Cytotoxic T Lymphocyte-associated Antigen 4 Ig-induced Asthma in the Treatment of Rheumatoid Arthritis

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To the Editor:

The CD28-CD80/CD86 costimulatory pathway is essential in enhancing and optimizing T cell activation and cytokine production in rheumatoid arthritis (RA). Cytotoxic T lymphocyte-associated antigen 4 (CTLA4) is a homolog of CD28. It can competitively bind to CD80/CD86 and downregulate naive and memory T cell proliferation, cytokine production, and humoral immune response. Its human soluble fusion protein, CTLA4-Ig, was approved for the treatment of active RA by the US Food and Drug Administration in 2005. Several animal studies suggest benefits of CTLA4-Ig in other immunologic diseases such as asthma. However, we describe here 2 cases of RA complicated with relapse of asthma while undergoing CTLA4-Ig therapy.

A 53-year-old Chinese woman had a 9-year history of refractory RA, and was treated with methotrexate (MTX) 7.5 mg per week and prednisone 3 mg daily. She had started CTLA4-Ig 10 mg/kg in combination with stable dosages of MTX and prednisone on August 20, 2009, because of her high RA activity. Four days later, she presented with productive cough, tachypnea, and chest distress. She did not complain of fever, rash, or joint pain. Although she was diagnosed with asthma in 1989, she did not experience any episodes of asthma in the previous 20 years. Upon admission, the laboratory examination revealed an abnormal arterial blood gas with partial pressure of oxygen 53.3 mm Hg, partial pressure of carbon dioxide 33.9 mm Hg, and oxygen saturation 88.7% on room air. The chest radiograph was normal. No evidence of bacteria (including mycobacterium tuberculosis) or fungi was noted. Her chest examination revealed diffuse wheezing in all lung fields. Episode of asthma was diagnosed. Then CTLA4-Ig was stopped, and intravenous methylprednisolone 80 mg/day was initiated with concurrent bronchodilators. The symptoms of asthma disappeared in 5 days. Steroid was tapered gradually during followup. She has had no recurrence of asthma.

In another case, a 53-year-old Chinese woman was diagnosed with RA in 1989. She still had active arthritis after multiple therapies including infliximab infusion and MTX treatment. She had no other systemic complaints although she had a few episodes of asthma during her childhood. She received 4 doses of CTLA4-Ig 10 mg/kg at Weeks 0, 2, 4, and 8, combined with MTX 10 mg weekly between July 30 and September 24, 2009. She had a good response to CTLA4-Ig, with 50% improvement in 1 month before asthma flared. However, in our 2 cases, no infection was found. They had no other systemic complaints except active arthritis before CTLA4-Ig treatment. They had not developed asthma for at least 20 years until they received CTLA4-Ig infusion. The mechanism underlying these side effects is unknown. We are not certain that the modulation of costimulatory molecules is relevant to the recurrence of asthma.

REFERENCES

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