

**A patient with steroids and antihistaminic drug allergy and newly occurred chronic urticaria
angioedema: What about Omalizumab?**

A Kutlu, E Karabacak, E Aydin, S Ozturk and B Bozkurt

Hum Exp Toxicol published online 7 November 2013

DOI: 10.1177/0960327113510539

The online version of this article can be found at:

<http://het.sagepub.com/content/early/2013/11/06/0960327113510539>

Published by:



<http://www.sagepublications.com>

Additional services and information for *Human & Experimental Toxicology* can be found at:

Email Alerts: <http://het.sagepub.com/cgi/alerts>

Subscriptions: <http://het.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

>> [OnlineFirst Version of Record](#) - Nov 7, 2013

[What is This?](#)

A patient with steroids and antihistaminic drug allergy and newly occurred chronic urticaria angioedema: What about Omalizumab?

A Kutlu¹, E Karabacak², E Aydin³, S Ozturk¹ and B Bozkurt⁴

Abstract

In this case report, successful use of omalizumab in the treatment of chronic urticarial and angioedema in a 24-year-old female patient with an allergic reaction history to almost every drug including steroids and antihistamines was presented. She also had allergy against a large number of foods, which were confirmed by oral provocation, specific Immunoglobulin E and allergy skin test.

Keywords

Allergy, drug, omalizumab

Introduction

Immunoglobulin E (IgE)-mediated allergic reactions to drugs are usually against a drug or a group of drugs, and multiple drug allergy syndrome is a rare condition.¹ The definition of multiple drug allergy syndrome varies in literature and is mainly defined as adverse reactions associated with two or more unrelated medications. In the provocation tests of the majority of patients with a history of multiple drug allergy syndrome, it is seen that reactions do not recur in most cases.²

In this case report, successful use of omalizumab in the treatment of chronic urticarial and angioedema in a 24-year-old female patient with an allergic reaction history to almost every drug including steroids and antihistamines was presented. She also had allergy against a large number of foods, which were confirmed by oral provocation, specific IgE and allergy skin tests.

Case

A 24-year-old female patient was referred to our clinic because of allergic reactions followed by a variety of drugs and food intake. The patient developed extensive urticarial rash following intake of eradication for *Helicobacter pylori* with triple therapy (amoxicillin, clarithromycin, and lansoprazole)

as well as after taking hydroxyzine, famotidine, and ranitidine. Oral contraceptive drugs containing progesterone were administered due to ovarian cysts, but these drugs caused urticarial complaints. Colchicine was administered after the patient was diagnosed for Familial Mediterranean fever by genetic studies. The patient described allergic reactions such as urticaria and angioedema after using a large number of nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics.

During the patients follow-up period in our clinic in order to determine the safety of antibiotics and NSAIDs, provocation tests were performed for many drugs with incremental doses. After provocation tests, variable degrees of urticarial reactions against

¹Department of Allergy and Immunology, GATA Haydarpaşa Training Hospital, Ankara, Turkey

²Department of Dermatovenereology, GATA Haydarpaşa Training Hospital, Istanbul, Turkey

³Department of Dermatovenereology, Kasimpasa Military Hospital, Istanbul, Turkey

⁴Department of Allergy and Immunology, Fatih University, Ankara, Turkey

Corresponding author:

Ali Kutlu, Department of Allergy and Immunology, GATA Haydarpaşa Training Hospital, Ankara, Turkey.

Email: kotiloglu@hotmail.com

ciprofloxacin, amoxicillin, ceftideron, doxycycline, nimesulide, paracetamol, benzydamine, codeine, and sodium salicylate were observed. In provocation tests for clarithromycin and ultracaine, no reaction was monitored. High serum IgE (sIgE) level was reported against ampicillin, amoxicillin, penicillin G, penicillin V, sulfamethoxazole, cephalosporin, tetracycline, and erythromycin (> 100 kU/L).

