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Case report

Disseminated tuberculosis with acute respiratory distress syndrome lacking granuloma formation in the lung

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ABSTRACT

A 66-year-old woman, who had been treated with systemic corticosteroids for four months for vasculitis of unknown etiology, was referred to our department due to a fever, dyspnea and patchy ground-glass opacities on chest computed tomography. As transbronchial biopsy specimens were suggestive of interstitial pneumonia, the prescribed dose of corticosteroids was increased. However, the patient developed pyrexia and presented diffuse ground-glass attenuation in the lungs bilaterally. Antituberculous drugs were administered because a previous blood interferon-gamma release assay was positive, however, the patient died of severe respiratory failure within several days, and cultures of her blood, urine and bone marrow posthumously revealed *Mycobacterium tuberculosis*. An autopsy revealed multiple foci of air-space pneumonia containing numerous acid-fast bacilli without granuloma formation, accompanied by diffuse alveolar damage. An immunosuppressive condition might inhibit air-space pneumonia to become granulomatous inflammation as an initial stage of pulmonary tuberculosis.

1. Introduction

Miliary tuberculosis is defined as millet seed sized tuberculosis lesions diffusely distending into at least two organs through hematogenous dissemination of the tubercle bacillus, and a chest image presenting with diffuse small nodular shadows. Although such miliary shadow is known to become indistinct when complicated with acute respiratory distress syndrome (ARDS), we herein report a case of disseminated tuberculosis histologically presenting with tuberculous pneumonia and diffuse alveolar damage without any granulomatous formation.

2. Case report

A 66-year-old woman was admitted to a hospital due to 1-month history of persistent pyrexia and nodular erythema in her lower legs in July 201X. The patient did not have a smoking or alcohol history, and routinely saw a doctor for hypertension, hyperlipidemia and knee osteoarthritis. She was diagnosed with vasculitis of unknown etiology, mostly suggestive of polyarteritis nodosa, according to skin biopsy findings and was treated with a systemic corticosteroid (prednisolone; initial dose 1.0 mg/kg/day in August 201X) for four months. A blood interferon-gamma release assay (QuantiFERON-TB Gold®) performed before the steroid initiation was positive, however, the polymerase chain reaction and culture of her bone marrow aspirate was negative for *Mycobacterium tuberculosis* (*M. tuberculosis*). There was no finding of previous pulmonary tuberculosis, therefore, the prophylactic administration of antituberculous drug was not performed during steroid therapy. The patient did not have any history of cancer or diabetes mellitus, including steroid-induced diabetes, and she was negative for human immunodeficiency virus infection. Her erythema improved, but in early December 201X, she developed an intermittent fever and chest computed tomography (CT) showed patchy ground-glass opacities in the lungs (Fig. 1A). Causative agents suggestive of an infection, including *M. tuberculosis*, were not identified in the blood and urine cultures, however, chest CT revealed a worsening condition approximately two weeks later (Fig. 1B). Laboratory tests showed an elevated level of serum KL-6 (2399 U/ml), normal level of β-D-glucan, and negative finding of cytomegalovirus antigen. *Pneumocystis jirovecii* or other microorganism, including

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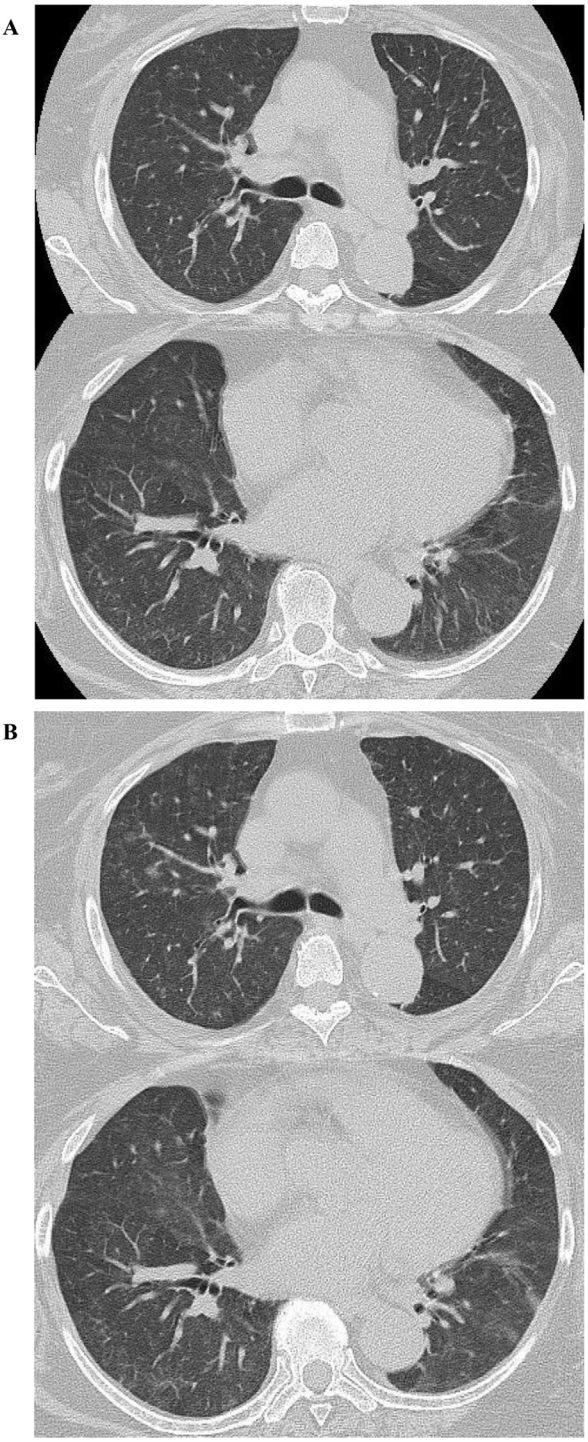

