

LETTER TO THE EDITOR

Omalizumab-induced triphasic anaphylaxis in a patient with chronic spontaneous urticaria

Editor

A 37-year-old woman presented with multiple itchy hives. She had been diagnosed with chronic spontaneous urticaria (CSU) and angioedema 2 years earlier and had been taking high-dose H₁ antihistamines and intermittent systemic steroids without an efficient response. The urticaria activity score was 11. Her medical history was non-contributory. Complete blood and eosinophil counts, liver, renal, and thyroid function tests, and C3 and C4 complement levels were normal. The serum IgE level was 133 IU/mL (normal 0–87). Anti-thyroid and antinuclear antibodies were negative. A chest x-ray and pulmonary function tests were normal. Omalizumab treatment (300 mg, every 4 weeks) was started. Severe angioedema of the face, tongue, and larynx, dyspnea, tachypnea, hypotension, tachycardia, conjunctival injection, flushing, and cyanosis occurred a few minutes after the first injection. The patient was immediately given intramuscular injections of 0.25 mg adrenalin, 40 mg methylprednisolone, and 45.5 mg pheniramine maleate. After 15 min, another 0.25 mg of adrenalin was injected. All of the symptoms were relieved within 30 min. However, additional anaphylactic reactions recurred 24 and 36 h after the omalizumab injection. The same treatment regimen was given and both instances resolved within 20 min. No further anaphylaxis was reported at the 10-day follow-up.

Chronic spontaneous urticaria is a disorder characterized by itchy wheals that last for more than 6 weeks, with or without angioedema, and that has no external stimulus.¹ Although histamine release from cutaneous mast cells is the key factor in its pathogenesis, basophils and IgE may also play prominent roles.¹

Non-sedating H₁ antihistamines are the main therapy for chronic urticaria. Unfortunately, few cases have a satisfactory response to H₁ antihistamines, even when administered in high doses.¹ Omalizumab, a recombinant humanized monoclonal antibody, is becoming increasingly popular as an effective treatment option for refractory CSU.² Omalizumab binds to circulating IgE, reduces the free IgE levels, and downregulates the IgE receptors (FcεRI) on mast cells and basophils, interrupting the subsequent allergic inflammatory cascade.²

Although omalizumab is generally safe and well tolerated, it may cause anaphylaxis.³ The incidence of omalizumab-induced

anaphylaxis ranged from 0.09% to 0.2%.^{4–6} These rates were found similar to the incidence of anaphylaxis for penicillins and nonsteroidal anti-inflammatory drugs, and also to the incidence of anaphylaxis reported in general population (about 0.05–2%).⁷ The majority of the reactions (68%) occurred in the first three administrations of omalizumab; 39% with the first dose, 19% with the second, the remainder after the third and subsequent doses.⁸ Twenty four percent of omalizumab-induced anaphylaxis cases had a previous history of anaphylaxis.⁸ Our patient had no history of anaphylaxis.

Anaphylaxis is a potentially fatal allergic reaction with multiple organ-system involvement that typically follows a uniphasic course, but may be biphasic.⁹ The second attack typically occurs 1–24 h after the first phase.⁹ In our patient, anaphylaxis followed a triphasic pattern. To our knowledge, triphasic anaphylaxis during omalizumab treatment for chronic urticaria had not been reported.

To the best of our knowledge, all the cases of anaphylaxis associated with omalizumab administration have occurred in the patients with asthma.⁸ Asthma patients receiving omalizumab should be observed for 2 h after the first three injections and for 30 min after the fourth or subsequent injections, as anaphylactic reactions due to omalizumab mostly occur within these periods.³ Furthermore, delayed symptom onset and protracted progression of anaphylaxis due to omalizumab may be seen in asthma patients.⁸

In conclusion, anaphylaxis due to omalizumab may occur in CSU patients, and it may follow a triphasic pattern for 36 h after omalizumab administration. We suggest that dermatologists must follow their patients for at least 48 h to detect late reactions.

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