During the dental examination, because of contact with latex gloves, urticarial angioedema developed on patient's tongue, lips, and face. The patient described similar reactions after contacting low latex containing material such as steering wheel and gear lever. The allergy skin test was positive for grass pollen mixture and latex. Our patient did not have asthmatic complaints and described short-term mild rhinitis complaints in spring. The patient has noted to have many allergic reactions against nuts, peanuts, soy beans, wheat flour, and also against banana, kiwi, tomatoes, potatoes, peaches, and known to be cross-sensitive with latex. Positive sIgE antibody (class IV and above) results were found against all the above-mentioned foods (17.5 kU/L). The patient stated having angioedema reactions shortly after using cetirizine during follow-up period, urticaria attacks raised after oral provocation tests administered with cetirizine (tablet and suspension form), desloratadine, and rupatadine. During dental surgery following methylprednisolone injection, shortness of breath, hoarseness, and short-term loss of consciousness were developed due to serious allergic reaction. Dexamethasone, deflazacort, and prednisolone allergy skin tests were positive.

During the follow-up period, the patient who had numerous urticarial angioedema attacks only after contact with detected allergens (drug or food) in general, began to experience spontaneous urticaria, angioedema attacks almost every day despite the fact that she paid excessive attention to the recommended diet formed by considering latex, nickel, salicylate allergies, and food sIgE values for the last 2 months. Due to the patient's current steroid and antihistamine drug allergies, optimal treatment of urticaria-angioedema has not been possible during these attacks. Although only the feniramine maleate (IV) has provided short-term relief of symptoms, the disease could not be taken under control and adrenaline was administered for some attacks. Taking the patient's IgE-mediated reactions against many food and drugs into consideration, omalizumab treatment was considered to be

beneficial and according to the asthma treatment protocol, 300 mg anti-IgE therapy per month was administered. Following the second dose, the patient started to see benefits of the treatment significantly, and after the third dose, this benefit has been maximized. The patient's dermatological quality of life index was calculated to be 22 points before omalizumab administration and six points at the third month of the treatment.³

Discussion

Drug hypersensitivity reactions are classified as allergic or nonallergic according to the immune system joining the reaction. Patients who describe allergic reactions for three or more chemically, pharmacologically, and immunogenetically irrelevant drugs and allergy tests for these drugs with negative results (skin prick tests (SPTs) and sIgEs) fit the situation called "multiple drug intolerance syndrome" (MDIS).⁴ These patients believe themselves to be allergic to all drugs. The vast majority of patients with drug allergies are allergic to one drug or a group of drugs. Multiple drug allergy syndrome is defined as allergic reaction against two or more structurally unrelated drugs and is a rare condition.¹

Our patient with no significant psychosomatic complaints was thought to have MDIS in the first place, but high sIgE levels against many different groups of antibiotics, positive results in skin tests for steroids, and also positive oral provocation test results for many drugs with allergic reaction history showed that our patient had the rare condition of "multiple drug allergy syndrome".

Multiple antibiotic allergies can be mentioned for individuals having allergic reactions against two or more irrelevant antibiotic groups in SPT or sIgE tests. These patients form a very small fraction of patients with a history of drug sensitivity. In fact, it is known that in patients with multiple antibiotic allergy history, IgE-mediated reactions can rarely be demonstrated.⁵ Our patient having high-sIgE level against beta lactam antibiotics, erythromycin, and tetracycline suggests that the patient has the capacity to develop allergic reactions to almost every antibiotic.

Although the fact that a large number of latex cross-reactive or non-cross-reactive food-allergic reactions as well as the drug allergies are observed in our latex allergic patient, it gives us the impression of cross-reactivity between foods and drugs; the concept of cross-reactivity to food and drugs in multiple

drug allergy patients is often quoted but not supported by the current literature.⁶

Coexistence of allergic reactions to steroid and antihistaminic drugs in our patient, which is a rare condition, suggests a possible sensitivity to drug additives. Numerous additives including food proteins used as preservatives and coloring substance during the production phase can cause reactions as hidden allergens. In some cases, patients who had anaphylactic reactions after systemic steroid administration and have cow's milk hypersensitivity, the main agent causing reaction was shown to be lactose used as an additive.⁷ Our patient had no problems after milk and dairy products intake. Although it is not easy to demonstrate the role of additives in allergic reactions, sufficient data are available showing that the patient had IgE-mediated multiple drug allergy.

