

Hypothesis & Experience  
Case Report



# Successful treatment of a patient with adult food allergy and severe asthma using omalizumab

Miyuki Nishie <sup>1,2</sup>, Katsunori Masaki <sup>1,2,\*</sup>, Shinichi Okuzumi <sup>1,2</sup>,  
Takao Mochimaru <sup>2,3</sup>, Hiroki Kabata <sup>1,2</sup>, Jun Miyata <sup>2,4</sup>,  
Hayato Takahashi <sup>2,5</sup>, and Koichi Fukunaga <sup>1,2</sup>

<sup>1</sup>Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Tokyo, Japan

<sup>2</sup>Keio Allergy Center, Keio University Hospital, Tokyo, Japan

<sup>3</sup>Department of Respiratory Medicine, National Hospital Organization Tokyo Medical Center, Tokyo, Japan

<sup>4</sup>Division of Infectious Diseases and Respiratory Medicine, Department of Internal Medicine, National Defense Medical College, Saitama, Japan

<sup>5</sup>Department of Dermatology, Keio University School of Medicine, Tokyo, Japan

OPEN ACCESS

Received: Jan 20, 2021

Accepted: Jul 6, 2021

\*Correspondence to

Katsunori Masaki

Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, 35 Shinanomachi, shinjuku-ku, Tokyo 160-8582, Japan.  
Tel: +81-3-5363-3793  
Fax: +81-3-3353-2502  
Email: masakik@keio.jp

Copyright © 2021. Asia Pacific Association of Allergy, Asthma and Clinical Immunology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Miyuki Nishie   
<https://orcid.org/0000-0003-1930-3477>

Katsunori Masaki   
<https://orcid.org/0000-0003-0909-9409>

Shinichi Okuzumi   
<https://orcid.org/0000-0002-4092-238X>

Takao Mochimaru   
<https://orcid.org/0000-0002-1505-6651>

Hiroki Kabata   
<https://orcid.org/0000-0001-8853-6149>

Jun Miyata   
<https://orcid.org/0000-0002-3189-1702>

Hayato Takahashi   
<https://orcid.org/0000-0001-6768-8821>

## ABSTRACT

Food allergy is a typical immediate-onset allergic disease in which symptoms are provoked by exposure to the sensitized antigens. Although previous reports have shown that omalizumab has helped children with egg or milk allergy achieve oral immunotherapy safely, there is still no established method for induction of remission in adult food allergy. A 51-year-old woman with oral steroid-dependent severe asthma was treated with omalizumab for 6 years. She had shellfish and wheat food allergy and oral allergy syndrome induced by kiwi and other foods associated with latex-fruit syndrome. Since omalizumab treatment, her food allergy symptoms had disappeared. After 7 years of this treatment, disseminated erythema suddenly appeared; omalizumab was discontinued because of suspected drug-induced eruption. After omalizumab interruption, she felt an itching sensation in her throat with worsened asthma control immediately after wheat ingestion. Readministration of omalizumab improved these symptoms. Thus, we raised the possibility that omalizumab not only improved asthma control but also induced pharmacological remission of the patient's food allergy. Omalizumab may be considered as a treatment option for adult patients with food allergies and severe asthma.

**Keywords:** Omalizumab; Food allergy; Oral allergy syndrome; Latex-fruit syndrome; Asthma; Quality of life

## INTRODUCTION

Food allergy and asthma often coexist and are significantly associated with each other [1]. The frequency of food sensitization to eggs, milk, soy, peanuts, wheat, and fish is higher in asthmatic patients compared to that in nonasthmatic patients [2]. Patients with multiple and severe food allergies often present with poorly-controlled asthma [3]. The complication rate of food allergy among adult asthma patients in Japan is 30% [4]. Moreover, food allergy has been identified as a risk factor for developing asthma. The prevalence of food allergy is estimated to be 6%–8% in children and 2%–5% in adults [5]. Shellfish is the most common antigen in adult food allergy patients (17.1%), followed by wheat (16.2%), fish (14.5%), and

Koichi Fukunaga   
<https://orcid.org/0000-0001-7460-1990>

### Conflict of Interest

K. Fukunaga received lecture fees from AstraZeneca and Boehringer-Ingelheim. The other authors have no conflict of interest to declare.

