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CASE REPORT

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Early-stage diffuse panbronchiolitis in a young patient confirmed by video-assisted lung biopsy: A case report

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Abstract

A 29-year-old man presented with sputum and cough, which were pointed out by his neighbors. A high-resolution chest computed tomography scan showed well-defined multiple centrilobular nodules and a tree-in-bud pattern. Chest auscultation revealed coarse crackles. He did not report any nasal sinus symptoms. We subsequently performed a video-assisted lung biopsy; the specimen confirmed diffuse panbronchiolitis. Subsequently, sinusitis was confirmed by an otolaryngologist. His symptoms gradually improved following treatment with erythromycin. We report a case of early-stage diffuse panbronchiolitis in a young patient, with multiple intralobular nodules, no bronchiectasis, and a good clinical course.

KEYWORDS

centrilobular nodule, diffuse panbronchiolitis, pathology

1 | INTRODUCTION

Diffuse panbronchiolitis is a distinct clinicopathologic entity with upper and lower respiratory tract symptoms. It occurs exclusively in East Asian populations, particularly among the Japanese. Diffuse panbronchiolitis typically develops in the fourth to sixth decade of life. The prognosis of patients with diffuse panbronchiolitis was poor prior to the development of macrolide therapy.[1] Pathological confirmation is often not necessary if the case fulfills the diagnostic criteria, although it is important to make a definitive diagnosis. The diagnostic criteria taken from a working group of the Ministry of Health and Welfare of Japan consist of (i) persistent cough, sputum, and exertional dyspnea, (ii) history of chronic paranasal sinusitis, (iii) bilateral diffuse small nodular shadows on a plain chest radiograph or centrilobular micronodules on chest computed tomography images, (iv) coarse crackles, (v) forced expiratory volume in one-second/forced vital capacity (FEV_1/FVC) <70% and partial pressure of arterial oxygen (PaO_2) <80 mm Hg; and (vi) titer of cold hemagglutinin >64.[2] The present case fulfilled the five criteria at the time of initial admission. However, a video-assisted lung biopsy was performed because he was very young, the presence of chronic sinusitis was unclear from his history, and he wanted a definitive diagnosis. We think that cases with definitive diagnosis of diffuse panbronchiolitis are now rare, as macrolides are prescribed for several other diseases in clinical practice. We herein describe a case of early-stage diffuse panbronchiolitis without bronchiectasis and cystic opacities that was confirmed using video-assisted lung biopsy and was effectively treated with erythromycin.

2 | CASE

A 29-year-old man presented at a hospital with sputum and a cough, which were pointed out by his neighbors. A chest X-ray showed a bilateral abnormality in the lower lung field. At the hospital, a prednisolone therapy was started because he was suspected to have hypersensitivity pneumonia on the basis of the transbronchial biopsy and the absence of acid-fast bacilli in the bronchoalveolar lavage fluid. However, the steroid therapy was not effective. He was referred to our hospital for further investigation. He was a nonsmoker and did

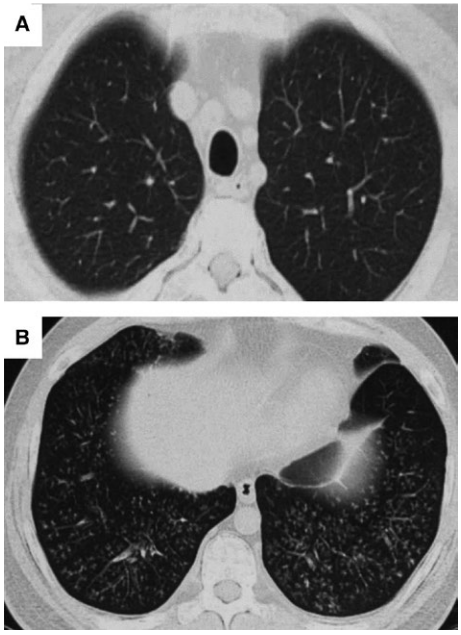

FIGURE 1 Chest CT in the upper lung (A) and in the lower lung (B) on admission showed bilateral well-defined multiple centrilobular nodules and tree-in-bud appearance, predominantly in the lower lung

