Official Case Reports Journal of the Asian Pacific Society of Respirology
Respirology Case Reports
OPEN ACCESS
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Organizing pneumonia associated with multicentric reticulohistiocytosis

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Keywords
Multicentric reticulohistiocytosis, organizing pneumonia.

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Received: 05 June 2015; Revised: 01 August 2015; Accepted: 18 August 2015.

Respirology Case Reports **2015; 3(4): 125–127**

doi: 10.1002/rcr2.125

Abstract

Organizing pneumonia (OP) is a clinicopathological entity that occurs idiopathically or in association with several conditions such as connective tissue diseases. Multicentric reticulohistiocytosis (MRH) is a systemic disease characterized by polyarthritis and mucocutaneous lesions, but lung involvement is uncommon. We report a patient with MRH associated with OP. This case may be of interest when considering the pathophysiological mechanisms of both diseases.

Introduction

Multicentric reticulohistiocytosis (MRH) is a rare disease of unknown etiology characterized by destructive polyarthritis and mucocutaneous lesions. Histologically, numerous multinucleated giant cells and histiocytes appear as a dense infiltrate in the dermis [1]. Although MRH is considered to be a systemic disorder, lung involvement is uncommon. Organizing pneumonia (OP) is a clinicopathological entity that occurs idiopathically or in association with several conditions [2]. We recently encountered a patient with MRH-associated OP. This case may be suggestive when considering the pathophysiological mechanisms of both diseases.

Case Report

A 65-year-old woman was referred to our hospital because of polyarthralgia and cutaneous nodules. About 6 months previously, she had developed arthralgia of the knees, proximal interphalangeal (PIP) joints, and metacarpophalangeal (MP) joints. She experienced morning stiffness that lasted for about 10 min, and her serum rheumatoid factor level was elevated. Chest X-ray showed tiny consolidations in the right lower lung field. Under a presumptive diagnosis of rheumatoid arthritis, methotrexate (8 mg/week) was started 5 months before presentation to our hospital and resulted in partial resolution of her joint symptoms. Several months later, she developed multiple cutaneous nodules on her fingers (Fig. 1A). Her medical history included cerebral infarction and hypertension, for which she had been treated with aspirin and amlodipine for several decades.

At the current presentation, she had no respiratory symptoms. Physical examination revealed multiple small erythroid papules of the periungual regions and dorsal aspects of her fingers. Her knees, PIP joints, and MP joints were swollen. Her body temperature was 35.8°C, and crackles were not audible on auscultation. Laboratory findings showed a white blood cell count of 5100/μL and a C-reactive protein level within the normal range. Her rheumatoid factor level was elevated at 62 IU/mL, but antibodies to cyclic citrullinated peptide and antinuclear antibody were negative. Radiographic imaging of her hands showed destruction of the distal interphalangeal joints and slight erosion of the PIP joints, which had progressed for about 5 months. Skin biopsy demonstrated a well-circumscribed dermal nodule infiltrated by numerous

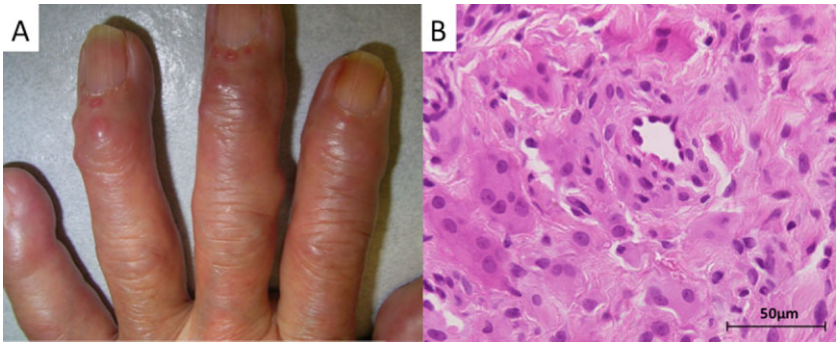

Figure 1. (A) Multiple small erythroid papules of the periungual regions of the fingers. (B) High-power magnification of the skin biopsy specimen demonstrating the presence of histiocytes and multinucleated giant cells with eosinophilic ground glass cytoplasm.

