular thickening and irregular vascular opacities.[10-12] Nagai[1] and Baughman et al.[7] reported that 20-25% of all cases of sarcoidosis lacked BHL. Solitary nodular opacity, cavity formation, cystic formation and diffuse granular opacities have also been reported.[2-6] The absence of BHL on chest radiograph often leads to difficulty in the diagnosis of the disease.[3,13-15] In this case, the absence of BHL and the solitary mass opacity on chest radiograph caused diagnostic confusion. Nakatsu et al.[16] described "sarcoid galaxy" sign as typical HRCT findings in sarcoidosis. At the same time, Johkoh et al.[17] described pseudo-alveolar pattern. Even if each different, to put their opinions together, the collection of numberlss nodular opacities is the typical sign of sarcoidosis. In this case, we observed these features in the RLL on HRCT. Initially, we considered that there was no relationship between these findings and the nodular opacities. However, as the RLL lesion progressed during observation, we then considered that both findings were associated and sarcoidosis with a pseudo-alveolar pattern was diagnosed. An air-bronchogram could be seen in the right upper lung field on the HRCT image, but the circumference of the opacity did not reflect homogeneous consolidation, which is often seen in bacterial pneumonia.[13]

As sarcoidosis progresses, the number of epithelioid cell granulomas increases in alveolar septa and around small blood vessels and bronchioles. Numerous granulomas may occupy and replace alveoli or bronchioles, resulting in air space reduction. During this process, the opacity on chest radiograph or HRCT can be recognized as an alveolar pattern or air space consolidation. Our present case was useful for considering the mechanism of pseudo-alveolar patterns in sarcoidosis.

Sarcoidosis with a pseudo-alveolar pattern has been reported to respond well to steroid therapy.[17,18] There are various opinions on the criteria that comprise the early stage of the disease.[14,17-19] The laboratory data in our patient showed no abnormalities consistent with sarcoidosis. No symptoms of eye, skin or respiratory involvement were evident. No abnormal findings were noted at a medical check one year earlier. Thus, we determined that he was in the early stage of the illness, and therefore might still show reversibility. At the latest clinical examination, the abnormal shadow on the chest radiograph had disappeared. Since there was no distortion of lung structure in the right upper lung lobe, and ground glass opacity with micronodular opacity comprised the main part of the disease on HRCT inspection, it was not surprising that the mass-like opacity had disappeared.[17-19]

The absence of BHL and the solitary mass-like opacity on chest radiograph in this case were not specific for sarcoidosis, which resulted in a delay in arriving at the correct diagnosis. We could not find previous reports of sarcoidosis showing a pseudo-alveolar pattern without BHL. Why the aggregate of the micronodular opacity on HRCT did not transform into a consolidation shadow is unknown; however, the usefulness of HRCT inspection is a notable feature of this case.

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