not report any allergies. His past medical and family history were unremarkable. A physical examination showed that he had a body temperature of 36.3°C, blood pressure of 112/70 mm Hg, pulse rate of 68 beats/min, respiratory rate of 18 breaths/min, and peripheral oxygen saturation of 92% in room air. A chest auscultation revealed coarse crackles. Laboratory studies showed that his white blood cell count was 11 400/μL with 92% neutrophils, hemoglobin was 15.4 g/dL, platelet count was 36.4×10^6/μL, serum total protein was 7.6 g/dL, albumin was 4.6 g/dL, and C-reactive protein was 0.58 mg/dL, with no apparent liver or renal dysfunction. Other laboratory data showed that his cold hemagglutinin titer was 1:128, and tests for anti-human T-cell lymphotropic virus type 1 antibody and rheumatoid factor gave negative results. A sputum culture showed Haemophilus influenza without acid-fast bacilli. Pulmonary function tests showed a forced vital capacity of 2.84 L (65.4%) and forced expiratory volume in 1 s of 1.21 L (52.6%). A chest X-ray showed bilateral multiple nodular opacities in the lower lung field. High-resolution computed tomography revealed pure multiple centrilobular nodules without bronchiectasis, often extending to small branching linear areas of attenuation (tree-in-bud pattern) (Figure 1). We suspected diffuse panbronchiolitis, but there were no significant nasal sinus symptoms or related family history at the time of admission. In addition, we considered other diseases described in the Discussion.

We subsequently performed a video-assisted biopsy at the costophrenic edge of the right lower lobe because of his rejection of a long-term macrolide therapy without a definitive pathological diagnosis. The specimen showed massive infiltration of the respiratory bronchioles by lymphoid cells and foamy macrophages, confirming a diagnosis of diffuse panbronchiolitis (Figure 2). Subsequently, chronic sinusitis was confirmed from the purulent mucus in the accessory nasal sinus by an otolaryngologist. The patient was treated with 600 mg/d of erythromycin for 4 years. His symptoms and chest X-ray improved. He has not experienced a relapse in the 2 years since the discontinuation of erythromycin therapy.

3 | DISCUSSION

We presented a case of histologically confirmed diffuse panbronchiolitis—a clinicopathologic entity characterized by three-layer

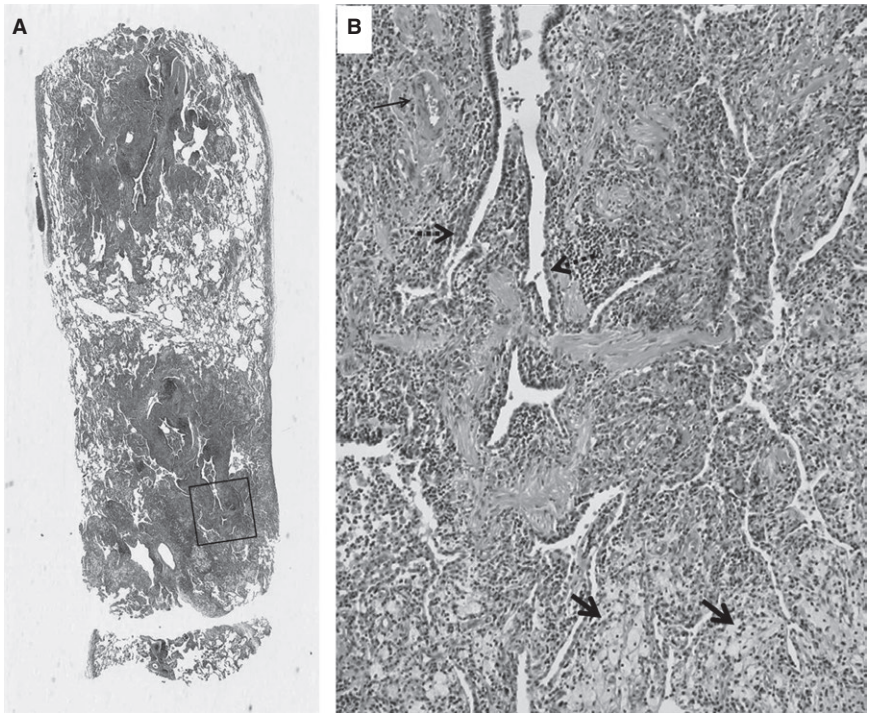

FIGURE 2 (A) The pathological specimen showed two nodular lesions centered on a bronchiole. Panoramic view, hematoxylin-eosin (HE). (B) An extended view of the square part of (A) showed massive infiltration of the respiratory bronchioles by lymphoid cells resulting in stenosis (dotted arrows). The thin arrow indicates a muscular artery. Many foamy cells were seen (thick arrows). ×100, HE

