

Loading-Dose Dupilumab May Function as a Prophylactic Agent for Food-Induced Anaphylaxis: A Case and Review of the Literature

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Abstract

Recent advances in targeted therapy using monoclonal antibodies have revolutionized care in many fields, and dupilumab for the treatment of moderate-severe atopic dermatitis is no exception. While on a trial of loading dose dupilumab, a 25-year-old white male with a past medical history significant for anaphylaxis after ingesting peanuts and tree nuts did not experience anaphylaxis after accidentally consuming almonds. Similarly to anti-IgE, the large-scale inhibition of IL-4 and IL-13 signaling to various immune cells involved with type II hypersensitivity reactions using loading dose dupilumab may have played a role in preventing anaphylaxis in this patient. The role of loading dose dupilumab as a potential prophylactic agent against food-induced anaphylaxis could be explored cautiously as a novel way to reduce both morbidity and mortality in patients with these allergies.

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INTRODUCTION

In the United States, IgE-mediated food allergies are estimated to affect 10% of adults and 8% of children, with a rising prevalence observed in the last two decades.^{1,2} The most common food allergies are caused by sensitivities to milk, eggs, soy, wheat, peanuts, tree nuts, fish, and shellfish, with 50% of all fatalities due to food-induced anaphylaxis caused by peanuts and tree nuts.² Patients with peanut and tree nut allergies typically have severe responses to even minor quantities of these allergens, and are historically unlikely to out-grow these allergies.¹ Food-induced anaphylaxis is a potentially fatal response by the body that begins as a mild allergic reaction which rapidly progresses within an hour of allergen exposure—sometimes persisting or recurring in a biphasic pattern for several hours despite treatment with epinephrine and intravenous fluids.^{2,3} Here we present a case of a 25-year-old white male who did not experience anaphylaxis after accidentally ingesting almonds while on loading-dose dupilumab.

CASE

A 25-year-old white male with a history of anaphylaxis with peanut and tree nut consumption was seen by paramedics 10 minutes after the accidental ingestion of almond-containing food. His most recent anaphylactic event occurred due to accidental tree nut dust consumption during elementary school, which resolved using epinephrine on-site. Additionally, the patient last had allergy testing performed in 2016 which supported the persistence of his food allergies into adulthood. At that time, all tree nut antigens were equally cross reactive. This patient’s history of well-controlled chronic asthma and moderate-severe atopic dermatitis refractory to topical triamcinolone warranted his use of dupilumab. A loading dose of 600 mg was self-administered 5 days prior to the allergen exposure. After the accidental consumption, epinephrine was not administered before the arrival of the paramedic team, and it was held by paramedics at the request of the patient due to being asymptomatic. Vitals were taken at the time of the encounter and every 5 minutes until the patient was cleared by paramedics (Table 1).

Time of Measurement	Blood Pressure	Pulse	Respiratory Rate	spO ₂	End-Tidal CO ₂
0 Minutes	142/92 mmHg	90	14	99%	34 mmHg
5 Minutes	160/100 mmHg	92	12	99%	32 mmHg
10 Minutes	138/82 mmHg	86	14	99%	33 mmHg
15 Minutes	134/76 mmHg	82	13	99%	35 mmHg

Table 1. *Vitals taken from paramedics.*

The preservation of airway function as demonstrated through the maintained nasal waveform capnography readings between 32-35 mmHg, as well as repeated normotensive and hypertensive blood pressure measurements, support that anaphylaxis did not occur. Additionally, the patient failed to develop any symptoms of an allergic reaction throughout observation in the ambulance. Upon follow-up, he reported remaining asymptomatic beyond 48 hours post-ingestion, including an absence of enterocolitis and proctocolitis.

