

Case Report

Passive Transient Transfer of Peanut Allergy by Liver Transplantation

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We report a case of transient symptomatic transferred IgE-mediated peanut allergy after elective blood-group compatible liver transplantation. We show that the allergy was transient and therefore passive, authorizing further uneventful peanut consumption. Skin tests with commercial peanut extract and native peanut were performed in the recipient. Circulating specific IgE against peanut and recombinant peanut allergens (rArah1, rArah2, rArah3) was measured in stored serum samples collected from the recipient between 6 months before and 8 months after liver transplantation. Specific IgE levels in the donor were measured at the time of multiorgan donation. In the recipient, diagnosis of IgE-mediated peanut anaphylaxis was based on the clinical history and detection of specific IgE against peanut and recombinant major peanut allergens (rArah1, rArah2 and rArah3). Skin tests were negative and specific IgE undetectable 6 months after the clinical reaction. Oral peanut challenge was negative excluding persistent peanut allergy. This case confirms that IgE-mediated peanut allergy can be transferred by liver transplantation and

shows that it may be transient and therefore passively acquired.

Key words: Ara h 1 allergen-peanut, Ara h 2 allergen-peanut, Ara h 3 allergen-peanut, food hypersensitivity, liver transplantation, peanut hypersensitivity

Abbreviations: IgE, Type E immunoglobulin; rArah1, Recombinant Ara h 1 allergen; rArah2, Recombinant Ara h 2 allergen; rArah3, Recombinant Ara h 3 allergen; Th1, Type 1 helper lymphocyte; Th2, Type 2 helper lymphocyte.

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Introduction

Peanut allergy is a major public health concern in Europe and the United States (1,2), being the most common cause of fatal allergic reactions, mostly among teenagers and young adults (1,3). We report a case of transferred symptomatic IgE-mediated peanut allergy following elective blood-group-compatible liver transplantation, and demonstrate that the allergy was transient and therefore passive.

A 20-year-old man with a history of atopy (allergic asthma and peanut allergy) suffered brain damage in a car crash. Brain death was confirmed a few hours later and his liver was transplanted into a 62-year-old woman with nonalcoholic fatty liver disease. She denied any food or drug allergy. Anesthesia and surgery were uneventful. Initial immunosuppression consisted of mycophenolate mofetil, cyclosporine and methylprednisolone. Two months after the transplant she experienced an immediate burning tongue sensation while chewing a peanut. On swallowing the peanut she developed hoarseness and palmar pruritus, followed by generalized pruritus, dyspnea and dizziness less than 5 minutes later. She was admitted to the emergency department within 15 min. On admission, she had arterial hypotension (70/47 mmHg), moderate tachycardia (97 bpm) and swallowing difficulties. She rapidly received colloid infusion (500 mL), methylprednisolone and dexchlorpheniramine. Her cardiovascular disturbances resolved within 30 min, along with her other manifestations. Serum tryptase was not measured. She was

discharged home the next day and advised to avoid all peanut-containing food.

Materials and Methods

Six months later, with her consent, skin tests were performed (4, 5). Prick-tests were negative with commercial peanut extract (Stallergènes, Antony, France), crushed Curly[®] snack (freshly ground peanuts), native peanut and roast peanut. Circulating specific IgE against peanut and recombinant peanut allergens (rArah1, rArah2, rArah3; ImmunoCAP 250, Phadia, Uppsala, Sweden) was measured in stored serum samples collected from the recipient between 6 months before and 8 months after the transplant (Table 1).

Results and Discussion

No specific IgE was found in pretransplant sera, while anti-rArah3 IgE was detectable as early as 24 h after transplantation. IgE against peanut and the three recombinant peanut components was detected 3 weeks posttransplantation, but was no longer present when tested 3 and 6 months after the clinical reaction. Specific IgE levels in the donor are reported in Table 1. The clinical circumstances of the reaction and the detection of specific IgE against peanut allergens pointed to IgE-mediated peanut anaphylaxis. Subsequently, the negative skin tests and undetectable specific IgE authorized oral food challenge (5). With the patient's informed consent and under medical supervision, labial challenge was performed, followed by graded oral challenge with Curly[®] snack and native peanut. No reaction was observed, formally excluding persistent peanut allergy. The patient was thus authorized to eat nuts and nut-containing and subsequent peanut consumption was uneventful.