Fig. 1. Chest computed tomographic scans after four months treatment with systemic corticosteroids for vasculitis of unknown etiology, showing patchy ground-glass opacities in the lungs (A). Two weeks later, worsening of these shadows is observed (B).

M. tuberculosis, was not detected in the bronchoalveolar lavage fluid. As transbronchial biopsy specimens were suggestive of interstitial pneumonia, the prescribed dose of corticosteroid was increased. However, the patient presented diffuse ground-glass attenuation in the lungs bilaterally (Fig. 2) with a high fever and severe hypoxemia in late December 201X. Although antituberculous drugs and high-dose corticosteroids were administered, the

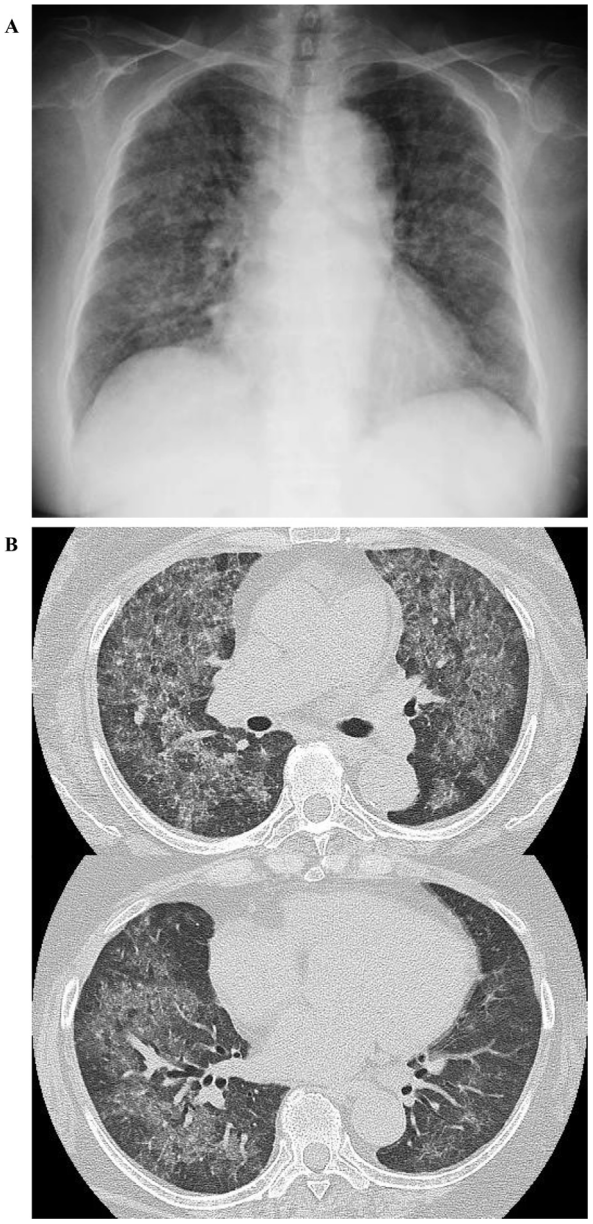

Fig. 2. A chest roentgenogram (A) and computed tomography (B) one week before death, showing diffuse ground-glass attenuation bilaterally.

patient died of severe respiratory failure within several days, and the cultures of her blood, urine and bone marrow posthumously revealed *M. tuberculosis* alone. An autopsy (only for the lung according to the family's consent) revealed multiple foci of alveoli filled with neutrophils and nuclear debris containing a large number of acid-fast bacilli without granuloma formation, accompanied by hyaline membranes in the wall of the distal airways, which suggested the acute phase of diffuse alveolar damage (Fig. 3A-C). In addition, septic embolization was observed in the pulmonary artery (Fig. 3D), which contained numerous acid-fast bacilli (data not shown).

3. Discussion

Tuberculous pneumonia, originally referred to as caseous pneumonia, is known as pulmonary tuberculosis presenting with infiltrative shadow in a chest image. This form of tuberculosis is