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Case Report

A case of acute respiratory failure in a rheumatoid arthritis patient after the administration of abatacept

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Abstract

Drug-induced pulmonary disease is an important consideration in the differential diagnosis of patients with rheumatoid arthritis (RA) who present with respiratory symptoms. We report a patient with RA who developed acute respiratory failure two weeks after the administration of abatacept. The clinical findings were consistent with drug-induced acute respiratory failure, most likely acute eosinophilic pneumonia. Pulse steroid was administered at 1000 mg/kg/day in the emergency department. Chest X-ray and arterial blood gas values revealed significant improvement on the second day of hospitalization. However, in the second week, the patient's fever rose up to 40°C, procalcitonin level increased to 15 ng/mL (<0.5 ng/mL is normal), and the patient died because of sepsis in the fourth week. This is the second report of respiratory failure, after the abatacept administration in the literature. We have reported an acute respiratory failure that occurred after use of the biological agent abatacept. With the increasing use of novel immunomodulatory agents, it is important for clinicians and pathologists to add the possibility of a drug reaction to the traditional differentials of acute respiratory failures occurring in these settings.

Keywords: Abatacept, arthritis, rheumatoid, respiratory insufficiency

Introduction

Rheumatoid arthritis (RA) is a generally progressive, systemic autoimmune disease characterized by chronic symmetrical erosive synovitis. The lung and pleura are also frequent sites of extra-articular involvement by RA.

Comorbid pulmonary disease is common in patients with RA and may also be a complication of therapy (1). Therapeutic agents with a potential for causing adverse pulmonary effects include methotrexate (MTX), leflunomide (LEF), tumor necrosis factor inhibitor (TNFi), sulfasalazine, parenteral gold, abatacept, and rituximab (RTX).

Drug-induced pulmonary disease is an important consideration in the differential diagnosis of patients with RA who present with respiratory symptoms (2). We report a case of RA who developed acute respiratory failure 2 weeks after the administration of abatacept.

Case Presentation

A 70-year-old female patient was admitted to the emergency department with dyspnea, which was present for the last 2 days. She did not complain of any cough, sputum, and chest pain. There were diffuse crackles in both lungs at the physical examination. Routine blood tests were nonspecific. Arterial blood gas analysis revealed severe hypoxemia. Chest X-ray revealed diffuse infiltrates in both lungs, although it was normal 15 days ago (Figure 1). The patient with a diagnosis of RA has been followed up by the rheumatology department for nearly 20 years. A total of two doses of abatacept (10 mg/kg) (Orencia; Bristol-Myers Squibb medical, New York, USA) were administered in 15-day intervals. Two weeks after the second dose, the patient was brought to the emergency room by an ambulance because of the deterioration of general condition. The patient did not use other drugs. The clinical findings were consistent with drug-induced acute respiratory failure, most likely acute eosinophilic pneumonia. Pulse steroid was administered at 1000 mg/kg/day for 3 days in the emergency department. Non-invasive mechanical ventilation was performed, but there was no response. The patient was admitted to the intensive care unit and was intubated. Because we could not distinguish infections such as *Pneumocystis carinii*, broad-spectrum antibiotics were also administered. Bronchial lavage cytology was not significant; cultures were negative. Chest X-ray and arterial blood gas values revealed significant improvement on the second day (Figure 2). Steroid dose tapered off 60 mg/day after the third day. After 3 days, the dose reduced to 50 mg/day. However, in the second week, the patient's fever rose up to 40°C, procalcitonin level increased to 15 ng/mL (<0.5 ng/mL is normal), and the patient died because of sepsis in the fourth week.

