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Learning from errors

Organising pneumonia as the first manifestation of rheumatoid arthritis

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Summary

Organising pneumonia (OP) is an inflammatory lung disease with distinctive clinicopathological features. OP can be evident during the course of rheumatoid arthritis (RA) with increased disease activity. The authors report an OP associated with RA case in which pulmonary symptoms preceded the onset of joint symptoms. An OP patient with elevated serum anticyclic citrullinated peptide antibody is likely to manifest RA in the near future, reflecting its high disease activity. Thus, an early rheumatologic consultation should be taken into consideration to make an early decision to initiate disease-modifying antirheumatic drugs therapy.

BACKGROUND

Organising pneumonia (OP) is a distinct type of intestinal pneumonia. In 1983, Davidson *et al* introduced the term cryptogenic OP (COP)[1] and in 1985, Epler *et al* described the same disease under the term of bronchiolitis obliterans with OP (BOOP).[2] The term COP has currently been preferred to BOOP because BO is a secondary or minor pathological finding which result from extension of OP to the bronchiolar lumen and there is other pathological entity 'constrictive BO' which should be differentiated from 'proliferative BO' in BOOP.[3]

The diagnosis of COP is based on the lack of any identified cause of OP characterised by typical pathological findings. While OP can also be seen in association with several other conditions such as infections, drugs and connective tissue disorders.[4] An association of OP with rheumatoid arthritis (RA) has also been described.[5–8] In most cases, OP developed during the follow-up period of joint involvement of RA. Here, we report a 71-year-old man who developed OP as the first manifestation of RA. The diagnosis of OP and how to manage for such a patient that OP precedes the onset of joint symptoms are discussed on the basis of our experience.

CASE PRESENTATION

A 71-year-old man was admitted to our hospital because of antibiotic-resistant pneumonia. Ten days before admission, he visited a general practitioner with a 4-day history of high fever, non-productive cough and malaise. He had no recent history of medication, travel or exposure to sick person, pets or other animals. Chest radiograph showed a consolidation in the right lower lung field. He was treated with levofloxacin for 7 days without benefit and was referred to our hospital. He had habitually smoked one package of cigarettes a day since he was 20-year old. On admission, the blood pressure was 126/70 mm Hg, pulse rate was 80 beats per minute, respiratory rate was 20 breaths per minute and body temperature was 37.7°C. Oxygen saturation by pulse oximetry was 96%. Auscultation of the chest revealed inspiratory crackles on the right side.

INVESTIGATIONS

On laboratory examinations, leucocytosis of 9.900/μl with normal differential counts, elevated C reactive protein of 12.3 mg/dl and elevated erythrocyte sedimentation rate of 121 mm/h were noted and the other data on blood chemistry were within normal limits. Serological findings showed that despite the absence of any articular symptoms, elevated immunoglobulin M (IgM)-rheumatoid factor (RF) of 159 IU/ml and anticyclic citrullinated peptide antibody (anti-CCP Ab) of greater than 100 U/ml, while antinuclear antibody was negative and serum levels of Kerbs von Lungren (KL)-6, a serum marker for interstitial lung disease and IgE levels were within normal levels. Sputum cultures yielded no pathogenic bacteria and sputum PCR examination for tubercle bacilli was negative. Chest radiograph showed patchy opacities in the right lower lung zone (figure 1). Chest CT revealed multiple non-segmental reticular opacities in the periphery of the right lung (figure 2). On the 6th hospital day (20-day after the pulmonary onset), he abruptly developed arthritis of the bilateral wrist joints and subsequently bilateral knee joints. Transbronchial lung biopsy (TBLB) on the 13th hospital day showed excessive proliferation of granulation tissue within the alveolar spaces ('intra-alveolar buds') and chronic inflammation in the surrounding alveoli (figure 3), consistent with OP pathology. On bronchoalveolar lavage fluid analysis, the differential white cell count showed mixed pattern of increased cellularity with 45% lymphocytes, 40% neutrophils and 15% plasma cells without the presence of eosinophils.

