

Passive Transfer of Nut Allergy After Liver Transplantation

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An anaphylactic reaction to cashew nut developed in a nonatopic 60-year-old man 25 days after receiving a liver allograft from a 15-year-old atopic boy who died of anaphylaxis after peanut ingestion. The liver recipient had no history of nut allergy. Post-transplantation skin prick test results were positive for peanut, cashew nut, and sesame seed, and the donor had allergen-specific IgE antibodies to the same 3 allergens. Contact tracing of the recipients of other solid organs from the same donor disclosed no other development of allergic symptoms after ingestion of peanut or cashew nut. Results of molecular HLA typing did not detect any donor-origin leukocytes in the recipient after transplantation, which excluded peripheral microchimerism. The patient inadvertently ingested peanut-contaminated food and suffered a second anaphylactic reaction 32 weeks after the transplantation. This case illustrates that transfer of IgE-mediated hypersensitivity can occur after liver transplantation and have potentially serious consequences. We therefore recommend that organ donors undergo screening for allergies, and that recipients be advised regarding allergen avoidance. *Arch Intern Med.* 2003;163:237-239

Immunoglobulin E-mediated allergy to peanuts is a major cause of anaphylaxis and death in the United States and Europe.¹ Long-term transfer of allergen-specific IgE-mediated hypersensitivity after allogeneic bone marrow transplantation is well recognized.²⁻⁵ The transferred allergy can persist for up to 1 year and is thought to result from adoptive transfer of IgE-producing donor-derived B cells.⁵ In contrast, transfer of allergy after solid-organ transplantation is rare and has been reported previously only once in the recipient of a combined liver-and-kidney allograft.⁶

REPORT OF A CASE

The liver donor was a 15-year-old boy with atopic dermatitis, moderately se-

vere asthma, and intolerance to a number of food additives. Although he had always avoided nuts and nut-containing foods, he had never undergone skin prick testing (SPT) and had never received a formal diagnosis of nut allergy. Immediately after eating fried rice with satay sauce, redness, flushing, severe wheezing, and dyspnea developed. Out-of-hospital respiratory arrest resulted in irreversible anoxic brain damage. Anaphylaxis due to peanut ingestion was diagnosed by means of an elevated serum tryptase level of 18.9 µg/L (reference range [RR], 0.0-15.0 µg/L), elevated total IgE level of 15000 kU/L (RR, 0-200 kU/L), and high levels of allergen-specific IgE antibodies to peanut, cashew nut, and sesame seed. Multiple organs were donated.

The recipient of the liver was a 60-year-old man with chronic hepatitis B virus infection, cirrhosis, and a solitary 3 × 3-cm hepatoma. His postoperative course was complicated by an episode of acute cellular rejection that was treated

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Results of Skin Prick Tests at 6, 8, and 48 Weeks After Liver Transplantation

	Test Result, mm		
	6 wk	8 wk	48 wk
Histamine control	5 × 5	5 × 5	8 × 6
Isotonic sodium chloride solution (control)	0 × 0	0 × 0	0 × 0
Peanut extract	10 × 8	9 × 7	7 × 6
Cashew nut extract	10 × 14	7 × 6	3 × 4
Sesame seed extract	3 × 3	ND	ND

Abbreviation: ND, not done.

with intravenous methylprednisolone sodium succinate, and he was discharged from hospital on day 24 receiving a triple immunosuppressive regimen of prednisolone, azathioprine sodium, and tacrolimus. The next day, anaphylaxis developed within 15 minutes of ingesting cashew nuts, although these had been a regular part of his diet before transplantation. He reported redness and flushing of the face, tightness in the throat, dizziness, and blurred vision. This was immediately followed by severe nausea, vomiting, and profuse watery diarrhea. He was treated with promethazine hydrochloride and admitted for observation.

