

Brief Report

TRANSFER OF SYMPTOMATIC PEANUT ALLERGY TO THE RECIPIENT OF A COMBINED LIVER-AND-KIDNEY TRANSPLANT

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PEANUTS are one of the commonest causes of food allergy in the United States and Europe.¹⁻³ They are also a leading cause of food-induced anaphylaxis and death, which usually follow inadvertent exposures.^{4,5} Allergy to peanuts is an IgE-mediated, mast-cell-dependent, immediate-hypersensitivity reaction. There are several reports of the transfer of allergen-specific IgE-mediated hypersensitivity by bone marrow transplantation.⁶⁻⁹ We report a case of peanut allergy transmitted through combined liver-and-kidney transplantation.

CASE REPORT

A 22-year-old man with a history of allergic reactions to peanuts was admitted to our hospital in a coma. After inadvertently ingesting satay sauce, which contains peanuts, during a Chinese meal, he had become unwell and had had a cardiorespiratory arrest that resulted in cerebral anoxia, coma, and brain death. A high level of peanut-specific IgE was detected in his serum by a radioallergosorbent test (Pharmacia Diagnostics, Uppsala, Sweden). Multiple organs were subsequently procured. The donor's HLA phenotype was A1,24;B8,44;DRB1*03,13.

On November 21, 1989, the donor's liver and right kidney were given in transplantation to a 35-year-old man, and the left kidney and pancreas were given to a 27-year-old woman. The man (HLA phenotype, A2,19;B12,-;DRB1*07,13) had end-stage renal failure due to subacute glomerulonephritis and had begun hemodialysis in 1970. He received a first cadaveric kidney transplant in May 1981. Because of chronic rejection, his renal function slowly deteriorated. He also had chronic active hepatitis due to hepatitis C virus, and cirrhosis was diagnosed in 1987. The woman (HLA phenotype, A1,24;B8,44;DRB1*03,04) had chronic renal failure due to type I diabetes mellitus and had begun hemodialysis in February 1988. Both transplant recipients received

immunosuppressive induction therapy with muromonab-CD3 (OKT3) and corticosteroids, azathioprine, and cyclosporine. Neither had ever had any allergy to peanuts. They had not been told the cause of the donor's death. Both had an uneventful postoperative course.

Three months after transplantation, the recipient of the liver-kidney transplant reported a skin rash and laryngeal dyspnea after eating peanuts. Allergy to peanuts was diagnosed on the basis of the clinical findings; the absence of specific IgE antibodies before transplantation, their presence at the time the symptoms appeared, and their decline thereafter; and a positive basophil degranulation test (Fig. 1).

The woman who received the pancreas-kidney transplant confirmed that since her transplantation she had not had any symptoms similar to these after eating peanuts. After giving informed consent, she ingested peanuts under close medical supervision, but no symptoms were noted. She had no peanut-specific IgE antibodies in her serum, and a basophil degranulation test was negative.

Tests for systemic donor-recipient microchimerism were performed in the two recipients. DNA was extracted from peripheral-blood cells and from skin in the forearm by a phenol-chloroform procedure; it was precipitated in ethanol and resuspended in distilled water. The identity of the *HLA-DRB1* alleles was determined with allele-specific amplification by the polymerase chain reaction with sequence-specific primers, as previously described.¹⁰ A positive internal control specific for a non-HLA locus was present during each amplification so that we could assess the quality of the reaction. This sensitive technique allows donor:recipient DNA ratios of 1:4000 to be detected. Microchimerism was not found in the blood but was found in the skin of the recipient of the liver-kidney transplant, as shown by the presence of both the donor's *DRB1*03,13* allele and the recipient's *DRB1*07,13* allele. No microchimerism was detected in either blood or skin from the kidney-pancreas recipient.

In vitro proliferation assays were performed in an attempt to identify peanut-specific T cells in the recipient of the liver-kidney transplant. Peripheral-blood lymphocytes were isolated by Ficoll-Hypaque density-gradient centrifugation. They were cultured in 96-well plates at a final concentration of 1 million per milliliter in RPMI 1640 medium supplemented with 10 percent normal AB-positive serum, in the presence of 10 or 20 μ g of crude peanut extract per milliliter (the gift of Dr. W. Burks, Little Rock, Ark.), or 10 μ g of purified protein derivative (Pasteur-Mérieux Institut, Paris) per milliliter as a positive control. After six to eight days, 1 μ Ci of tritium-labeled thymidine was added. The cultures were continued for 18 hours, after which radioactivity incorporated into DNA was counted. Although a substantial proliferative response to purified protein derivative was observed, there was no peanut-specific proliferation above the negative control value.

The patient with the allergy was of course advised to avoid peanuts permanently, and specific IgE antibodies rapidly disappeared from his serum. Seven years later, his liver and kidney were functioning well.