Food allergy transfer after solid organ transplantation has occasionally been described in adult recipients but is more common in children (6). The four previous reports of peanut allergy in adult liver or lung transplant recipients are summarized in Table 2 (7–10). None of the recipients had been peanut-allergic before transplantation. Legendre (7) reported the first case: 3 months after combined liver–kidney transplantation, the recipient, a 35-year-old man, developed a skin rash and laryngeal dyspnea after eating peanuts. Peanut-induced anaphylaxis was diagnosed on the basis of clinical findings, the absence of specific IgE before transplantation, its presence at the time of the reaction, its subsequent decline and a positive basophil activation test. Phan (8) reported a similar case involving a 60-year-old male liver transplant recipient. He experienced two episodes of peanut-induced allergic reactions, the second of which he self-treated with epinephrine. Peanut allergy was confirmed by skin tests, which were still positive for peanut 48 weeks after transplantation, even though specific IgE was undetectable. Vagefi (10) reported walnut-induced anaphylaxis in a 54-year-old male liver recipient 4 weeks posttransplantation, confirmed by positive food

challenge. Finally, Khalid (9) reported four peanut-induced reactions in a 42-year-old female lung recipient; peanut allergy was confirmed by positive skin tests with peanut extract 7 months posttransplant. Interestingly, in three of these reports, no peanut allergy was reported in the recipients of kidney and/or pancreas–kidney grafts from the same donors (7–9). In the present case, the recipient of the same donor's lungs experienced an allergic reaction following peanut ingestion 3 months after the transplant, and peanut allergy was confirmed by an allergological assessment. In contrast, the recipients of the donor's heart, kidneys and pancreas reported no allergic reactions. Interestingly, the other liver recipient (the donor's liver was split for a double transplant) also experienced no allergic reaction.

Finally, all the affected liver recipients described in the literature, including our patient, had mucocutaneous, cardiovascular and/or gastrointestinal signs (7,8,10), whereas the lung was the main target organ in the lung recipient (Table 2) (9). The patients were all advised to avoid consumption of nuts and nut-containing foods. Our case is the first in which the transient nature of transferred peanut allergy following liver transplantation was demonstrated, authorizing further uneventful peanut consumption by the recipient.

IgE-mediated peanut allergy was diagnosed in our patient on the basis of the clinical detection of specific IgE at the time of the reaction. Diagnosis of food allergy is based on the clinical history, skin tests, specific IgE assay and food challenge (4,5,11). Disorders with acute symptom onset after food ingestion are typically IgE-mediated (2). Phan (8) reported that skin tests were positive respectively 4 weeks and 4 months after the first and second clinical reactions. In our patient, skin tests performed 6 months after the clinical reaction were negative, and specific IgE was undetectable at 3 and 6 months. However, circulating IgE is undetectable in nearly one-third of patients with true food allergy (12), whereas prick tests are usually positive (5).

Peanut contains up to 32 different proteins, of which at least eight (Arah1 to Ara h8) have been shown to bind specific IgE; the three major allergens are Arah1, Arah2 and Arah3 (13–15). Recombinant (r) allergens (genetically engineered isoforms resembling native allergen molecules) are useful diagnostic tools (16). In our patient, passively transferred IgE against rArah3 was detectable as early as 24 h after liver transplantation. Interestingly, serum IgE against native peanut allergen and two other peanut components (rArah1 and rArah2) detected when first tested 3 weeks after transplantation. This suggests that several mechanisms may be involved in the transient appearance of IgE of various specificities after solid organ grafting. The combined presence of anti-rArah1 or anti-rArah3 IgE with anti-rArah2 IgE is known to be associated with severe reactions (11), as in our patient.