With the patient's consent, investigations were performed to elucidate the nature of his allergic reactions. Allergy to nuts was confirmed 6 weeks later when results of SPT were positive for peanut, cashew nut, and sesame seed (**Table**). He was advised to avoid all nuts and nut-containing foods and prescribed an epinephrine hydrochloride autoinjector. Despite these precautions, he was inadvertently exposed to peanuts 32 weeks later; on this occasion the allergic reaction was terminated by self-administered epinephrine. The SPT was repeated at 48 weeks, and results indicated that he was still reactive to peanut and, to a lesser extent, cashew nut (**Table**).

The recipients of the heart, kidney, and kidney-and-pancreas transplants were then contacted. Severe postoperative complications had developed in the heart transplant recipient, who had died. However, the kidney and kidney-and-pancreas transplant recipients reported no allergic symptom after eating peanuts or cashew nuts. Test results of serum obtained from all 3 recipi-

ents were negative for allergen-specific IgE antibodies to peanut, cashew nut, and sesame seed. We then obtained DNA from peripheral blood leukocytes and skin of the liver recipient for molecular typing of the classes I and II HLA locus by means of polymerase chain reaction using sequence-specific primers to detect donor-origin leukocytes. The donor's HLA genotype was A*01/02, B*08/44, DRB1*01/03, and DRB3*pos. The recipient's HLA genotype was A*02/11, B*60/62, DRB1*09/11, DRB3*pos, and DRB4*pos. No donor-specific HLA alleles were found in the blood or the skin of the recipient after transplantation. Measurement of immunoglobulin levels before and after transplantation showed a fall in IgG (from 1650 to 610 mg/dL; RR, 620-1410 mg/dL), IgA (from 533 to 79 mg/dL; RR, 60-396 mg/dL), and IgM (from 214 to 70 mg/dL; RR, 48-304 mg/dL) antibody levels. Serum total IgE levels did not vary significantly (18 kU/L and 12 kU/L before and after transplantation, respectively).

COMMENT

Transfer of allergy after solid organ transplantation is a rare occurrence reported only once previously.⁶ The consequences, however, are potentially fatal, and we suggest including screening for allergies in the donor selection process. This can be achieved by obtaining a rigorous history, examination of the medical records, SPT, and measurement for serum allergen-specific IgE levels where appropriate. In our patient and the previously reported case, both occurred after liver transplantation, and there was no evidence of transfer to the recipients of other solid organs.⁶ In the

other reported case, Legendre et al⁶ demonstrated peripheral microchimerism in the skin of their patient, and proposed that adoptive transfer of donor-origin B cells that were present in the liver, but not the other organs, was responsible for the transfer of the allergy. In contrast, we were unable to detect any donor-specific HLA alleles in our patient. Although we have not excluded central microchimerism in the bone marrow, this implies that peripheral microchimerism, at least, is not necessary for transfer of the allergy.

The allergic reaction in our patient occurred soon after transplantation, when aggressive immunosuppression resulted in suppression of endogenous antibody production. An alternative explanation, therefore, may be passive transfer of exogenous (donor) IgE. Although the donor liver was perfused with University of Wisconsin solution, considerable quantities of IgE might have been present in the hepatic sinusoids and extravascular space. Although serum IgE has a half-life of 2 to 4 days,⁷ IgE bound to mast cells has a long biological half-life.⁸ This is consistent with the observation that passive transfer of IgE in the Prausnitz-Küstner^{9,10} and Walzer reactions¹⁰ can persist for up to 6 months. Passively transferred donor IgE could, therefore, conceivably bind to and prime the recipient's mast cells, causing them to degranulate when exposed to cashew nuts at 25 days and peanuts at 32 weeks after transplantation. This explanation would also be consistent with the decreased SPT responses elicited at 48 weeks (**Table**).

In summary, liver transplantation is associated with transfer of symptomatic nut allergy from the donor to the recipient. It is possible that reactivity to other allergens such as antibiotics may also be transferred after liver transplantation. The exact mechanism responsible for the transfer of allergy remains to be elucidated. Nevertheless, increasing awareness of this phenomenon may lead to more careful screening of the donor and the prevention of potentially serious allergic reactions after liver transplantation.

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