Respiratory Medicine Case Reports 21 (2017) 147–150

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Re-administration of abatacept for the control of articular symptoms of rheumatoid arthritis during anti-tuberculous therapy

Hironori Kawamoto, M.D. [a, *], Jin Takasaki [b], Satoru Ishii [b], Manabu Suzuki [b], Eriko Morino [b], Go Naka [b], Motoyasu Iikura [b], Shinyu Izumi [b], Yuichiro Takeda [c], Haruhito Sugiyama [b]

[a] Division of Respiratory Diseases, Department of Internal Medicine, The Jikei University School of Medicine, Tokyo, Japan
[b] Division of Respiratory Diseases, Department of Internal Medicine, National Center for Global Health and Medicine, Tokyo, Japan
[c] Division of Respiratory Diseases, Department of Internal Medicine, Kohnodai Hospital, National Center for Global Health and Medicine, Tokyo, Japan

ARTICLE INFO

Article history:
Received 21 February 2017
Received in revised form
9 April 2017
Accepted 10 April 2017

Keywords:
Tuberculosis
Biological agent
Abatacept
Paradoxical reaction
Rheumatoid arthritis

ABSTRACT

This case report describes the re-administration of abatacept to successfully reduce the articularsymptoms of a patient with rheumatoid arthritisduring the intensive phase of anti-tuberculous therapy. A 75-year-old man developed active pulmonary tuberculosis during the administration of abatacept for rheumatoid arthritis. The patient experienced a paradoxical reaction and exacerbation of rheumatoid arthritis that caused us to discontinue the abatacept. Later re-administration of abatacept along with anti-tuberculosis treatment led to well-controlled rheumatoid arthritis without exacerbation of the tuberculosis. This case shows that re-administration of abatacept may be much safer than TNF inhibitor to treat patients who are infected with mycobacteria during thetreatment of immunological diseases such asrheumatoid arthritiswith biological agents.

1. Introduction

Biological agents such as abatacept are widely used in patients with moderate-to-severe active rheumatoid arthritis (RA). However, biological agents increase the risk of reactivation of the latent tuberculosis (TB) infection [1]. The American College of Rheumatology proposes that biological agents can be re-administered to patients with active TB after completion of anti-TB therapy [2]. The British Society of Rheumatology recommends that patients who are treated with biological agents should receive full anti-TB chemotherapy if clinically indicated [3].

Stopping treatment with biological agents increases the risk of exacerbating the disease attributable to the recovery of the biological agent-dependent inflammation. When RA patients are treated with biological agents that exacerbate pre-existing tuberculous lesions or cause the development of new lesions, this is termed a paradoxical reaction. Patients with a paradoxical reaction typically show fever, pulmonary infiltrates, and hypoxemia [4]. It is necessary to control the active TB as well as the RA in a paradoxical reaction.

Here, we describe a RA patient who developed active TB during the initiation of abatacept, which is not an anti-tumor necrosis factor (TNF) agent, and whose RA and TB were successfully controlled by the re-administration of abatacept after anti-TB treatment.

2. Case report

A 75-year-old man was diagnosed as having RA 2 years ago because of polyarthralgia and increases in inflammatory reactions, rheumatoid factor and anti-cyclic citrullinated peptide antibody. At first, prednisolone (PSL) was prescribed at 5 mg per day, and salazosulfapyridine and methotrexate were added shortly thereafter because his RA was not under good control. After half a year, abatacept was also added because the above-mentioned medicines were still not enough to control the RA. After the addition of abatacept, his RA had been well controlled.

Two years later, he complained of a cough and slight fever. Laboratory data indicated increased inflammatory reaction, and a chest X-ray and computed tomography (CT) scan revealed consolidation in the right upper field lung (Fig. 1A and B). The patient's

* Corresponding author. Department of Respiratory Medicine, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo, 162-8655, Japan.
E-mail address: h5amm1212@yahoo.co.jp (H. Kawamoto).

http://dx.doi.org/10.1016/j.rmcr.2017.04.013

previous physician suspected bacterial pneumonia, discontinued the abatacept, and prescribed new quinolone antibiotics. However, the patient's pulmonary symptoms and laboratory data did not improve, and his RA was getting worse. Thereafter, *Mycobacterium tuberculosis* was confirmed by polymerase chain reaction and culture of his sputum. The isolated *M. tuberculosis* was susceptible to all anti-TB drugs. The result of a T-SPOT® TB test was indeterminable, and his C-reactive protein and matrix metalloproteinase 3 levels were elevated (Table 1).

After the diagnosis of TB, an anti-TB regimen comprising isoniazid, rifabutin, ethambutol and pyrazinamide was initiated. His cough improved although he still had a slight fever after the anti-TB regimen. On the 21st day of therapy, he experienced breathlessness, and oxygen at 2 L was necessary to maintain his blood oxygen level. A chest X-ray and CT scan showed progression of consolidation in the right upper field lung and new consolidation in the left upper field lung (Fig. 2A and B). A paradoxical reaction was suspected because consolidation in the pre-existing lesions had worsened and a new lesion appeared even though his clinical symptoms had improved with the anti-TB regimen. We added steroid pulse therapy (methylprednisolone at a daily dose of 1000 mg for 3 days) to the ongoing anti-TB therapy, after which his chest X-ray, oxygen saturation and RA symptoms immediately improved. After steroid pulse therapy, PSL 60 mg per day was used as steroid maintenance therapy. After steroid therapy for one month, almost all consolidations in the bilateral upper lung fields had disappeared (Fig. 3). We began to gradually taper the dose of PSL every week because his clinical course was uneventful.