METHODS

We completed a search through PubMed on October 4, 2023 to identify other reported cases of anaphylaxis prevention after dupilumab usage. The search strategy was ("dupilumab anaphylaxis" OR "anaphylaxis dupilumab" OR "dupixent anaphylaxis" OR "anaphylaxis dupixent") AND ("anaphylaxis prevented by dupilumab") AND ("anaphylaxis prophylaxis") in PubMed. There were three cases identified that described the resolution of active anaphylaxis with dupilumab administration, one case that detailed anaphylaxis prevention in Food-Dependent, Exercise-Induced Anaphylaxis (FDEIA), one case that described a prophylactic effect against idiopathic anaphylaxis, and one case that discussed anaphylaxis prevention in a patient with food-induced anaphylaxis (corn and peanuts). Thus, our patient may be the first reported case that characterizes a prophylactic effect against tree nut-induced anaphylaxis from dupilumab usage.

DISCUSSION

Anaphylaxis is a severe allergic reaction that is the constellation of several inflammatory symptoms, which can present after contact with an antigen or idiopathically, most commonly after intensive exercise. This reaction can be characterized clinically by the presence of: hives, pruritis, erythema, and edema on the skin and/or the mucosal tissue, stridor, shortness of breath, and hypoxia; hypotension and arrhythmias; as well as vomiting, abdominal pain, and colitis.^{2,4} Anaphylaxis is primarily mediated by a number of chemical and cellular factors including: IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, TNF- α , IFN- γ , TNFR1, MCT, histamine, antigen-specific IgE, Th2 cells, mast cells, basophils, and eosinophils.⁵⁻⁷ Notably, IL-4 and IL-13 are critical

for the propagation of respiratory symptoms associated with allergic reactions and for the generation of factors responsible for manifesting and maintaining anaphylaxis via Th2 activation, despite not being found to play a significant role in determining the scale of active anaphylaxis.⁵

Dupilumab is a human monoclonal antibody that targets IL-4 receptors, inhibiting IL-4 and IL-13 signaling to various immune cells involved with type II hypersensitivity reactions.⁸ This ultimately makes dupilumab an attractive agent for treating both IgE-mediated atopic dermatitis and asthma. Interestingly, long-term dupilumab has been shown to decrease food-specific IgE levels in patients with atopic dermatitis and comorbid food allergies by over 80%.⁹ Additionally, several case studies have further suggested the potency of dupilumab in both preventing idiopathic anaphylaxis, and in resolving treatment resistant anaphylaxis—including cases of food-dependent reactions. One case study identifies dupilumab at being effective for the prevention of idiopathic anaphylaxis, another details its prevention of anaphylactic symptoms in a child with the rare FDEIA disease, and three other recent case studies describe the potency of subcutaneous dupilumab in resolving treatment-resistant anaphylaxis.¹⁰⁻¹³ One proposed mechanism for anaphylaxis prophylaxis with dupilumab implies that IL-4 and IL-13 play a larger role in mounting an anaphylactic response than previously believed.¹⁴ Further investigation will be required to measure the capacity for these mediators to rapidly and potently help the immune system recruit such a large sum of key reactive factors and propagate the respiratory response observed in anaphylaxis. This may be of particular interest in the coming years due to the growing popularity of biologic agents, such as dupilumab, and other novel targeted therapies.

Despite the evidence that dupilumab may be effective in preventing and clearing anaphylaxis, the ability for dupilumab to function as a prophylactic agent against strictly food-induced anaphylaxis has only recently begun to be described in the literature. The most notable case involved a patient who developed adult-onset food allergies, which resulted in anaphylaxis. These new onset allergies to corn and nuts were confirmed using specific IgE measured by ImmunoCAP and a food challenge test with pistachios—both of which occurred prior to the patient initiating dupilumab therapy for severe atopic dermatitis. After initiating dupilumab therapy and going on the adult maintenance dose (300 mg every 2 weeks), a repeat food challenge test was conducted after the patient accidentally ingested pistachios with no reported reaction. The results of this test using corn showed tolerance to ingesting high quantities of the allergen without reaction.¹⁵

Due to findings such as these, it is no surprise that dupilumab has been investigated in clinical trials both as a monotherapy (NCT03793608) and in combination therapy with peanut oral immunotherapy (NCT03682770) for preventing peanut-mediated anaphylaxis in children aged 6-17 years old. In the Phase 2 clinical trial NCT03793608, each patient received 200 mg dupilumab subcutaneously every 2 weeks after a loading dose of 400 mg. Levels of peanut-specific IgE were found to be reduced by roughly 49% after 24 weeks of therapy, and two of the twenty-four patients passed a double-blind, placebo-controlled food challenge (NCT03793608).¹⁶ They successfully ingested 444 mg of peanut protein without signs of an allergic reaction after 24 weeks of therapy (NCT03793608). At this time, no results have been published from NCT03682770, as it is still ongoing.