OUTCOME AND FOLLOW-UP

At that time, we were not sure whether such a recent-onset arthritis could be diagnosed with RA because of lack of experience. Oral prednisolone 30 mg/day was initiated without disease-modifying antirheumatic drugs

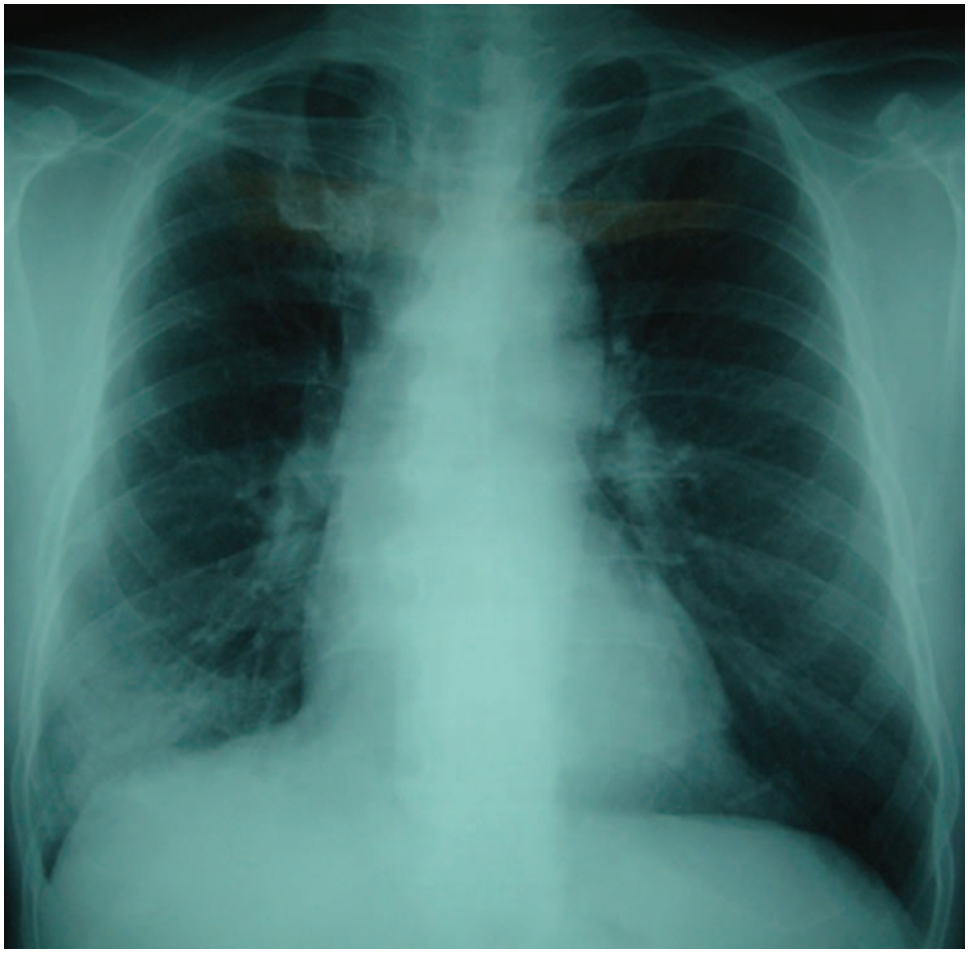

Figure 1 Chest radiograph showed patchy opacities in the right lower lung zone.

(DMARDs) for OP, which resulted in rapid improvement in clinicoradiographic findings of OP with resolution of the articular symptoms. On T1-weighted MRI of the right wrist 7-week after the onset of joint symptoms, several carpal erosions, which was not yet evident on plane radiograph, were noted under treatment with predonisolone tapered to 15 mg/day despite no recurrence of articular symptoms. As the MRI findings raised the possibility of a definite diagnosis of RA,[9] we contacted a rheumatologist and outpatient appointment was scheduled next week.

When the dose of prednisolone was tapered to 10 mg/day just before the rheumatology appointment, the joints involvements including multiple proximal interphalangeal and metacarpophalangeal joints, bilateral wrist and knee joints flared 8-week after the first joint symptoms, while no recurrence of OP was evident. A definite diagnosis of RA was made by the rheumatologist and combination therapy of 8 mg/week methotrexate with 200 mg/day bucillamine, an analogue of d-penicillamine[10] used as a popular DMARD in Japan, was initiated[11] with the informed consent of the patient.