When the PSL was reduced to 15 mg per day, he experienced exacerbation of left knee joint pain, and was no longer able to walk.

Table 1
Laboratory data on admission.

Hematology	
White blood cells	8170/μL
Hemoglobin	12.4 g/dL
Platelets	28.3×10^4/μL
Serology	
Albumin	3.4 g/dL
AST	19 U/L
ALT	18 U/L
Creatinine	0.78 mg/dL
C-reactive protein	6.3 mg/dL
Hemoglobin A1c	6%
Biochemistry	
Anti-CCP antibody	783.4
MMP-3	300.4
RF	228.3 IU/mL
T-spot TB	Indeterminable

AST, aspartate aminotransferase; ALT, aspartate aminotransferase; CCP, cyclic citrullinated peptide; MMP-3, matrix metalloproteinase 3; RF, rheumatoid factor; TB, tuberculosis.

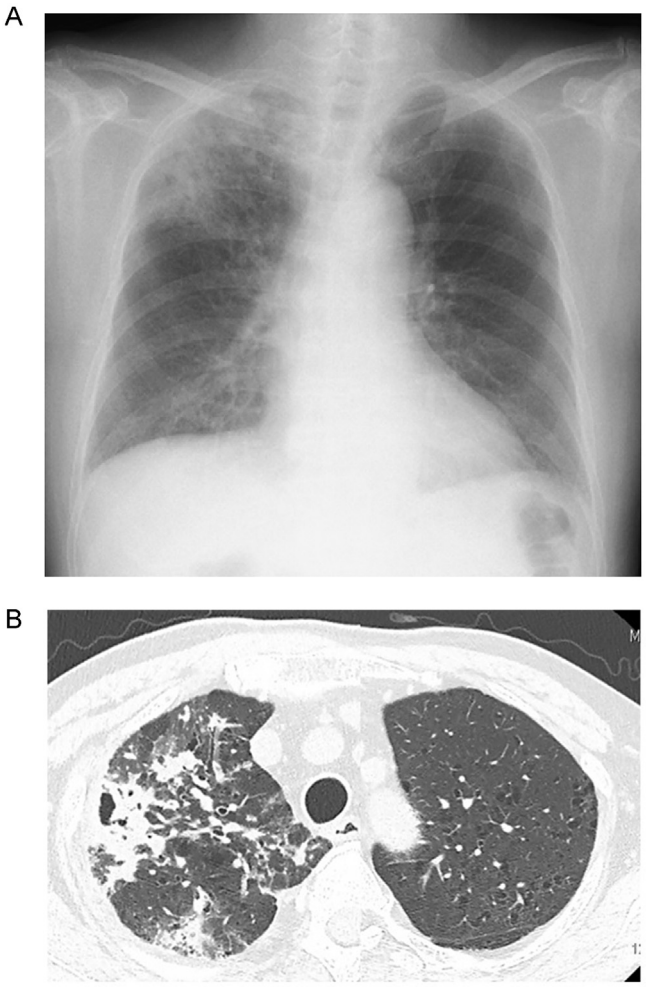

Fig. 1. (A) Chest X-ray shows consolidation in the right upper lung field and ground glass opacity in the bilateral lung bases. (B) Chest computed tomography shows emphysema, consolidation and granular shadows in the right upper lobe.

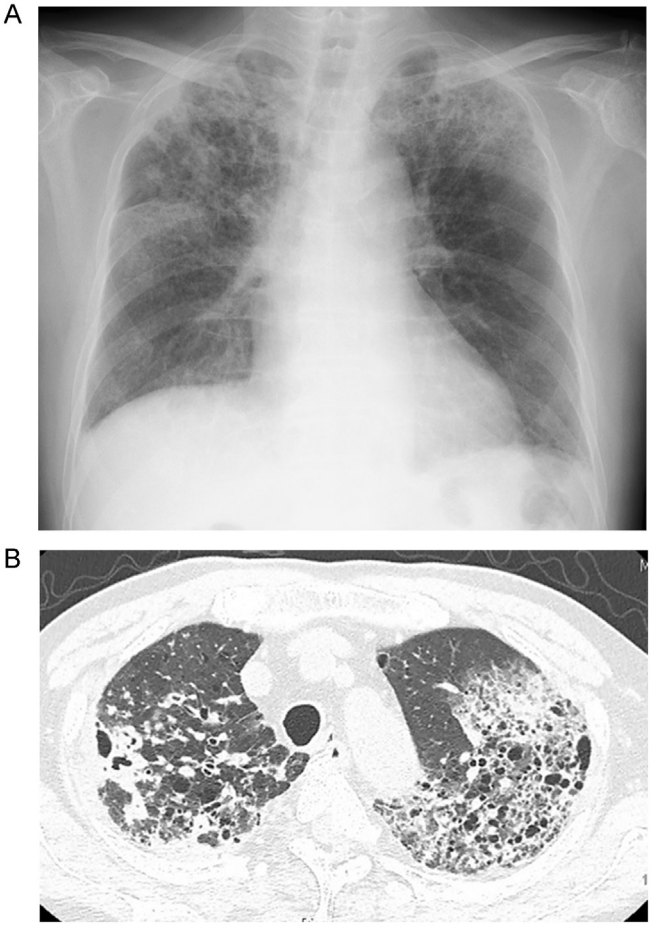

Fig. 2. (A) Chest X-ray shows exacerbation of the consolidation in the right upper lung field and the spread of consolidation to the left upper lung field. (B) Chest computed tomography shows the spread of consolidation in the bilateral lung lobes.