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Anaphylaxis due to food-related anaphylaxis treated with omalizumab.

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Abstract

Anaphylaxis is a systemic allergic reaction that is acute and could be life-threatening. Once diagnosed, avoidance of allergen and carrying an epinephrine auto-injector are recommended. Most anaphylactic reactions are immunoglobulin E (IgE)-mediated and the major triggers include food, medication, insect stings, exercise and vaccines. Here, we present a case of a 38-year-old male, a surgeon, diagnosed as food-related anaphylaxis with a convincing clinical history and the positive serum-specific IgE level to *Dermatophagoides pteronyssinus* and *Dermatophagoides farina* allergens. This patient was treated with omalizumab administered subcutaneously. Routine lymphocyte subsets and CD23+ B cells of this patient were evaluated monthly for the consecutive ten months and one year after the last treatment. Our data showed that there was a correlation between the level of CD23+ B cells and the efficacy of omalizumab treatment. The patient had higher percentage of CD23+ B cells and CD23 expression level (86.5 % and MFI 371.9, respectively) during the onset of anaphylaxis. With the omalizumab treatment, both CD23+ B cells and CD23 expression level decreased gradually. The basal levels of CD23+ B cells and CD23 expression dropped to 25.1% and 72.6 MFI, respectively when the patient became recovered one year after the last treatment. Our findings highlight the potential of CD23+ B cells to be the useful parameter to predict the treatment effect of omalizumab in food-related anaphylaxis.

Keywords: Anaphylaxis, Omalizumab, CD23+ B cells.

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Introduction

Anaphylaxis is a systemic allergic reaction that is acute and could be life-threatening [1]. The most common triggers for allergic reactions are represented by food (35%) followed by drugs and biologics (20%), insect stings (20%), exercise (5%), and vaccines (3%) [2]. The symptoms of anaphylaxis involve several organ systems including skin, causing mainly urticaria (80~90%), respiratory tract (70%), gastrointestinal tract (30~45%), cardiovascular (10~45%) and central nervous system (10-15%) [3]. The mechanisms of food allergy are primarily associated with the immunoglobulin E (IgE)-mediated type I allergic reaction, but also with all the other three types of allergy [4]. Once diagnosed, avoidance of allergen and carrying an epinephrine auto-injector are recommended [3,5]. In addition to epinephrine, diphenhydramine is often used for anaphylaxis by injection [6]. Diphenhydramine is an anti-histamine used to treat allergies and was commonly used for acute allergic reactions in the emergency department as of 2007 [7].

Recently, the reports of food-dependent exercise-induced anaphylaxis has been increasing, it is a special type of IgE-mediated food allergy [8] and develops after starting to exercise following food allergen exposure [9]. It has been reported that omalizumab is mainly used to treat asthma, urticaria, eczema and other allergic diseases, and it has shown a favorable safety and tolerability profile [10,11]. Omalizumab is a recombinant humanized monoclonal antibody against IgE, which can lower the level of free IgE in plasma and inhibit a series of biological effects caused by IgE by selectively binding to high-affinity IgE receptors. At the same time, it can regulate the behavior of basophilic granulocytes, mast cells and B cells [10,11]. It is expected that omalizumab could bring new hope for the treatment of allergic diseases. However, the precise mechanism of omalizumab action remains unclear. Here, we described a case of food-related anaphylaxis successfully treated with omalizumab and investigated his

level of CD23+ B cells in relation to the treatment effect of omalizumab.

Case Report

A 38-year-old Taiwanese male surgeon was admitted to the emergency department by ambulance when he developed anaphylaxis following exercise outdoors. He ate some fried rice, almond soup and French fries. Approximately 40 minutes after eating the food, he went outdoor for running. Within 15 minutes of onset of physical activity, he developed lip swelling then stopped running. He also presented with periorbital edema, urticarial rash, generalized pruritus, and abdominal pain. In the emergency department, the vital sign was low blood pressure of 60/40 mmHg. Therefore, he was diagnosed as food-related anaphylaxis. He was then treated with Benadryl (diphenhydramine) and intramuscular epinephrine and his symptoms resolved within approximately three hours. He regularly exercises and never had the issues with postprandial activity. He was not exposed to alcohol, or medication (including NSAIDs and aspirin) several hours prior to exercise. Positive serum-specific IgE level to *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farina*e (Der f) allergens was found. Noticeably, he had similar symptoms of anaphylaxis after exercise four months later. Therefore, omalizumab (150 mg) was prescribed for this patient. Now the patient had no more anaphylaxis episodes.