DISCUSSION

In RA, pulmonary involvement is one of the extra-articular manifestations. In a study of CT findings of RA patents, four major patterns were identified with usual interstitial pneumonia, non-specific interstitial pneumonia, bronchiolitis and OP.[12] In a review of OP associated with RA in the literature from 1987 through 2006,[7] most OP developed in cases with persistent RA for at least several years, while only a few cases that pulmonary manifestations preceded or simultaneously occurred with the onset of joint involvements have been described.[6–8] According to the review, development of OP was likely a significant relationship with disease activity of RA because many OP patients with RA had a high titre of RF.[7]

The radiographic features of OP are distinctive; multiple patchy airspace consolidation, small nodular opacities and small linear opacities are usually seen with the subpleural or peribronchial distribution.[13] The definitive diagnosis of OP depends on the typical pathological feature. An open lung biopsy or video-assisted thoracoscopy is preferred to obtain specimens enough for the diagnosis to be made,[14] while TBLB occasionally fails to provide an adequate sample to rule out other disorders. In the present case, a diagnosis of OP was made because in addition to the typical OP pathology, the clinical, laboratory and radiographic findings could rule out other conditions such as infectious disease, drug reaction, fume or toxic exposures, hypersensitivity pneumonitis, eosinophilic lung disease and other connective tissue diseases. However, if the future clinical course would be unusual for OP, an open or thoracoscopic lung biopsy would be reconsidered.

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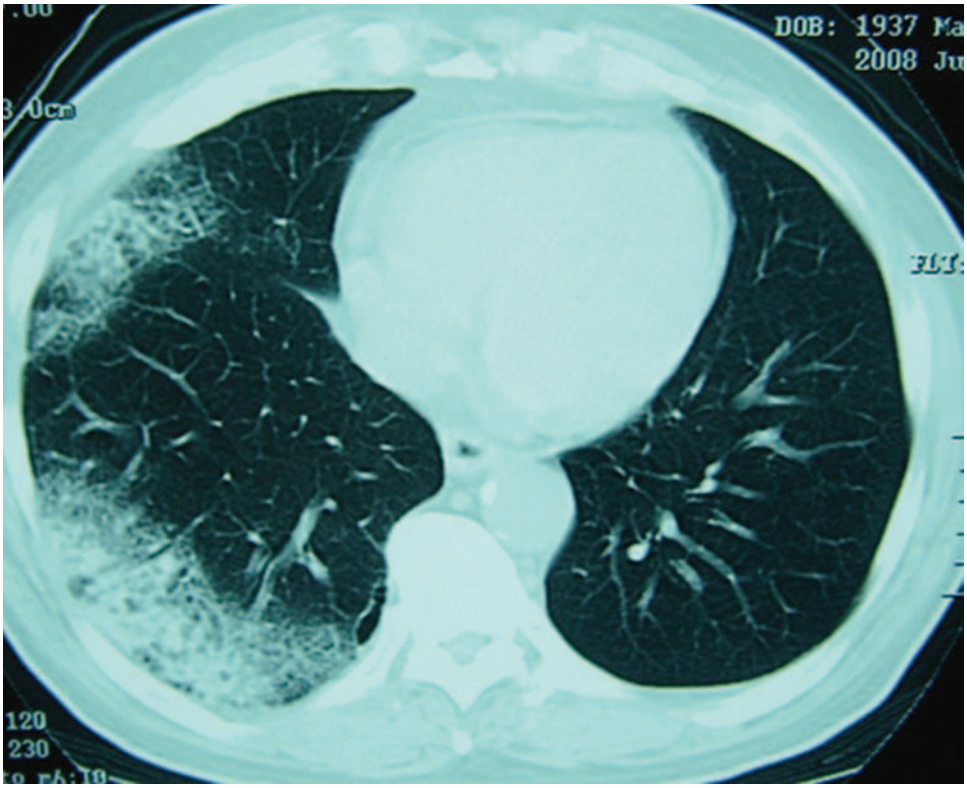

Figure 2 Chest CT revealed multiple non-segmental reticular opacities in the periphery of the right lung.

