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Multi-drug-resistant tuberculosis with galaxy and cluster signs on high-resolution computed tomography

Keitaro Nakamoto, Yuka Sasaki, Hiroyuki Kokuto, Masao Okumura, Takashi Yoshiyama & Hajime Goto

Department of Respiratory Medicine, Fukujuji Hospital, Japan Anti-Tuberculosis Association, Kiyose, Japan.

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Correspondence
Keitaro Nakamoto, 3-1-24, Matsuyama, Kiyose, Tokyo, 204-8522, Japan. E-mail: keichon2000@yahoo.co.jp

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Abstract

The galaxy sign and cluster sign were first reported in pulmonary sarcoidosis. From those reports, these two signs became known as one of the characteristic computed tomography (CT) findings of sarcoidosis. We report a patient with pulmonary tuberculosis who had these two signs. A 44-year-old man was referred to our hospital for general fatigue, cough, and low-grade fever lasting about two months. Thoracic CT showed a large parenchymal nodule arising from coalescent small nodules (galaxy sign) and clusters composed of numerous small nodules (cluster sign) in the bilateral lungs. Three specimens of sputum acid-fast smear were negative. However, we performed a bronchoscopy, and *Mycobacterium tuberculosis* was proven to be positive by the acid-fast culture test of the obtained bronchoalveolar lavage fluid. Moreover, drug sensitivity testing revealed this to be a case of multi-drug-resistant tuberculosis. Patients with these signs must be examined carefully to differentiate tuberculosis from pulmonary sarcoidosis.

Introduction

The galaxy sign and cluster sign are reported as characteristic thoracic computed tomography (CT) findings of pulmonary sarcoidosis. Nakatsu et al. first reported the CT finding termed the sarcoid galaxy sign, which described large nodules arising from a coalescence of small nodules [1]. Pathologically, this sign represented numerous coalescent granulomas. In contrast, Herráez Ortega et al. described the sarcoid cluster sign as the presence of clusters of multiple small punctiform nodules in the periphery of the lungs [2].

Galaxy and cluster signs are considered useful signs indicative of pulmonary sarcoidosis. However, pulmonary tuberculosis may also show these findings. We report a patient with multi-drug-resistant tuberculosis (MDR-TB) with galaxy and cluster signs requiring differentiation from sarcoidosis through high-resolution CT.

Case Report

A 44-year-old man was referred to our hospital for general fatigue, cough, and low-grade fever lasting about two months. He had no prior appreciable medical history but had 24 pack-years of cigarette smoking. He worked in a cleaning business. On examination, his body temperature was 37.3 °C, pulse rate 93/min, blood pressure 109/84 mmHg, and his respiratory rate was 20/min, with an O_2 saturation of 96% on room air. Lungs were clear on auscultation.

Chest X-ray showed bilateral lung infiltrates and right pleural effusion (Fig. 1A). Thoracic CT showed a large parenchymal nodule arising from coalescent small nodules and clusters composed of numerous small nodules in the bilateral lungs (Fig. 1B–D), along with right pleural effusion (Fig. 1D). Laboratory findings showed an increased white blood cell count (normal range 4000–8000/μL) of 10,970/μL (76.4% neutrophils (normal range 48–61%)). C-reactive protein level (normal range 0–0.3 mg/dL) was high at 5.85 mg/dL. Serum angiotensin-converting enzyme (normal range 8.3–21.4 IU/L) and soluble IL-2 receptor levels (normal range 124–466 U/mL) were also increased at 23.5 IU/L and 943 U/mL, respectively. Interferon-gamma release assay was positive. Pulmonary tuberculosis and sarcoidosis were considered based on the imaging and laboratory findings. However, three sputum acid-fast smear specimens were negative. The adenosine deaminase

