

Teenager Suffered from Idiopathic Anaphylaxis and Chronic Spontaneous Urticaria Successfully Treated with Omalizumab: A Case Report

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Anaphylaxis is a serious and probably lethal systemic reaction. When a trigger cannot be determined, idiopathic anaphylaxis is considered. It can occur as a complication of chronic spontaneous urticaria (CSU). In idiopathic anaphylaxis presenting with frequent attacks, long-term prophylaxis with H1-antihistamines and steroid treatment is recommended but rarely effective. Omalizumab, a humanized monoclonal antibody drug that decreases free immunoglobulin E molecules in the circulation, is approved for the treatment of chronic severe persistent allergic asthma and CSU. We report a 15-year-old female patient suffering from CSU concomitant with idiopathic anaphylaxis. Omalizumab at a dose of 300 mg once every 4 weeks was administered for 6 months. The patient has remained asymptomatic during therapy and 3 months after the end of the therapy.

Introduction

ANAPHYLAXIS IS A rare but potentially life-threatening syndrome that may progress to anaphylactic shock, including airway insufficiency secondary to bronchospasm or circulatory collapse. When a trigger cannot be determined, idiopathic anaphylaxis is considered.¹ It can occur as a complication of chronic spontaneous urticaria (CSU). Recently approved for CSU management, omalizumab is a fully humanized recombinant monoclonal antibody that binds to the fragment crystallizable (Fc) region of the immunoglobulin E (IgE) molecule that itself binds to FcεRI.^{2,3}

Case Report

A 15-year-old female presented a 2-year history of spontaneous urticaria with angioedema. The last 2 episodes were complicated by anaphylactic symptoms.

The first episode of urticaria occurred in 2012. The symptoms were diffuse nettle rash, itching, abdominal pain, and swelling of lips and tongue, started minutes after using drotaverine because of periodic abdominal pain. The symptoms resolved within 4 days due to treatment with H1-antihistamines (single dose). She was recommended discontinuation of drotaverine.

In 2013, she again experienced urticaria, itching, cramping abdominal pain, and angioedema of lips. The symptoms subsided after oral corticosteroid and H1-antihistamines. In

the Department of Allergy and Pediatrics, she underwent thorough testing and medical examination. Laboratory findings included normal values for complete blood count with differential, comprehensive metabolic panel, including anti-nuclear antibody, thyroid-stimulating hormone level, C4 level, and C1 inhibitor function and level. Also, C4 levels were all in normal range during the angioedema attacks. Skin prick tests, total IgE level, and specific IgE levels excluded atopic diseases. Celiac diseases and infection of parasites were also excluded. The patient did not attribute her urticaria with angioedema to certain foods. She had no other diseases and family medical history was unremarkable. The diagnosis of CSU was established and second-line therapy with dual dose of H1-antihistamines was administered.

The patient continued the therapy for 2 months without symptoms of CSU. Owing to headache she took ibuprofen (200 mg), and after 2 h itchy hives were observed. In the hospital, ibuprofen provocation test was performed—it was negative and the dose of H1-antihistamines was increased up to 4 times the standard dosage. The patient was asymptomatic only for 1 month. She was admitted to the emergency department because of symptoms of anaphylaxis: diffuse urticaria, pruritus, and angioedema of lips and tongue as on onset of the disease, then shortness of breath, dizziness, hypotension were presented. She needed anti-anaphylactic treatment (epinephrine, corticosteroids, bronchodilators). Self-injectable epinephrine was prescribed and the quadruple dose of H1-antihistamines was sustained.

Nonetheless, after 6 weeks she experienced one more attack necessitating epinephrine self-injection. Owing to previous unsuccessful therapies, according to recommendation of CSU treatment,² the decision for omalizumab therapy was made. The patient was administered 300 mg of omalizumab every 4 weeks. H1-antihistamines were progressively reduced to single dose daily. According to the pharmaceutical company's recommendation, omalizumab was administered for 6 months. During the treatment and 3 months later, the patient has not presented CSU or anaphylaxis symptoms. The single dose daily of H1-antihistamines as prevention was maintained.