### Author Contributions

Conceptualization: Katsunori Masaki. Formal analysis: Miyuki Nishie, Katsunori Masaki. Investigation: Miyuki Nishie, Katsunori Masaki. Methodology: Miyuki Nishie, Katsunori Masaki. Project administration: Katsunori Masaki, Koichi Fukunaga. Writing - original draft: Miyuki Nishie, Katsunori Masaki. Writing - review & editing: Miyuki Nishie, Katsunori Masaki, Shinichi Okuzumi, Takao Mochimaru, Hiroki Kabata, Jun Miyata, Hayato Takahashi, Koichi Fukunaga.

fruits (12.8%) [6]. Once physicians diagnose asthma, they should actively interview and evaluate the patients for the presence of any food allergies. Contrastingly, adult food allergies are difficult to undergo remission and lifelong avoidance of their antigens is required. Thus, having an adult food allergy with a high risk of anaphylaxis lowers patients' quality of life (QoL). There have been few case reports of omalizumab for adult food allergy [7-9], with a large-scale study terminated owing to occurrences of adverse events [10]. Thus, accumulation of observational studies like the present case is warranted to evaluate the efficacy of omalizumab for adult food allergies. Here, we report an adult treated with omalizumab for food allergy and latex-fruit syndrome.

## CASE REPORT

A 51-year-old woman had been taking prednisolone (5–20 mg per day) to manage her severe asthma. Based on previous tests, her asthma did not have type 2 dominant factors because her peripheral blood eosinophil count was 81.2/ $\mu$ L and fractional exhaled nitric oxide was 3 ppb. She was diagnosed with food allergy to shellfish and wheat, based on previous episodes of her throat and eyelids swelling after ingesting these foods. Additionally, latex-fruit syndrome was diagnosed because she had an itchy mouth and lips after eating kiwi, pineapple, and melon. Serum immunoglobulin E (IgE) radioallergosorbent tests for shellfish, wheat, and latex were positive (**Table 1**). Omalizumab (300 mg every 2 weeks) was initiated for severe asthma because she had a total IgE of 1,400 IU/mL and body weight of 67.2 kg. Since then, her asthma control improved, and pharmacological remission of allergic symptoms was achieved.

After 7 years of this treatment, the patient suddenly presented with disseminated erythema. Secondary rash induced due to drugs or infectious disease was considered as one of the differential diagnoses; all drugs including omalizumab were discontinued because the erythema occurred 6 days after its administration. A lymphocyte transforming test (LTT) was performed on the suspected drugs, including antibiotics and nonsteroidal anti-inflammatory drugs that she took several days before this event. However, their reactive responses were all negative (**Table 2**). Thus, we could not identify the specific cause of disseminated erythema. On the other hand, her

**Table 1.** Serum antigen specific IgE radioallergosorbent test

Class 4: Mites, Japanese Cedar pollen
Class 3: Cat dander
Class 2: Shrimp
Class 1: Crab, Wheat, Latex, Banana
Class 0: Gluten, $\omega$ -5 gliadin

**Table 2.** Drug-induced lymphocyte stimulation test

Drug	Maximum stimulation index	Maximum response value (cpm)
L-Carbocysteine		
Negative	1.5	374
Esomeprazole magnesium hydrate		
Negative	1.5	377
Amoxicillin hydrate		
Negative	1.0	264
Acetaminophen		
Negative	1.3	328
Loxoprofen sodium hydrate		
Negative	1.1	167
Diclofenac sodium		
Negative	1.1	158

asthma symptoms, including cough and dyspnea, worsened; frequent short-acting  $\beta$ -agonist rescue inhalation was needed after omalizumab was discontinued. Furthermore, she developed an itchy throat immediately after wheat ingestion, similar to her previous symptoms. Based on the history and laboratory results, omalizumab was unlikely to be the suspect drug; therefore, omalizumab administration was cautiously restarted to improve asthma symptoms. After this therapeutic change, asthmatic and allergic symptoms during wheat intake disappeared. Moreover, she could safely eat wheat with no incidence of oral symptoms.