DISCUSSION

We report the transfer of allergy to peanuts along with the combined transplantation of a liver and a kidney. Several mechanisms of transfer may be envisaged. Passive transfer of donor IgE is unlikely, because the half-life of IgE is only a few days, whereas the allergic reaction occurred three months after transplantation. However, we cannot rule out the possibility that donor IgE bound to the recipient's mast cells and basophils could have persisted for more than a few days.

The transfer of allergen-specific donor lympho-

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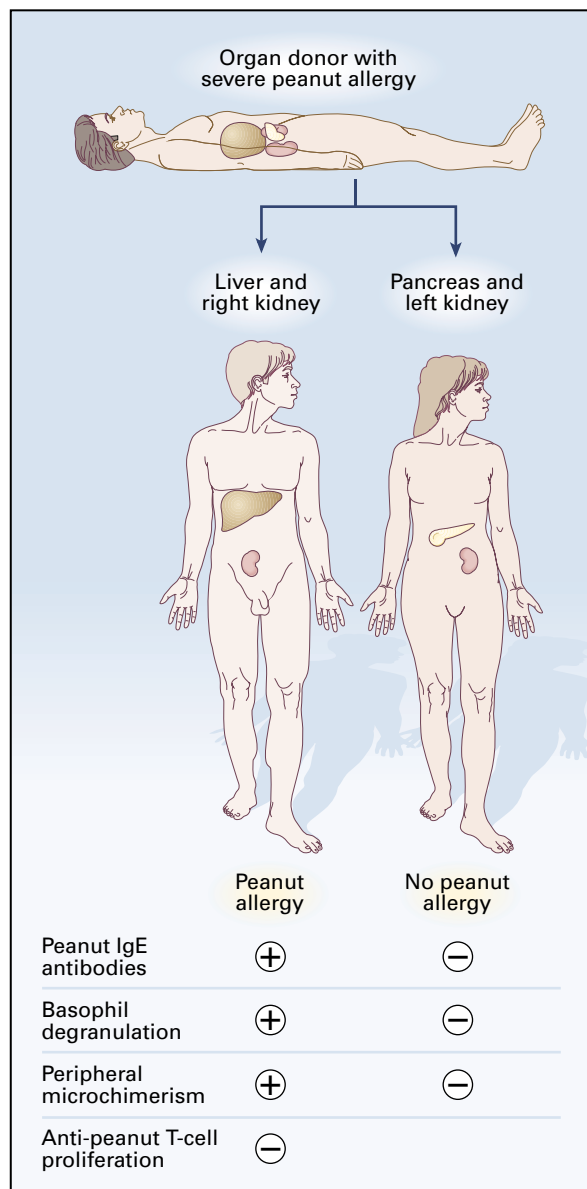


Figure 1. Results of Tests for Peanut IgE Antibodies, Basophil Degranulation Tests, Tests of Peripheral-Blood Cells for Microchimerism, and Assays for Anti-Peanut T-Cell Proliferation in the Recipients of Organ Transplants from a Donor Allergic to Peanuts.

cytes is a more likely possibility. In mice, a secondary hapten-specific IgE response can be elicited by the adoptive transfer of primed B lymphocytes, T lymphocytes, or both.¹¹ The occurrence of immune hemolytic anemia and autoimmune thrombocytopenia after liver transplantation from donors with such diseases indicates that the transfer of functionally active donor-type B or T lymphocytes can occur in hu-

mans.¹² The production of IgE by B cells depends on the presentation of allergens by antigen-presenting cells and on cooperation between B cells and regulatory T-helper lymphocytes of the Th2 type. In our patient there may have been transfer of peanut-specific IgE-producing B cells or of peanut-specific Th2 lymphocytes that induced the recipient's B cells to produce peanut-specific IgE. Unfortunately, it was impossible to verify the transfer of donor-type memory B cells because of the difficulty in demonstrating allotypic differences in IgE antibodies. Although the lack of *in vitro* proliferation of the recipient's T lymphocytes argues against the persistence in the host of donor peanut-specific memory T cells, one cannot exclude the possibility that these negative results were due to the absence in the culture of adequate (donor type) antigen-presenting cells.

It is relevant that the allergy was transferred from the liver-kidney transplant, but not from the pancreas-kidney transplant. Pluripotential hematopoietic stem cells and dendritic cells are known to be normally resident in the liver.^{13,14} These passenger cells can migrate from the graft to the recipient's lymphoid organs, and multilineage hematopoiesis derived from donor cells can persist for several months after liver grafting. Such cells may have immunomodulatory effects that result in donor-specific immune tolerance¹⁵ or a graft-versus-host reaction. In the present case, migration of donor-derived cells into the recipient's skin is suggested by the presence of microchimerism in the skin, and the skin was indeed the site of the allergic reaction. It is thus tempting to speculate that the passenger cells present in the donor's liver, but not in his kidneys or pancreas, were responsible for the transfer of the allergy to our patient.

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