Discussion

CSU is a common autoimmune skin disease characterized by spontaneously recurring hives, which may also be accompanied by deeper cutaneous swelling. The urticarial skin lesions occurred intermittently or continuously for more than 6 weeks.^{2,3} CSU is associated with significant psychosocial morbidity with a markedly negative impact on overall quality of life.⁴ Our patient had chronic urticaria of unknown triggers and 2 episodes of anaphylaxis, each preceded by hives. Because of the refractory lesions, omalizumab was administered. The patient experienced major improvement in her quality of life. She has not presented symptoms during 6 months of treatment and 3 months after discontinuation of omalizumab.

Omalizumab is a monoclonal antibody against IgE, nowadays approved for the treatment of persistent severe IgE-mediated asthma and as a third-line therapy for management of CSU.^{2,5} There are a few articles that report the effectiveness of omalizumab in prevention of idiopathic anaphylaxis.^{6,7} Omalizumab binds to circulating IgE, irrespective of allergen specificity. Reduction in circulating IgE and the complexes IgE-anti-IgE, make the complement system is not activated. Omalizumab has also been shown to downregulate FcεRI on basophils, mast cells, and dendritic cells, thus preventing the release of inflammatory mediators.³

At present, the results of many clinical and experimental researches have demonstrated clinically significant efficacy of omalizumab in the treatment of refractory CSU. It seems to be safe, the anaphylactic potential of omalizumab is very low. The most common adverse side effects reported by patients include viral infections, headaches, and sinus inflammation. Omalizumab is approved for children >12 years of age.⁸ In patients with recurrent anaphylaxis but without a clear identification of the causative agents, self-injectable epinephrine in the self-treatment is strongly recommended. Medical prophylaxis with glucocorticoids and H1-antihistamines might be helpful, but not always effective.¹

There is evidence that omalizumab could be effective in the treatment and prevention of idiopathic anaphylaxis. Demirtürk et al. reported a 46-year-old female patient with severe allergic asthma and idiopathic anaphylaxis who received omalizumab successfully at a dose of 375 mg once every 2 weeks.⁹ Lee presented a 41-year-old man who experienced recurrent anaphylactic events. The anaphylactic events were prevented completely by monthly injection of 300 mg of omalizumab, and the preventive effect lasted more than a month.¹⁰ Netchiporouk et al. described 4 pediatric cases (3 of them <12 years of age) presenting with severe CSU with or without delayed pressure urticaria and

with complete remission after treatment with subcutaneous omalizumab injections.¹¹

Furthermore, the use of omalizumab has been reported recently in a few cases of solar urticaria (SU).^{12,13} SU is a rare chronic photodermatosis, characterized by erythema and itchy hives on sun-exposed areas usually few minutes after ultraviolet radiation. On the basis of the pathogenetic mechanism of SU, hypothesized to be IgE mediated, the use of omalizumab has been attempted. Arasi et al. described the case of a 16-year-old girl with an 18-month history of SU, unresponsive to conventional therapies but fully responsive to omalizumab.¹² Likewise, Levi et al. reported a 6-year-old child with severe SU and angioedema.¹³ They administered 300 mg of omalizumab twice a month and observed complete remission, no side effects, and negative photoprovocation. As for now, duration of treatment is still unknown and further studies are needed to identify both effective treatment schedule and doses for eligible patients suffering from SU or CSU unresponsive to conventional treatment.

In conclusion, we reported the first case of successful usage of omalizumab as a prevention therapy for idiopathic anaphylaxis concomitant with CSU in a teenager. This report shows that anti-IgE therapy might be considered as an option to prevent anaphylactic events in patients for whom the causative agents cannot be identified or avoided.

Author Disclosure Statement

No competing financial interests exist.

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Received for publication September 21, 2015; accepted after revision November 7, 2015.

This article has been cited by:

1. Pajno Giovanni B.. 2016. Through the Looking Glass: Chronic Urticaria Treated with Anti-IgE Therapy. *Pediatric Allergy, Immunology, and Pulmonology* **29**:1, 56-57. [[Citation](#)] [[Full Text HTML](#)] [[Full Text PDF](#)] [[Full Text PDF with Links](#)]