## DISCUSSION

In the present case, omalizumab not only improved asthma control but also induced clinical remission of food allergy and latex-fruit syndrome. We were not able to identify the genuine cause of erythema based on the LTT; however, omalizumab was not the culprit, since the reintroduction of omalizumab did not provoke skin erythema. The LTT is commonly used for auxiliary diagnosis of drug allergies [11]. However, the LTT may produce false-positive or false-negative results, and its value in the diagnosis of drug allergies appears to vary greatly depending on the drug in question [12, 13]. Previous studies found that the LTT had poor sensitivity and specificity in diagnosing omalizumab allergy and drug eruptions. Our patient had severe asthma and oral allergic symptoms to shellfish, wheat, and fruits. Shellfish and wheat are also the antigens that cause exercise-induced food anaphylaxis that restrained her activities. Adult patients with food allergies should continuously avoid diets containing sensitized antigens because adult food allergies cannot be cured spontaneously. Thus, food allergies remarkably damage patients' QoL; patients are continually at risk for anaphylaxis due to the possibility of consuming food contaminated with a hidden antigen.

Oral immunotherapy (OIT) has recently been used to aggressively induce remission in children with food allergies [14]. Some researchers have reported that omalizumab could reduce the risk of anaphylaxis during OIT because OIT may often cause allergic symptoms, such as urticaria, asthma attack, or even anaphylactic shock [15-18]. In addition, omalizumab alone seemed to be effective for food allergy; since food allergies are typical IgE-dependent conditions, omalizumab might inhibit anaphylactic reactions. Indeed, Sampson et al. [10] tried to investigate the efficacy of omalizumab for peanut allergy with a phase II, randomized, double-blinded, placebo-controlled study among children and adult patients; however, this study was terminated early because of safety concerns during the screening food challenge before omalizumab administration. Some observational studies and case reports have suggested that omalizumab could improve patients' threshold for eliciting allergic reaction to each food (egg, milk, baked milk, or wheat) intake [7-9]. Etokimab, an anti-interleukin-33 antibody, has been reported to be effective for an active pharmacological remission in adult patients with peanut allergy [19]; however, the drug is not yet available in clinical practice.

In this case, the administration of omalizumab enabled the patient to safely ingest foods that she had avoided in the past, improving her QoL. Omalizumab may be considered as a treatment option for adult food allergy patients with severe asthma.

## ACKNOWLEDGEMENTS

We are deeply grateful to Dr. Keiko Ohgino for her assistance.