Omalizumab is a humanized, monoclonal IgG anti-IgE antibody that binds specifically to circulating IgE molecules, thus interrupting the allergic cascade, and it is licensed for use in severe asthma. However, a growing number of reports suggest that anti-IgE treatment may also be beneficial to patients suffering from other IgE-related conditions, including cold urticaria, solar urticaria, chronic spontaneous and autoimmune urticaria, symptomatic dermatographism, idiopathic angioedema, peanut allergy, latex sensitivity, systemic mastocytosis, and so on.^{8–15}

Anti-IgE therapy with omalizumab decreases serum free IgE levels and downregulates expression of High-affinity immunoglobulin E receptors (FcεRI) on mast cells and basophils. The downregulation of FcεRI expression is associated with a loss of sensitivity to allergen challenge and a reduction in mediator release.⁸

Büyükoztürk et al. proposed that omalizumab is a treatment agent in treatment-resistant chronic spontaneous urticaria (CSU) and idiopathic angioedema patients who feel hopeless and restricted because of their disease.⁹ Their results show that omalizumab therapy was also effective in a real-life setting for refractory CSU and idiopathic angioedema. Therefore, our patient who had allergic reactions against almost every drug including antihistamines and steroids had to be treated with the omalizumab also. For this reason, we used omalizumab as the only option for the chronic urticaria treatment. The fact that our patient benefited significantly from omalizumab treatment shows the important role of IgE for urticaria-angioedema reactions in the etiology.

Conflict of interest

The authors declared no conflicts of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Macy E and Ho NJ. Multiple drug intolerance syndrome: prevalence, clinical characteristics, and management. *Ann Allergy Asthma Immunol* 2012; 108: 88–93.
2. Ramam M, Bhat R, Jindal S, et al. Patient reported multiple drug reactions: clinical profile and results of challenge testing. *Indian J Dermatol Venereol Leprol* 2010; 76: 382–386.
3. Finlay AY and Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; 19: 210–216.
4. Schiavino D, Nucera E, Roncallo C, et al. Multiple-drug intolerance syndrome: clinical findings and usefulness of challenge tests. *Ann Allergy Asthma Immunol* 2007; 99: 136–142.
5. Macy E. Multiple antibiotic allergy syndrome. *Immunol Allergy Clin North Am* 2004; 24: 533–543.
6. Dewachter P, Mouton-Faivre C, Castells MC, et al. Anesthesia in the patient with multiple drug allergies: are all allergies the same? *Curr Opin Anaesthesiol* 2011; 24: 320–325.
7. Savvatanos S, Giavi S, Stefanaki E, et al. Cow's milk allergy as a cause of anaphylaxis to systemic corticosteroids. *Allergy* 2011; 66: 983–985.
8. Holgate S, Casale T, Wenzel S, et al. The anti-inflammatory effects of omalizumab confirm the central role of IgE in allergic inflammation. *J Allergy Clin Immunol* 2005; 115: 459–465.
9. Büyükoztürk S, Gelincik A, Demirtürk M, et al. Omalizumab markedly improves urticaria activity scores and quality of life scores in chronic spontaneous urticaria patients: a real life survey. *J Dermatol* 2012; 39: 439–442.
10. Metz M, Bergmann P, Zuberbier T, et al. Successful treatment of cholinergic urticaria with anti-immunoglobulin E therapy. *Allergy* 2008; 63: 247–249.
11. Metz M, Altrichter S, Ardelean E, et al. Anti-immunoglobulin E treatment of patients with recalcitrant

- physical urticaria. *Int Arch Allergy Immunol* 2011; 154: 177–180.
12. Kaplan AP, Joseph K, Maykut RJ, et al. Treatment of chronic autoimmune urticaria with omalizumab. *J Allergy Clin Immunol* 2008; 122: 569–573.
 13. Douglass JA, Carroll K, Voskamp A, et al. Omalizumab is effective in treating systemic mastocytosis in a nonatopic patient. *Allergy* 2010; 65: 926–927.
 14. Demirtürk M, Gelincik A, Colakoğlu B, et al. Promising option in the prevention of idiopathic anaphylaxis: omalizumab. *J Dermatol* 2012; 39: 552–554.
 15. Sampson HA, Leung DY, Burks AW, et al. A phase II, randomized, double-blind, parallel-group, placebo-controlled oral food challenge trial of Xolair (omalizumab) in peanut allergy. *J Allergy Clin Immunol* 2011; 127: 1309–1310.