Table 1: Time course of circulating IgE against peanut and recombinant peanut allergens (rArah1, rArah2, rArah3)

Donor		Recipient						
IgE antibodies	Day 0	6 months before Day 0	Day 0	Day 0 + 24 h	Day 0 + 3 weeks	Day 0 + 2 months	Day 0 + 5 months	Day 0 + 8 months
Clinical event			Liver transplantation			Peanut-induced clinical reaction		Negative skin tests and food challenge
Peanut (N < 0.1 kU/L)	199	<0.1	<0.1	<0.1	2.48	NA	<0.1	<0.1
rAra h1 (N < 0.1 kU/L)	87	<0.1	<0.1	<0.1	1.59	NA	<0.1	<0.1
rAra h2 (N < 0.1 kU/L)	56.1	<0.1	<0.1	<0.1	0.84	NA	<0.1	<0.1
rAra h3 (N < 0.1 kU/L)	38.6	<0.1	<0.1	0.42	0.49	NA	<0.1	<0.1

NA = not available.

Various mechanisms of sensitization transfer have been suggested. One possibility is passive transfer of donor IgE, although Legendre (7) pointed out that the half-life of circulating IgE is only a few days. However, reactions have been reported soon after transplantation (10) and might be explained by retention of specific IgE in donor liver sinusoids, leading to recipient mast-cell sensitization (6). Long-term binding of donor-derived specific IgE to recipient mast cell and basophil high-affinity receptors increases its half-life

(6–8) and could thus lead to mediator release with clinical repercussions during a period of several months after transplantation. In our patient, circulating anti-rArah3 IgE was detectable as early as 24 h after transplantation and was undetectable when tested 3 and 6 months after the clinical reaction, although it might have disappeared earlier. Other mechanisms could have contributed to the observed increase in rArah2- and rArah3-specific IgE 3 weeks after the transplant. The decline in type 1 helper (Th1)

Table 2: Donor and recipient characteristics in reported cases of transferred food allergy in adult solid organ recipients

Donors			Recipients				
References	Sex, age	Cause of death	Sex, age, organ	Onset delay of clinical signs/organ transplantation	Allergen and onset delay of clinical signs/allergen ingestion	Clinical features	Treatment
Legendre 1997 (7)	Male, 22	Peanut-induced anaphylaxis	Male, 35 liver and kidney	3 months	Peanut, ?	Erythema, laryngeal dyspnea	?
Phan 2003 (8)	Male, 15	Peanut-induced anaphylaxis	Male, 60 liver	25 days	Cashew nut, 15 min	Facial flushing, throat tightness, dizziness, blurred vision GI symptoms	Promethazine
				32 weeks	Peanut, ?	Clinical signs not detailed	Self-administered epinephrine
Khalid 2008 (9)	?, 12	Peanut-induced anaphylaxis	Female, 42 lung	4 days	Peanut, 'soon after'	Shortness of breath	Nebulized bronchodilators
				5 weeks	Peanut, immediately	Extreme shortness of breath, SpO ₂ : 88%	Not stated
				4 months	Peanut, ?	Wheezing, mild shortness of breath	Albuterol
				7 months	Peanut, immediately	Severe shortness of breath, wheezing, lip swelling, urticaria, dizziness, SpO ₂ : 78%, HR: 122 b.min ⁻¹	Epinephrine, albuterol, nebulization, methylprednisone, ranitidine, diphenhydramine
Vagefi 2009 (10)	Female, 24	Unknown allergen-induced anaphylaxis	Male, 54 liver	8 days	Nut, 20 min	Throat thickening, flushing pruritus, GI symptoms	None

GI = gastro-intestinal; HR = heart rate.

lymphocytes due to immunosuppression with agents such as tacrolimus might promote Th2 populations and thus favor immediate allergic hypersensitivity (6,17). However, among the five published reports of transferred hypersensitivity in adults (including our patient), only two patients had received tacrolimus (8,10). A more likely explanation is that transfer of allergen-specific T and B lymphocytes, as well as hematopoietic stem cells and dendritic cells able to survive for several months in the recipient, might lead to active production of specific IgE (6,7).

Graded food challenge is a useful diagnostic tool (5), as uneventful ingestion of a relevant amount of a suspect food rules out allergy. In the present case, food challenge, authorized by negative skin tests with commercial peanut extracts and native peanuts, was uneventful, confirming that the anaphylactic reaction was due to transient and therefore passive sensitization. The overall concordance between a positive prick-test and positive food challenge has been reported to be 59% and 92%, respectively, with commercial extracts and fresh foods (4). Thus, native food seems to be more reliable than commercial extracts for food allergy diagnosis (4). Khalid (9) used only commercial extracts, possibly explaining why food challenge was positive while skin tests were negative. In the case reported by Vagefi (10), in which food challenge was positive 7 years posttransplant, it was not mentioned whether skin tests were performed with peanut extracts as well as native peanuts. We confirm that IgE-mediated peanut allergy can be transferred by liver transplantation and demonstrate its transient nature, at least in our patient. In contrast, a case of peanut allergy transferred by lung transplantation was shown to persist 7 years later (9), suggesting that the mechanisms of acquired food allergy might vary from one patient to another.