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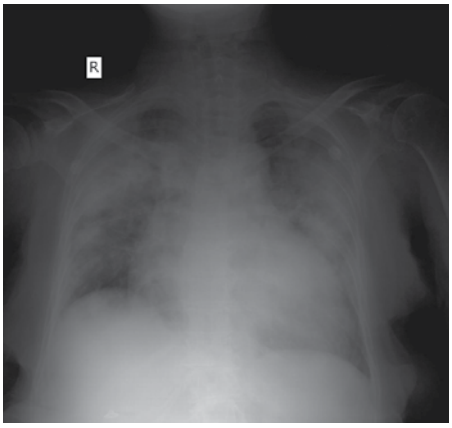

Figure 1. Chest X-ray revealed diffuse infiltrates in both lungs

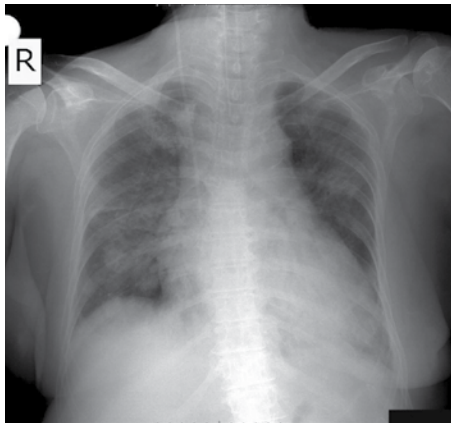

Figure 2. Chest X-ray revealed significant improvement on the second day

Discussion

It is known that non-biologic disease-modifying antirheumatic drugs (DMARDs) and biologics can induce or exacerbate interstitial lung disease (ILD) in RA.

The side effects related with the lung for MTX is already known, and it must also be considered that LEF, TNFi, RTX, and tocilizumab (TCZ) may induce pneumonitis or worsen RA-related ILD (3, 4).

Abatacept is a soluble fusion protein that is effective for the treatment of RA. It consists of the extracellular domain of cytotoxic T lymphocyte antigen 4 (CTLA4) and the Fc portion of immunoglobulin G1 (IgG1). CTLA4-Ig binds CD80 (B7-1) and CD86 (B7-2) on antigen presenting cells, thereby acting as a competitive inhibitor of the CD28-B7 costimulatory interaction. Because soluble CTLA4-Ig binds to CD80 (B7-1) and CD86 (B7-2), it prevents the second activation signal received by T cells via CD28 (5, 6). It has been approved by the United States Food and Drug Administration for the treatment of patients with moderately to severely active RA who have had an inadequate response to one or more DMARDs or TNFi (7).

This is the second report of respiratory failure, after the abatacept administration in the literature. The first case was reported by Wada et al. (8) in 2012.

It is believed that the immunosuppression induced by rheumatologic disease itself and exacerbation by immunomodulatory therapies predispose to infection and subsequently respiratory failure. Abatacept might be the cause of respiratory failure, but other possibilities such as flare-up RA itself, cardiogenic pulmonary edema, or viral-bacterial infections should be considered. Cardiogenic pulmonary edema was excluded via transthoracic echocardiography, and bronchial lavage cytology was not significant; cultures were negative. Viral and diffuse bacterial pneumonia and acute inhalational injuries are excluded. However, the patient's general condition deteriorated after abatacept administration; respiratory failure was more likely to depend on abatacept.

The underlying mechanism is unclear. It has been suggested that the interference with CTLA-4 signals in regulatory T-cells result in the impaired suppressive functions of those cells and in the exacerbation of T helper 17 (Th17) immunity (9). It is possible that abatacept shares immunomodulatory pathways with tumor necrosis factor (TNF) agents, resulting in neutrophil activation. Abatacept has been shown to have an impact on the T effector functions of Th1, Th2, and Th17 cells (10).

Further cases are needed to identify the relation between abatacept and interstitial pneumonia; however, this possibility should always be considered when we use abatacept. Development of new or worsening cough, dyspnea, and radiographic abnormalities should alert the clinician to the possibility of drug-induced ILD.

In conclusion, we have reported an acute respiratory failure that occurred after the use of the biological agent abatacept. With the increasing use of novel immunomodulatory agents, it is important for clinicians and pathologists to add the possibility of a drug reaction to the traditional differentials of acute respiratory failures occurring in these settings.

Ethics Committee Approval: N/A.

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