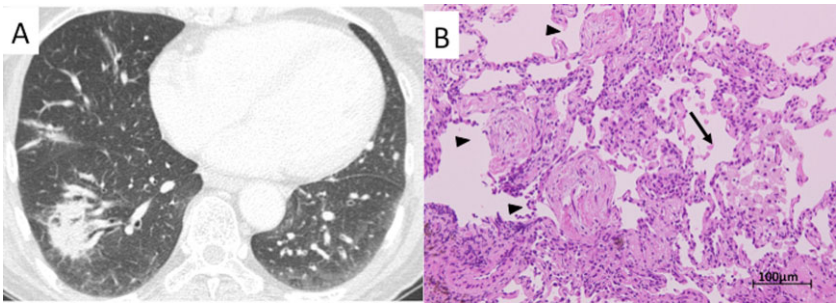

Figure 2. (A) Chest computed tomography scan showing consolidations in the right middle and lower lobes. (B) Histological findings of transbronchial biopsy obtained from the left lower lobe demonstrating organizing pneumonia (arrowheads). Foamy macrophages have accumulated in the alveolar spaces (arrow).

histiocytes and giant cells with eosinophilic ground-glass cytoplasm (Fig. 1B). Immunohistochemistry showed positivity for CD68, but negativity for CD1a. All clinical and pathological findings were consistent with MRH. Chest X-ray showed worsening of the right lower lobe consolidation with new airspace opacities in the right middle lung field. Computed tomography (CT) showed multiple consolidations with air bronchograms in the right middle and lower lobes (Fig. 2A). The mediastinal and hilar lymph nodes were enlarged. Bronchoalveolar lavage findings were negative for malignant cells and pathogenic organisms; the total cell count was 0.38×10^5 cells/mL (92.0% alveolar macrophages, 4.3% lymphocytes, and 0.7% neutrophils), and the CD4/CD8 ratio was 1.79. Transbronchial lung biopsy (TBLB) showed mild alveolitis with lymphoid cell infiltration and intra-alveolar organizations, which were consistent with OP; however, no vasculitis, granuloma formation, necrosis, or histiocyte infiltration was found (Fig. 2B). Endobronchial ultrasound-guided transbronchial needle aspiration of a mediastinal lymph node showed only scant lymphoid tissue and no malignant cells, histiocytes, or giant cells. Further evaluation for underlying malignancy was unrevealing. Methotrexate was discontinued because of no improvement in her cutaneous lesions, and salazosulfapyridine was started. About 6 months later, follow-up chest CT scans revealed that the lung infiltrations had spread to the left lower lobe without resolution of the right lung infiltrations, but she had no respiratory symptoms. Her skin lesions were not remarkably changed. Based on these clinical findings, we diagnosed our patient with MRH-associated OP.

Discussion

MRH is a rare systemic disorder of unknown etiology [1]. Orkin et al. [3] reported that about 20% of patients with MRH exhibit pulmonary infiltrations on chest roentgenograms; however, they did not include any details regarding tissue examinations. Only three patients with pulmonary parenchymal involvement by MRH have been described [4–6]. One case was accompanied by usual interstitial pneumonia (UIP) [6], one was accompanied with intra-alveolar granulation tissue [4], and one resembled OP. In the present case, the patient's chest CT and TBLB findings were typical of OP, but direct lung involvement by MRH was not detected histologically.

OP is a clinicopathological entity, and it is speculated that immunological and inflammatory processes are involved in its development [2]. West et al. [6] described a patient with MRH with UIP who had initially been diagnosed with undifferentiated connective tissue disease; the authors proposed the interplay between MRH and a systemic inflammatory process. Our case may support this hypothesis. However, further research is needed to fully elucidate the mechanism behind the link between MRH and OP.

Many kinds of medications can cause OP [2]. Thus, methotrexate may be a cause of OP. However, definitive diagnosis of drug-induced lung toxicity is difficult because clinical, radiologic, and pathological findings are nonspecific [7]. The typical clinical features of methotrexate pneumonitis include progressive dyspnea and cough that are often associated with fever [7]. Hypoxemia is always present [7], and chest CT findings frequently show bilateral ground-glass opacities and consolidations [8]. Our patient had no respiratory symptoms, and her chest X-ray findings of tiny consolidations in the right lower lobe progressed gradually and had been detected before methotrexate treatment. Her clinical findings were not typical for methotrexate pneumonitis, and we diagnosed her with OP associated with MRH. However, we could not completely exclude methotrexate as a contributor to the pulmonary infiltrates. Among the previous reports of MRH with pulmonary involvement [4–6], two patients were treated with methotrexate [4, 6]. Further investigations are needed to clarify whether methotrexate is associated with pulmonary involvement in patients with MRH.

Disclosure Statements

No conflict of interest declared.

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

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