Table 1. *The frequencies of different lymphocyte subsets (%) during the omalizumab treatment course.*

	T cell	B cell	NK cell	CD4	CD8
1[a]	67	12	17	40	27
2	72	15	14	44	27
3	77	16	6	48	27
4	70	10	14	39	27
5	67	14	16	40	26
6	67	12	18	40	26
7	64	14	21	42	20
8	70	12	15	41	25
9	68	12	18	42	26
10	67	15	17	41	26
11[b]	65	16	15	38	24

[a]Before the omalizumab treatment.

[b]One year after the last treatment of omalizumab.

In order to evaluate the effect of the omalizumab treatment and elucidate the possible mechanism of omalizumab action, routine lymphocyte subsets and CD23+ B cells were evaluated monthly for consecutive ten months and one year after the last treatment. Our data showed that the frequencies of lymphocyte population were normal and quite consistent during the entire treatment course (Table 1). Noticeably, there was a correlation between the level of CD23+ B cells and the efficacy of omalizumab treatment (Table 2). The patient had higher percentage of CD23+ B cells and CD23 expression level (86.5 % and mean fluorescence intensity (MFI) 371.9, respectively) during the onset of anaphylaxis. With the omalizumab treatment, CD23+ B cells and expression level decreased gradually. The basal level of CD23+ B cells and CD23 expression even dropped to 25.1%, 72.6 MFI, respectively when the patient became recovered one year after the last treatment. However, it is noticed that from 6th to 10th treatments, the percentage of CD23+ B cells and CD23 expression level were elevated to 71.6% (MFI 109.7), and then again gradually dropped to 36.5% (MFI 106.7). This suggested that the patient might be exposed to other allergen. Indeed, he suffered from urticaria when he came back for the 6th treatment. Therefore, the increase on the level of CD23+ B cells from the 6th treatment was associated with the onset of allergic reaction and more omalizumab treatment was thus urged. This study was approved by the institutional review board of Show Chwan Memorial Hospital, Taiwan.

Table 2. *The percentage and expression of CD23+ B cells during the omalizumab treatment course.*

	Percentage	Mean fluorescence intensity
1[a]	86.5	371.9
2	88.0	216.6
3	71.0	159.1
4	23.7	101.1
5	38.7	102.2
6	71.6	109.7
7	89.9	239.2
8	89.2	150.1
9	50.0	118.0
10	36.5	106.7
11[b]	25.1	72.6

[a]Before the omalizumab treatment.

[b]One year after the last treatment of omalizumab.

Discussion

According to the literature [12-14], omalizumab exerts its action in at least three different ways: (1) Binding free circulating IgE and thus significantly reducing the amount of IgE available on the surface of mast cells and basophils to bind antigen; (2) reducing the expression of IgE high-affinity receptor (FcεRI) on effector cells; and (3) suppressing the basophil response to allergens. However, the precise mechanism of omalizumab action, especially in chronic spontaneous urticaria remains unclear.

Similar to FcεRI, CD23 binds to IgE with equal affinity. It has been reported that OVA-specific IgE bound by CD23 on B

cells could help OVA-specific T cell expansion [15]. Moreover, CD23+ is considered as a negative regulator of IgE. Mice with overexpression of CD23 have decreased production of IgE, in contrast, CD23 deficient mice have higher IgE level [16,17]. However, in human, the role of CD23+ B cells for IgE remains controversial [18,19]. Gagro et al. had mentioned that CD23+ lymphocytes were positively correlated with serum IgE level. In addition, CD23+ B cells were decreased after hyposensitization in allergy children and had correlation with the severity in asthma patients after allergen challenge [20,21]. Serum IgE level is one of the parameters to evaluate the severe condition in allergy. However, it cannot be accounted as the reference during the omalizumab treatment. In this case study, we evaluated the CD23+ B cell expression following omalizumab treatment to determine whether the level of CD23+ B cells could replace serum IgE to assess the patient condition and the effect of omalizumab treatment. Indeed, our result revealed that CD23+ B cells might be the parameter to evaluate the efficacy of omalizumab treatment; however, it requires more data to confirm this discovery.

Conclusion

Our findings highlight the potential of CD23+ B cells to be the useful parameter to predict the treatment effect of omalizumab in food-related anaphylaxis. This may help develop improved therapeutic strategies for the treatment of anaphylaxis.

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