Organizing Pneumonia with a Positive Result for Anti-CCP Antibodies as the First Clinical Presentation of Rheumatoid Arthritis

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Abstract

We report an 86-year-old woman who presented with organizing pneumonia (OP) with a positive anti-cyclic citrullinated peptide (anti-CCP) antibodies as the first manifestation of rheumatoid arthritis (RA). She experienced dyspnea, chest X-ray showed diffuse alveolar exudates indicated OP histologically. Although she did not present with articular symptoms initially, anti-CCP antibodies measured for differentiation of RA were positive. Eight months later, she showed representative manifestations of RA. Even though OP following joint involvement is frequent in RA, in rare cases it could be the first manifestation. This is the first case showing OP with a positive result for anti-CCP antibodies as the first manifestation of RA.

Key words: anti-CCP antibodies, interstitial lung disease, organizing pneumonia, rheumatoid arthritis


Introduction

Interstitial lung disease (ILD) is a frequent extra-articular manifestation of rheumatoid arthritis (RA), and a source of substantial morbidity and mortality for affected patients. The histopathological and radiographic appearances of RA-associated ILD (RA-ILD) are heterogeneous, usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), and organizing pneumonia (OP). ILD with joint involvement is often diagnosed as RA (1, 2). However, pulmonary involvement such as OP is often observed during the follow-up period of joint pain associated symptoms. When pulmonary abnormality precedes joint symptoms, diagnosis of RA is not made immediately (3, 4). This delayed diagnosis may be a disadvantage for the prompt induction of effective treatment. We present a woman with clinical and histopathological diagnosis of OP with a positive result for anti-cyclic citrullinated peptide (anti-CCP) antibodies as the first manifestation of RA.

Case Report

An 86-year-old Japanese woman had symptoms of fever, dry cough, and progressive dyspnea in mid-March 2009. Her laboratory results upon admission were as follows: white blood cell count, 10,400 cells/μL; C-reactive protein (CRP), 10 mg/mL; Mycoplasma IgM antibodies (-); Legionella urinary antigen test (Binax NOW, Portland, ME, USA) (-); QuantiFERON-TB Gold (QFT-G) (-); KL-6, 236 U/mL; SP-D, 218 ng/mL. Because infectious disease was first assumed to be the cause of her symptoms, she received parenteral antibiotics, but showed no clinical improvement. Cultures of blood, sputum, and urine were performed on several occasions, but all were negative. The chest X-ray showed diffuse alveolar exudates with ground-grass opacities in both lungs, and a high-resolution computed tomography (HRCT) scan showed parenchymal exudates with
Figure 1. High-resolution computed tomography (HRCT) scan showed parenchymal exudates with ground-grass opacities in both lungs, predominantly in the upper lobes.

Figure 2. Fragment of a transbronchial lung biopsy (Hematoxylin and Eosin staining) showed intra-alveolar organization, alveolar thickening, and lymphocyte infiltrations.

Figure 3. A second HRCT scan showed partial resolution of alveolar exudates.

ground-grass opacities, suggesting an OP pattern in both lungs, predominantly in the upper lobes (Fig. 1) (5).

A transbronchial lung biopsy (TBLB) was performed and showed intra-alveolar organization, alveolar thickening, and lymphocyte infiltration (Fig. 2). The histology was compatible with OP, this is the preferred term rather than bronchiolitis obliterans organizing pneumonia (BOOP), because it should avoid confusion with other airway diseases such as constructive bronchiolitis (6). At this time, although no articular symptoms were present, the level of anti-CCP antibodies measured to differentiate OP as the first manifestation of RA was 50.8 U/mL, and other laboratory tests showed normal muscle enzymes, ANA (-), anti-SSA (-), anti-SSB (-), Jo-1 (-), RF 1/160, and matrix metalloproteinase-3 (MMP-3) was 119 ng/mL. Corticosteroid pulse therapy for progressive hypoxia was performed. Fever and dyspnea had disappeared in mid-April 2009. A second HRCT scan showed partial resolution of alveolar exudates (Fig. 3).

Because her general symptoms and respiratory status had improved markedly through the steroid pulse therapy alone, follow-up corticosteroid administration was not continued. She was discharged after confirming that there had been no relapse for two months.

Eight months later, she experienced arthralgias of finger joints and showed 6-hour duration morning stiffness which presented without respiratory symptoms. Physical examinations confirmed polyarthritis in both wrists, metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints. Laboratory tests revealed RF 1/160, anti-CCP antibodies 52.1 U/mL. X-ray of her hands showed dorsally dislocated ulnar heads. Thus, she was diagnosed as RA based on the diagnostic criteria of American College of Rheumatology.

Discussion

We present here a patient with clinical and histopathological diagnosis of OP with a positive result for anti-CCP antibodies as the first manifestation of RA. OP is defined pathologically by the presence of buds of granulation tissue progressing from fibrin exudates to loose collagen-containing fibroblasts in the distal air spaces (7). The lesions occur predominantly within the alveolar spaces, but are often associated with buds of granulation tissue occupying the bronchiolar lumen. OP may be a disorder occurring secondary to a determined cause, infectious agents, drugs, or in a specific context as a connective tissue disorder (CTD) (8). Therefore, evaluation of infectious disease and CTDs interpreting the profile of a new drug are clinically important. In this case, cultures of blood, sputum, and urine were performed on several occasions but were all negative, and there was no history of new drug administration; thus, CTDs were evaluated serologically. Although articular symptoms were not present, anti-CCP and RF results were positive.

Symptoms of CTDs usually precede lung involvement (9). ILD as the first presentation of CTDs, particularly in RA is rare (3). Recent studies have suggested that the UIP pattern is more common in the RA-ILD patient population (1). Accordingly, cases of RA preceded by OP are very rare. Cavalcas et al (4) reported a case in which a patient was diagnosed with RA six months after COP detection. In that report, OP was considered idiopathic at the beginning, and the patient received steroid treatment. The steroid dose was gradually tapered; however, six months later, the patient pre-
sented with fever and arthralgias.

We detected positive anti-CCP antibody at the time of OP occurrence in our patient. Although articular symptoms were not present initially, eight months later, she was diagnosed as RA following the diagnostic criteria of American College of Rheumatology met in this case. The anti-CCP antibody test is more specific than the commonly used RF test (95% vs 90%) and has comparable sensitivity (more than 70%) for the diagnosis of RA. These antibodies can be detected very early in the disease and have been reported to predict the development of erosive RA (10-12). In the present patient, OP with a positive result for anti-CCP antibodies is a clue of the further development of RA.

Recent studies have suggested that the majority of patients classified as idiopathic NSIP may be associated with various types of CTD including RA (9, 13). Although COP preceded articular symptoms in this case, cases of RA preceded by idiopathic UIP and NSIP could exist because the RA symptoms are usually dominant over the lung abnormalities in the population of RA-ILD patients (1, 2). In conclusion, in a patient with COP, idiopathic UIP and NSIP, the measurement of anti-CCP antibodies should be considered as a possible diagnosis of RA even if there are no articular symptoms.

References