Anaphylactic Reaction Requiring Epinephrine in a 10-Year-Old Patient Undergoing Peanut Challenge While on Dupilumab Therapy

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To the Editor,

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Peanut is one of the most frequent elicitors of anaphylaxis in childhood[1]. Reactions occur commonly in two organ systems and often involve the lower respiratory tract or the cardiovascular system[2], requiring an intramuscular administration of epinephrine[3]. Many patients with peanut allergy also suffer from other atopic diseases, especially atopic dermatitis (AD), which is a predisposing factor for the development of food allergy[4]. In recent years, new therapeutic modalities for AD have been developed: Dupilumab, a monoclonal antibody against interleukin-4-receptor-α, has been approved since 2017 and can now be used in infants with severe AD from 6 months of age[5]. Beyond its therapeutic success in AD, dupilumab is also used in the therapy of severe asthma and eosinophilic oesophagitis[6,7]. Its mechanism is based on the blockade of the interleukin-4 and interleukin-13 signalling pathways and thereby modulating two central cytokines in the Th2-mediated immune response[5]. The extent to which the expression of interleukin-4 and interleukin-13 has an influence on IgE-mediated food allergies is largely unexplored, but interleukin-4-expression seems to play a role in peanut allergy[8]. Dupilumab has an influence on peanut-specific and Ara h 2-specific IgE, which decrease significantly during therapy[9]. However, the clinical significance remains unclear. It can be hypothesized that patients will no longer exhibit severe reactions to food. A clinical trial assessing the efficacy and safety of dupilumab in children with peanut allergy as monotherapy or as adjunct to oral immunotherapy has been completed, but the results have not yet been published (NCT03793608 and NCT03682770, respectively).

The case of a 10-year-old male patient reported below shows that despite dupilumab and low peanut- and Ara h 2-specific IgE levels under this therapy, an anaphylactic reaction requiring the administration of epinephrine was elicited. The patient has suffered from severe AD since infancy. He has been treated with dupilumab subcutaneously every four weeks since May 2022, with a significant improvement of his disease. Basic therapy is still given twice daily, and tacrolimus 0.03% is applied topically to erythematous areas. With known sensitization to house dust mites, birch and grass pollen, the patient also suffers from allergic rhinoconjunctivitis and allergic asthma, which was treated with a combination preparation of inhaled corticosteroid and long-acting beta-agonist until May 2022. His therapy for asthma could be discontinued under dupilumab.

Furthermore, he has a clinically relevant hen's egg allergy, which could be confirmed by an oral hen's egg provocation at 5 years of age. With known sensitization to hazelnut and peanut with a maximum value of peanut-specific IgE of 21.4 kU/l in 2016 with a total IgE of 730 kU/l, an elimination diet has been practiced since infancy. An emergency kit including an adrenaline autoinjector, an antihistamine and a corticosteroid was already available. In order to evaluate the clinical relevance of peanut and hazelnut sensitization for the

first time, the patient was admitted in September 2023 for a double-blind, placebo-controlled food challenge (DBPCFC) with peanut and hazelnut.

The patient's admission status was unremarkable except for the skin findings; the atopic dermatitis presented with dry integument, partly crusty, slightly erythematous efflorescences on the extremities and retroauricularly, hands lichenified. The findings resulted in a SCORAD of 41 points. Total IgE and specific IgE against hen's egg, peanut and hazelnut, as well as their components on admission are shown in table 1.

The DBPCFC was performed following the PRACTALL recommendations[10]. During the peanut challenge, an objective reaction occurred after the 5th dose (300 mg peanut protein) with generalised urticaria, repetitive cough, dyspnoea and a systolic blood pressure drop of 18 mmHg. Adrenaline was administered intramuscularly and clemastine and prednisolone intravenously. During the challenge with hazelnut and placebo, all doses could be administered without reactions, so that we assumed clinical tolerance to hazelnut but peanut allergy with anaphylactic reaction. Before discharge, knowledge about the use of emergency medication was checked again and the family received detailed nutritional counselling.

Dupilumab is a highly effective biologic for the treatment of moderate to severe atopic dermatitis and severe asthma[5,6]. Our patient also showed significant improvement in eczema and asthma. Dupilumab also lowers food-specific IgE antibodies[9]. However, the clinical impact of the suppression is unclear. In our case, despite very low specific IgE antibodies to peanut and its components, the patient showed an anaphylactic reaction to peanut requiring treatment with epinephrine. Even though this is only a first case report and data from controlled studies are still pending, this case shows that clinical relevance should in any case be checked in a controlled setting despite reduced and low peanut IgE levels so that emergency measures can be initiated immediately in case of provocation.

Key words: anaphylaxis, dupilumab, epinephrine, peanut allergy, food allergy

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Immunology (ÖGAI), the Swiss Society for Allergy and Immunology (SGAI), the German Society of Anaesthesiology and Intensive Care Medicine (DGAI), the German Society of Pharmacology (DGP), the German Respiratory Society (DGP), the patient organization German Allergy and Asthma Association (DAAB), the German Working Group of Anaphylaxis Training and Education (AGATE). *Allergo J Int* . 2021;30(1):1-25. doi:10.1007/s40629-020-00158-y

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Table 1: Laboratory results on admission

Parameters	kU/l
Total IgE	39,30
Hen's egg-sIgE	1,46
Peanut-sIgE	1,59
Ara h1-sIgE	<0,10
Ara h2-sIgE	0,33
Ara h3-sIgE	<0,10
Hazelnut-sIgE	4,62
Cor a 14-sIgE	<0,10
Cor a 9-sIgE	<0,10