## REFERENCES

1. Emons JAM, van Wijk RG. Food allergy and asthma: is there a link? *Curr Treat Options Allergy* 2018;5:436-44.  
[PUBMED](#) | [CROSSREF](#)
2. Wang J, Visness CM, Sampson HA. Food allergen sensitization in inner-city children with asthma. *J Allergy Clin Immunol* 2005;115:1076-80.  
[PUBMED](#) | [CROSSREF](#)
3. Friedlander JL, Sheehan WJ, Baxi SN, Kopel LS, Gaffin JM, Ozonoff AI, Fu C, Gold DR, Phipatanakul W. Food allergy and increased asthma morbidity in a School-based Inner-City Asthma Study. *J Allergy Clin Immunol Pract* 2013;1:479-84.  
[PUBMED](#) | [CROSSREF](#)
4. Harada N, Harada S, Ito J, Atsuta R, Hori S, Takahashi K. Mobile health app for Japanese adult patients with asthma: clinical observational study. *J Med Internet Res* 2020;22:e19006.  
[PUBMED](#) | [CROSSREF](#)
5. Iweala OI, Choudhary SK, Commins SP. Food allergy. *Curr Gastroenterol Rep* 2018;20:17.  
[PUBMED](#) | [CROSSREF](#)
6. Imai T, Sugizaki C, Ebisawa M. A report on 2017 Nationwide survey of immediate type food allergies in Japan (supported by a grant from "Consumer affairs agency, government of Japan). *Alerugi* 2020;69:701-5.  
[PUBMED](#)
7. Fiocchi A, Artesani MC, Riccardi C, Mennini M, Pecora V, Fierro V, Calandrelli V, Dahdah L, Valluzzi RL. Impact of omalizumab on food allergy in patients treated for asthma: a real-life study. *J Allergy Clin Immunol Pract* 2019;7:1901-9.e5.  
[PUBMED](#) | [CROSSREF](#)
8. Vickery BP. Can omalizumab monotherapy benefit real-world food allergy patients? Lessons from an observational study. *J Allergy Clin Immunol Pract* 2019;7:1910-1.  
[PUBMED](#) | [CROSSREF](#)
9. Asero R. Disappearance of severe oral allergy syndrome following omalizumab treatment. *Eur Ann Allergy Clin Immunol* 2017;49:143-4.  
[PUBMED](#)
10. Sampson HA, Leung DYM, Burks AW, Lack G, Bahna SL, Jones SM, Wong DA. 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;127:1309-10.e1.  
[PUBMED](#) | [CROSSREF](#)
11. Nyfeler B, Pichler WJ. The lymphocyte transformation test for the diagnosis of drug allergy: sensitivity and specificity. *Clin Exp Allergy* 1997;27:175-81.  
[PUBMED](#) | [CROSSREF](#)
12. Mantani N, Kogure T, Sakai S, Goto H, Shibahara N, Kita T, Shimada Y, Terasawa K. Incidence and clinical features of liver injury related to Kampo (Japanese herbal) medicine in 2,496 cases between 1979 and 1999: problems of the lymphocyte transformation test as a diagnostic method. *Phytomedicine* 2002;9:280-7.  
[PUBMED](#) | [CROSSREF](#)
13. Watanabe M, Shibuya A, Satomichi A, Ono K, Tsuchihashi T, Hidaka H, Kokubu S, Seigenji K. Diagnostic value of drug lymphocyte stimulation test and evaluation of diagnostic criteria for drug induced liver injury. *Kanzo* 2001;42:448-54.  
[CROSSREF](#)
14. Pajno GB, Fernandez-Rivas M, Arasi S, Roberts G, Akdis CA, Alvaro-Lozano M, Beyer K, Bindslev-Jensen C, Burks W, Ebisawa M, Eigenmann P, Knol E, Nadeau KC, Poulsen LK, van Ree R, Santos AF, du Toit G, Dhimi S, Nurmatov U, Boloh Y, Makela M, O'Mahony L, Papadopoulos N, Sackesen C, Agache I, Angier E, Halcken S, Jutel M, Lau S, Pfaar O, Ryan D, Sturm G, Varga EM, van Wijk RG, Sheikh A, Muraro A; EAACI Allergen Immunotherapy Guidelines Group. EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy. *Allergy* 2018;73:799-815.  
[PUBMED](#) | [CROSSREF](#)
15. Nadeau KC, Schneider LC, Hoyte L, Borrás I, Umetsu DT. Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy. *J Allergy Clin Immunol* 2011;127:1622-4.  
[PUBMED](#) | [CROSSREF](#)
16. Crisafulli G, Caminiti L, Chiera F, Arasi S, Salzano G, Panasiti I, Barbalace A, Pajno GB. Omalizumab in children with severe allergic disease: a case series. *Ital J Pediatr* 2019;45:13.  
[PUBMED](#) | [CROSSREF](#)

17. Yanagida N, Sato S, Ebisawa M. Clinical aspects of oral immunotherapy for the treatment of allergies. *Semin Immunol* 2017;30:45-51.  
[PUBMED](#) | [CROSSREF](#)
18. Taniuchi S, Takahashi M, Soejima K, Hatano Y, Minami H. Immunotherapy for cow's milk allergy. *Hum Vaccin Immunother* 2017;13:2443-51.  
[PUBMED](#) | [CROSSREF](#)
19. Chinthrajah S, Cao S, Liu C, Lyu SC, Shindher SB, Long A, Sampath V, Petroni D, Londei M, Nadeau KC. Phase 2a randomized, placebo-controlled study of anti-IL-33 in peanut allergy. *JCI Insight* 2019;4:e131347.  
[PUBMED](#) | [CROSSREF](#)