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SYSTEMIC REACTION TO OMALIZUMAB

To the Editor:

A 76-year-old woman presented with a greater than 60-year history of steroid-dependent asthma and allergic rhinitis. She had received immunotherapy more than 30 years ago, which had been discontinued because of repeated systemic reactions. Her other comorbidities included arthritis, hypertension, and depression. Her current treatment included 500 and 50 μ g of salmeterol and fluticasone, respectively, sodium montelukast, a nasal corticosteroid, and 4 mg of methylprednisolone every other day. She received her first dose of omalizumab, 300 mg, in May 2004. She had no evident reaction until 75 minutes after the fourth dose, at which time she had sudden onset of weakness,

lightheadedness, and syncope. During her examination, before the injection, her blood pressure was 157/80 mm Hg with no evident symptoms. Immediately after her syncopal episode, her blood pressure was 60/40 mm Hg. She became cyanotic and had a brief generalized seizure. She quickly responded to epinephrine, oxygen, and volume expansion. There was no immediate evidence of rash or bronchospasm. She was transferred to the emergency department within 20 minutes, at which time she was awake and alert. Her arterial oxygen saturation was 94%, and her blood pressure was 110/78 mm Hg. The results of laboratory studies were normal except for a serum potassium level of 3.2 mmol/L, a white blood cell count of 12,400 K/ μ L, and a tryptase (α and β) level of 13 ng/mL (reference range, 2–12 ng/mL). These studies were performed approximately 180 minutes after the injection. She remained in the hospital for 36 hours with stable vital signs and no oxygen requirements.

Laboratory studies were performed 9 months after the reaction when permission was granted by Novartis to supply a specimen, with the following results: total IgE, 99.2 ng/mL; free IgE, 91.3 ng/mL; and omalizumab, 38.8 ng/mL. The level of IgE antibodies directed to anti-E25 Fc and anti-E25 Fab was 0. No further reactions have been reported.

The mechanism of this reaction is not clear. The patient had no demonstrable IgE antibody to either E25 Fc or E25 Fab. The elevated tryptase level suggests that mast cell degradation was one of the operative mechanisms in the systemic reaction. In the clinical trials, low titer of anti-IgE antibodies were detected in 1 of 1,723 patients (less than 0.1%) using an enzyme-linked immunosorbent assay. This finding did not correlate with risk of systemic reaction. More than 20,000 patients have been treated in the United States since the release of omalizumab in June 2003. The occurrence of adverse reactions is low but not zero (Table 1). This finding reinforces the need for observation after administration of the drug in a health care facility where acute reactions can be treated.

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Table 1. Anaphylaxis Cases in Omalizumab-Treated Patients*

Patient age, y/sex	Event	Treatment and outcome	Significant medical history
19/F	90 minutes after dose 1: hives, itchy ears, mild dyspnea	Epinephrine, IV steroids, antihistamine; full recovery in 8 days; omalizumab therapy discontinued	Allergies: "sneezing for 30 minutes" after immunotherapy injection
15/M	90 minutes after first infusion: moderate anaphylactoid	Epinephrine, oral steroids antihistamine, nebulized albuterol; full recovery in 1 day; omalizumab therapy discontinued	None
28/F	120 minutes after dose 4: injection site edema, periorbital swelling, throat and tongue swelling	Epinephrine, oral steroids, antihistamine; full recovery in 4 days; omalizumab therapy discontinued	Allergies: morphine, anaphylaxis associated with peanuts, chocolate, immunotherapy

Abbreviation: IV, intravenous.

* Data on file (Genetech and Novartis).