Source Title	Patient Characteristics	Observations
The Role of Dupilumab in Refractory Anaphylaxis Secondary to Food Allergy	40-year-old female suffering from treatment-resistant anaphylaxis post-consumption of green curry	<ul style="list-style-type: none"> Significant clinical improvement was observed with IV dupilumab, leading to anaphylaxis resolution.¹⁰
Effect of Dupilumab in a Patient with Severe Asthma Complicated with Recurrent Anaphylaxis: A Case Report	17-year-old female with a history of multiple hospitalizations due to severe uncontrolled asthma and anaphylaxis caused by various triggers	<ul style="list-style-type: none"> Switching from omalizumab to dupilumab due to worsening asthma with no further changes to her asthma management regimen led to a reduction in hospitalizations for asthma exacerbations and anaphylaxis.¹¹
Dupilumab for Treatment of Food-Dependent, Exercise-Induced Anaphylaxis: Report of One Case	11-year-old male with FDEIA in response to dietary mushrooms	<ul style="list-style-type: none"> Subcutaneous dupilumab was administered seven times in thirty-three weeks in addition to bimonthly mushroom exposure. No anaphylaxis was observed.¹²

Treatment of Idiopathic Anaphylaxis with Dupilumab: A Case Report	28-year-old female with recurrent biweekly episodes of idiopathic anaphylaxis since childhood	<ul style="list-style-type: none"> • A trial of dupilumab was started due to symptom recurrence after the discontinuation of omalizumab. • A near-complete resolution of symptoms over six months was observed.¹³
Dupilumab for Treatment of Food Allergy	30-year-old female with adult-onset food allergies to corn and peanuts confirmed via specific IgE measured by ImmunoCAP and open food challenge test	<ul style="list-style-type: none"> • The patient started dupilumab for atopic dermatitis. She accidentally ingested pistachios (peanuts) with no reported reaction while on maintenance-dose dupilumab. • The results of a follow-up open food challenge test using corn showed tolerance to ingesting high quantities of the allergen without reaction.¹⁵
Study to Evaluate Dupilumab Monotherapy in Pediatric Patients with Peanut Allergy (NCT03793608)	Twenty-four children aged 6-17 years old with peanut allergies	<ul style="list-style-type: none"> • Peanut-specific IgE were found to be reduced by roughly 49% after 24 weeks of therapy. • Two of the twenty-four patients passed a double-blind, placebo-controlled food challenge without signs of an allergic reaction after ingesting 444 mg of peanut protein at 24 weeks of therapy (NCT03793608).
Study in Pediatric Subjects with Peanut Allergy to Evaluate Efficacy and Safety of Dupilumab as Adjunct to AR101 (Peanut Oral Immunotherapy) (NCT03682770)	One hundred forty-nine children aged 6-17 years old with peanut allergies	<ul style="list-style-type: none"> • No results are available at this time, as this study is ongoing.

Table 2. Summary of current sources that discuss dupilumab usage against anaphylaxis.

CONCLUSIONS

Severe food-mediated allergies affect millions of Americans, and the accompanying risks for severe morbidity and mortality due to allergic reactions in this population warrant the utilization of prophylactic measures. As it currently stands, commonly used techniques for anaphylaxis prophylaxis in those with severe allergies include strict antigen avoidance, exposure-based desensitization, and the biologic omalizumab, an anti-IgE immunoglobulin. These have been shown to be highly efficacious at reducing the sequelae of allergen exposure and anaphylactic shock. However, each modality is associated with restrictive lifestyles, high time investment, or high cost. The potential for dupilumab to function as both a prophylactic and resolving agent against anaphylaxis could make it another life-saving tool for patients with severe food allergies beyond its current applications.

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