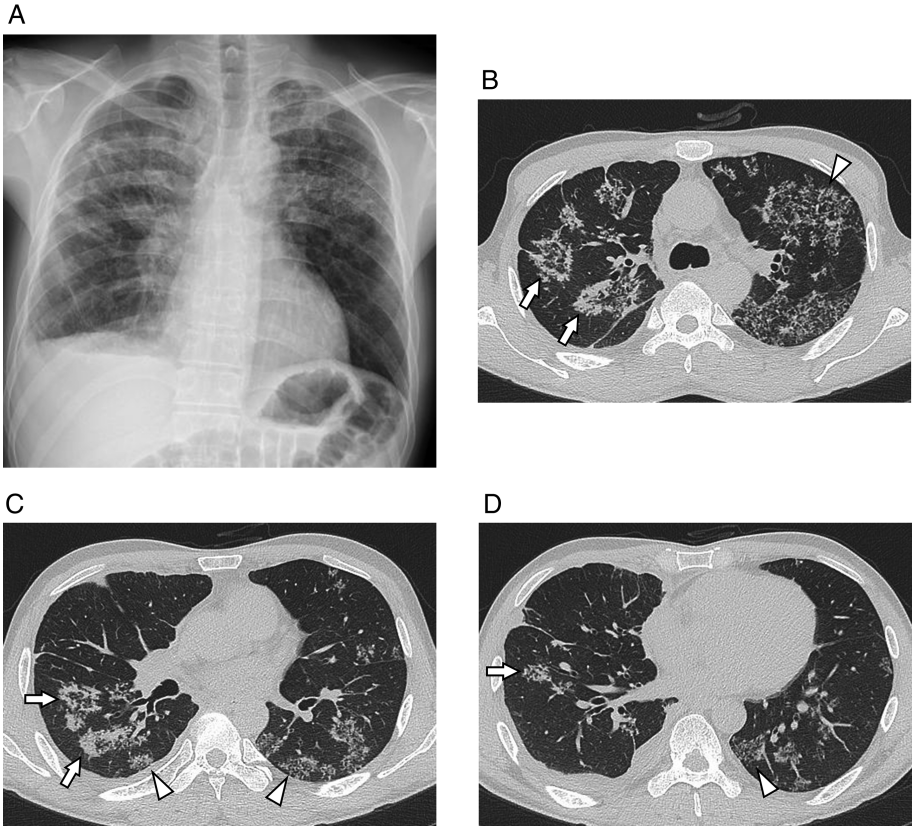

Figure 1. Chest X-ray showed infiltrates in the bilateral lungs and right pleural effusion (A). Thoracic computed tomography showed the galaxy sign (arrows) and cluster sign (arrowheads) in the bilateral lungs (B–D). Pleural effusion was also present (D).

level in pleural fluid was as high as 101.2 IU/L, with the proportion of lymphocytes in the pleural fluid increased to 90.5%. We performed a bronchoscopy to further aid in the diagnosis. Bronchoalveolar lavage fluid (BALF) obtained from the right middle lobe B4 showed a slightly increased total cell count of 21.6×10^4 cells/mL with accumulation of many macrophages (macrophages 88.0%, lymphocytes 11.2%, neutrophils 0.8%) and increased CD4/8 ratio of 5.0. The smear test of BALF was negative but later became positive for *Mycobacterium tuberculosis* in the acid-fast culture test. Moreover, drug sensitivity testing revealed the presence of multi-drug-resistant tuberculosis. Susceptibility testing results obtained using the standard proportion method with 1% Ogawa medium showed resistance to isoniazid, rifampicin, ethambutol, streptomycin, kanamycin, and ethionamide. Therefore, he was treated with antituberculous drugs (pyrazinamide, levofloxacin, para-aminosalicylic acid, cycloserine, linezolid, and delamanid), following which his symptoms and CT findings improved.

Discussion

Pulmonary tuberculosis is known to show various thoracic CT findings, such as micronodules, consolidation, cavitation, and pleural effusion [3]. In the present case, however, the patient had MDR-TB with thoracic CT findings characterized by the galaxy sign and cluster sign.

Originally, these two CT findings of the galaxy sign and cluster sign were known to be indicative of sarcoidosis. Nakatsu et al. reported the galaxy sign in 16 of 59 (27%) patients with sarcoidosis in their study [1]. Koide et al. also reported a galaxy sign incidence of 23.1% in patients with sarcoidosis [4]. Furthermore, in their report, the sarcoidosis patients with the galaxy sign were younger (median: 32 years, interquartile range (IQR) 28–38 years) than those without (median: 62 years, IQR 37.7–73.0; $P < 0.001$). Moreover, the CD4/8 ratio in BALF was also significantly lower in the former group (median: 2.6, IQR 2.0–3.9 vs. 5.8, IQR 3.7–8.6; $P < 0.001$). In contrast, Herráez Ortega et al. reported the presence of multiple small nodules without central coalescence in the lung, which was named the cluster sign [2]. In their report, nine of 91 patients with sarcoidosis had this sign. Our patient was young (44 years old) and showed both of these findings on thoracic CT. Therefore, this case needed to be differentiated from sarcoidosis.

These two signs are occasionally found in patients with tuberculosis. For instance, Ko et al. reported that 16% of 111 adults with active pulmonary tuberculosis had galaxy or cluster signs [3]. They also reported that these two signs were significantly more frequent in the perilymphatic group than

the centrilobular group on thoracic CT findings (30% vs. 0%, $P < 0.001$). In addition, the frequency of a positive acid-fast bacilli test was significantly lower in the perilymphatic group than the centrilobular group (32% vs. 70%, $P = 0.001$). In the article by Koide et al., two of 108 (1.9%) pulmonary tuberculosis patients had the galaxy sign, but the results of acid-fast bacilli staining test in both patients were negative. In our patient, three specimens of sputum acid-fast smear were also negative. These results indicated that patients with these signs may show a high proportion of negative acid-fast bacilli tests, and some physicians may not be able to accurately diagnose pulmonary tuberculosis. For this reason, the importance of further examinations such as bronchoscopy is suggested. Indeed, in our case, only the acid-fast culture test of BALF was positive for *M. tuberculosis* with multi-drug resistance. MDR-TB is a major global concern and is difficult to treat [5]. We believe that treatment in this patient was successful due to an accurate diagnosis.

In conclusion, we experienced a highly educational case indicating the importance of careful examination of patients with galaxy and cluster signs to differentiate tuberculosis from pulmonary sarcoidosis.

Disclosure statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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