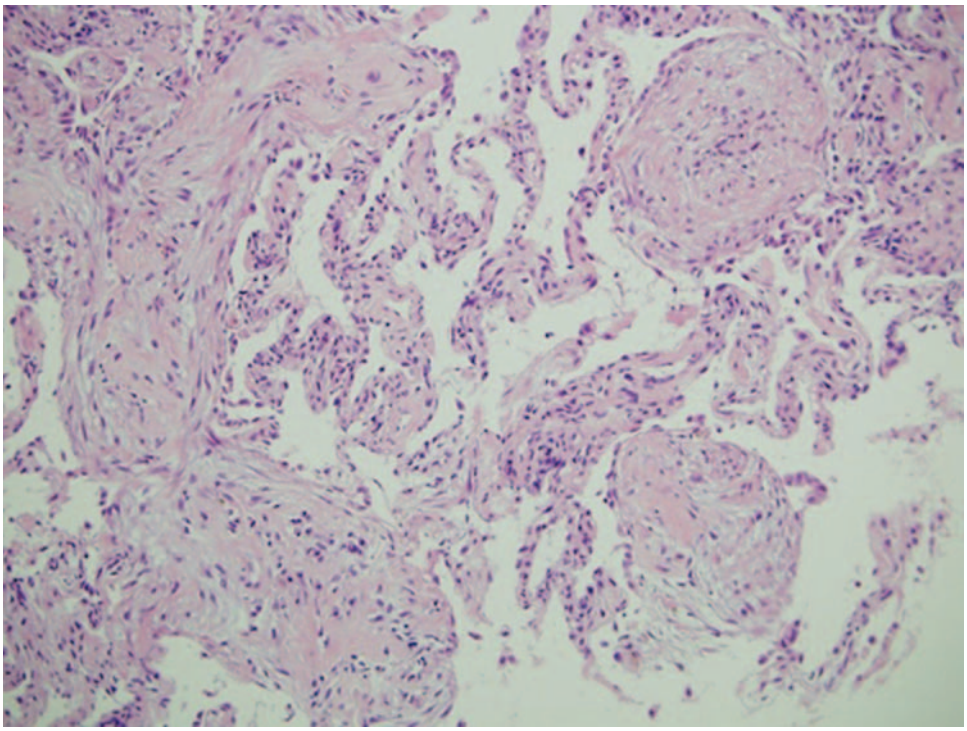

Figure 3 The histological findings of transbronchial lung biopsy showed excessive proliferation of granulation tissues within the alveolar spaces ('intra-alveolar buds') and chronic inflammation in the surrounding alveoli (H&E staining ×200).

The prognosis of OP associated RA is generally favourable because most patients rapidly respond to corticosteroid therapy.[7] However, corticosteroid can mask articular symptoms necessary for early diagnosis, as with the present case. In RA, ideally, DMARDs therapy should be initiated within 'a window of opportunity', during which aggressive DMARDs therapy could provide more optimum therapeutic effect,[15] and therapeutic delay could

result in substantially radiographic damage.[16] However, 1987 American College of Rheumatology (ACR) criteria was not considered optimal diagnostic tool for RA in early stage because of its low discriminative value in patients with undifferentiated arthritis (UA).[17 18]

Recently, the detection of serum anti-CCP Abs has proven to be a significant predictor of RA because of its higher specificity.[19] In an inception cohort of patients with recent-onset UA, testing for anti-CCP Abs allowed accurate prediction that 93% of patients eventually fulfilled the 1987 ACR criteria after 3-year of follow-up,[20] and these autoantibodies can be detected years before RA symptoms develop.[21] In addition, anti-CCP Abs testing results has been included in one of four major categories of the 2010 ACR/European League Against Rheumatism classification criteria for early diagnosis of RA published 2-year after we experienced the present case.[22]

Accordingly, when the patient first developed joint symptoms, we should have considered OP, even though its onset preceded articular manifestations, as an extra-articular manifestation of RA in the presence of high autoimmune activity and an early rheumatologic consultation, not initiation of prednisolone therapy alone, should have taken into consideration to make an earlier decision to initiate DMARDs therapy. In addition, an earlier diagnosis of RA associated OP might make us decide to slowly taper the prednisolone dosage, leading to the possible avoidance of the joint flare up.

We must admit that our diagnostic strategy was insufficient for an early initiation of DMARDs therapy, resulting in progression of the joint damage. Accordingly, by describing our trial-and-error diagnostic process in this case report, we would like to share our experience with clinicians, who possibly encounter such a patient with unusual first manifestation of RA.

In conclusion, in a case with OP, even without joint symptoms, serum anti-CCP Ab should be measured because elevated anti-CCP Ab is likely to manifest RA in the near future, reflecting its high disease activity. Thus, in such a case, an early rheumatologic consultation should be taken into consideration to make an early decision to initiate DMARDs therapy.

Learning points

- In a case with OP, even without joint symptoms, serum anti-CCP Ab should be measured.
- OP with elevated anti-CCP Ab is likely to manifest RA in the near future, reflecting its high disease activity.
- In such a case, an early rheumatologic consultation should be taken into consideration to make an early decision to initiate DMARDs therapy.

Competing interests None.

Patient consent Obtained.

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