inflammation of the respiratory bronchiole and inflammation of the upper and lower airways. It was reported that chronic sinusitis at presentation was found in at least 78% of patients with diffuse panbronchiolitis.[3] Unfortunately, we did not obtain information regarding sinusitis from his history. Because we suspected diffuse panbronchiolitis from the high-resolution computed tomography findings, it may have been better to consult an otolaryngologist before his biopsy. With a history of chronic paranasal sinusitis, he would have fulfilled all the diagnostic criteria.[2]

Typical findings of a high-resolution computed tomography scan include centrilobular nodular opacities, nodular, and linear (tree-in-bud) opacities corresponding to bronchioles with intraluminal mucus plugs, and thickened and dilated bronchial walls (bronchiolectasis). We diagnosed early-phase diffuse panbronchiolitis because the patient showed well-defined centrilobular nodular opacities and tree-in-bud opacities without bronchiectasis and did not demonstrate any large cystic opacities accompanied by dilated proximal bronchi, which are found in late-phase diffuse panbronchiolitis.[4] As differential diagnoses for diffuse panbronchiolitis, similar findings may be seen in patients with hypogammaglobulinemia, cystic fibrosis, primary ciliary dyskinesis, allergic bronchopulmonary aspergillosis, mycobacterial infection, granulomatosis with polyangiitis, sarcoidosis, diffuse aspiration bronchiolitis, human T-cell lymphotropic virus type 1-associated bronchiolitis, Young syndrome, and bronchiolitis obliterans.[5] This case showed no remarkable laboratory test results. With regard to the previous hospital's diagnosis of hypersensitivity pneumonia following imaging, it was reported that a high-resolution computed tomography scan generally showed ground-grass opacities and ill-defined centrilobular nodules reflecting cellular infiltration.[6] A transbronchial biopsy has a low sensitivity for diffuse panbronchiolitis because the histologic lesions of diffuse panbronchiolitis are centered around the respiratory bronchi. However, a bronchoscopy with bronchoalveolar lavage and transbronchial biopsy are helpful in identifying other processes (eg, infection, sarcoidosis). A lung biopsy can be performed for a definitive diagnosis of diffuse panbronchiolitis. However, it is often not necessary when a case fulfills the predescribed criteria.[2,3]

Pathological differential diagnoses include constructive bronchiolitis and follicular bronchiolitis. However, the main location of the lesion is a membranous bronchiole with fibrous obstruction or germinal center formation. In addition, a respiratory bronchiole is not usually affected. Another differential diagnosis is eosinophilic bronchiolitis characterized by massive infiltration of eosinophils within respiratory and membranous bronchioles. This case was diagnosed as diffuse panbronchitis because a prominent involvement of the respiratory bronchioles without infiltration of eosinophils is a distinctive characteristic of the condition.[7]

With regard to therapy, many studies have established the efficacy of erythromycin in improving symptoms, as was seen in the present case. The duration of treatment remains unclear.[5,8] This patient was treated for 4 years and has not had a relapse in the 2 years after stopping treatment.

Currently, cases with definitive diagnosis of diffuse panbronchiolitis may be rare because macrolides are routinely prescribed in clinical practice. We should differentiate diffuse panbronchitis and confirm whether the case fulfills the previously described diagnostic criteria in case of patients with persistent cough, sputum, and exertional dyspnea or with well-defined centrilobular nodules that are at least 5-10 mm from the pleural surfaces on chest computed tomography images.

We reported this rare case of early-phase diffuse panbronchiolitis, which was proven histologically. Our report demonstrates the importance of obtaining medical history, seeking expert opinion (ie, consultation of otolaryngology), and determining differential diagnosis of centrilobular nodules observed on images.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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