The first preventive measure for food allergy is culprit allergen avoidance, which implies careful reading of food labels, care when eating in restaurants, and avoidance of food cross-contamination during meal preparation. Transplant teams should be informed when a donor has a history of peanut allergy, and the recipients should be advised accordingly. All recipients of grafts from a food allergic donor may benefit from follow-up investigations. In cases of acquired food allergy, the patients should be advised on how to use epinephrine (18). In turn, a combination of negative skin tests, undetectable specific IgE and negative food challenge some months following the reaction may authorize safe reintroduction of the culprit food.

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References

- Moneret-Vautrin DA, Morisset M, Flabbee J, Beaudouin E, Kanny G. Epidemiology of life-threatening and lethal anaphylaxis: A review. *Allergy* 2005; 60: 443–451.
- Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol* 2010; 125(2 Suppl 2): S116–S125.
- Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol* 2001; 107: 191–193.
- Rance F, Juchet A, Bremont F, Dutau G. Correlations between skin prick tests using commercial extracts and fresh foods, specific IgE, and food challenges. *Allergy* 1997; 52: 1031–1035.
- Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: An updated practice parameter. *Ann Allergy Asthma Immunol* 2008; 100(3 Suppl 3): S1–S148.
- Atkins D, Malka-Rais J. Food allergy: Transfused and transplanted. *Curr Allergy Asthma Rep* 2010; 10: 250–257.
- Legendre C, Caillat-Zucman S, Samuel D, et al. Transfer of symptomatic peanut allergy to the recipient of a combined liver-and-kidney transplant. *N Engl J Med* 1997; 337: 822–824.
- Phan TG, Strasser SI, Koorey D, et al. Passive transfer of nut allergy after liver transplantation. *Arch Intern Med* 2003; 163: 237–239.
- Khalid I, Zoratti E, Stagner L, Betensley AD, Nemeh H, Allenspach L. Transfer of peanut allergy from the donor to a lung transplant recipient. *J Heart Lung Transplant* 2008; 27: 1162–1164.
- Vagefi PA, Blazick E, Hamilos D, Ades A, Cosimi AB, Hertl M. Transference of food allergy after adult liver transplantation. *Transplantation* 2009; 87: 1426.
- Astier C, Morisset M, Roitel O, et al. Predictive value of skin prick tests using recombinant allergens for diagnosis of peanut allergy. *J Allergy Clin Immunol* 2006; 118: 250–256.
- Fleischer DM, Conover-Walker MK, Christie L, Burks AW, Wood RA. The natural progression of peanut allergy: Resolution and the possibility of recurrence. *J Allergy Clin Immunol* 2003; 112: 183–189.
- Shreffler WG, Beyer K, Chu TH, Burks AW, Sampson HA. Microarray immunoassay: Association of clinical history, in vitro IgE function, and heterogeneity of allergenic peanut epitopes. *J Allergy Clin Immunol* 2004; 113: 776–782.
- Nicolaou N, Poorafshar M, Murray C, et al. Allergy or tolerance in children sensitized to peanut: Prevalence and differentiation using component-resolved diagnostics. *J Allergy Clin Immunol* 2010; 125: 191–197, e1–13.
- Asaranoj A, Moverare R, Ostblom E, et al. IgE to peanut allergen components: Relation to peanut symptoms and pollen sensitization in 8-year-olds. *Allergy* 2010; 65: 1189–1195.
- Skamstrup Hansen K, Poulsen LK. Component resolved testing for allergic sensitization. *Curr Allergy Asthma Rep* 2010; 10: 340–348.
- Boyle RJ, Hardikar W, Tang ML. The development of food allergy after liver transplantation. *Liver Transpl* 2005; 11: 326–330.
- Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol* 2010; 126 (Suppl): S1–S58.