



Transfer of Peanut Allergy Following Lung Transplantation: A Case Report

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ABSTRACT

This case study describes a patient who developed peanut allergy following lung transplantation. A 54-year-old woman underwent bilateral lung transplantation on June 2009 owing to severe chronic obstructive pulmonary disease. She had no history of food allergy before transplantation. The donor, however, was a 20-year-old man who was fatally injured during an automobile accident; he was allergic to peanuts. At 3 months after transplantation, the lung recipient presented with acute dyspnea and urticaria 15 minutes after consuming food containing peanut derivatives. Pre- and posttransplantation recipient blood samples analyzed for the presence of IgE antibodies specific for peanut allergens confirmed that the allergy had been passively transferred as a consequence of transplantation. Food allergy following solid organ transplantation is thought to be rare, mostly occurring in children. Two mechanisms may explain the observations described for the patient reported in this study: *de novo* development of peanut allergies after transplantation, or passive transfer of peanut allergies from a peanut-sensitized organ donor. This case report documenting pre- and posttransplantation IgE status in a lung transplantation case suggested that the allergic status of organ donors should be thoroughly assessed before transplantation, and potential allergy transfer risks must be discussed with the transplant team and the patient.

Food allergies are common diseases affecting ~6% of children >3 years of age and ~3.5% of adults in Western countries. However, food allergy prevalence among young children has doubled over the past 10 years in the United Kingdom. Peanut allergies are the most frequent ones among adults and second to egg allergies in children. Peanut allergy pathogenesis is caused by type I hypersensitivity responses associated with immunoglobulin E (IgE) specific to peanut allergens. T_H2 $CD4^+$ T lymphocytes also play a key role in mediating the pathogenesis. In addition to mast cells and eosinophils, they are responsible for the activation and recruitment of IgE-producing B cells.¹ Because transplant patients are required to take immunosuppressive drugs that dampen both cellular and humoral immune responses as a means of preventing graft rejection, these individuals would not be expected to (or at least to have a diminished incidence) of developing food allergies. In the present report, we describe a well documented case of peanut allergy that was transferred to a lung transplant recipient who had no history of allergies by a lung donor with asthma and peanut allergies. This observa-

tion provides an opportunity to highlight a rare immunologic food allergy response following solid organ transplantation.

CASE PRESENTATION

A 54-year-old woman underwent bilateral lung transplantation in June 2009 owing to severe chronic obstructive pulmonary disease related to smoking (40 packs/y) with no history of atopy. Induction immunosuppression consisted of intravenous basiliximab followed

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by an oral immunosuppressive regimen consisting of tacrolimus, mycophenolate mofetil, and methylprednisolone. The lung donor was a 20-year-old man who died of brain hemorrhage after an automobile accident. He had a history of both asthma (treated with beclomethasone) and peanut allergy. Three months after transplantation, the lung recipient consumed food containing peanuts. Thirty minutes later she presented with severe dyspnea, tachycardia, and a urticarial cutaneous rash (anaphylaxis severity grade III/IV). No dysphonia or drop in blood pressure was observed; O₂ saturation was 99% with nasal oxygen therapy at 3 L/min. Her symptoms improved after a bolus of intravenous methylprednisolone and antihistamine therapy without catecholamines. Before transplantation, foods containing peanuts had been a part of her diet and she did not display any overt signs of allergy. One month later, she was referred to the allergy clinic. Skin-prick tests (SPTs) to peanut allergens were positive. Specific IgE titers to peanut allergens were 3.44 kU/L for Ara h1 and 2.52 kU/L for Ara h2. SPTs to common dog and cat respiratory allergens were positive without clinical symptoms. Five months after the initial allergic episode, pretransplantation and posttransplantation recipient blood samples were tested for 103 food and respiratory allergens using an Immunocap ISAC array (Phadia, Uppsala, Sweden). Specific IgE to food or respiratory allergens undetectable in pretransplantation blood samples were positive in posttransplantation blood samples (Ara h1 2.6 ISU, Ara h2 3.1 ISU, and Ara h3 0.4 ISU). The metacholine challenge test showed no bronchial hyperresponsiveness and no increase in exhaled nitric oxide. It was therefore recommended that the patient remove peanuts and nuts from her diet. Ten months later, the SPT response to peanuts was increased and SPTs to other nut antigens were positive. Specific IgE titers to peanut antigens were still positive, but at lower levels: 2.01 kU/L for Ara h1, 1.17kU/L for Ara h2, and 0.32kU/L for Ara h3.

Other organ recipients from the same donor were also examined for their atopic status, with results summarized in Table 1. The liver recipient also developed anaphylaxis following consumption of peanuts at 2 months after transplantation, but cutaneous and blood tests were negative for peanut antigens at 6 months after the initial anaphylactic response. To the best of our knowledge, the other 4 organ recipients have not developed peanut allergies to date.

DISCUSSION

Transplant-acquired food allergies (TAFA) are now a well described phenomenon presenting in 2 primary ways. First and most common is TAFA primarily reported in children

who develop food allergies after solid organ transplantation from a donor with no history of food allergy. This phenomenon occurs at an unexpectedly high rate, ranging from 6% to 57%²⁻⁴ of cases compared with children not receiving a transplant, suggesting that development of food allergies is a risk factor associated with solid organ transplantation. The second scenario associated with the development of TAFA is thought to be related to the passive transfer of food allergies from a donor with food allergies to a previously nonallergic recipient. The difficulty in distinguishing between these two scenarios lies with the general lack of information regarding the atopic status of donors and recipients before transplantation; that is, neither SPTs nor results of specific IgE antibody responses have been described in earlier case reports.

Passive food allergy transfer has been reported mainly after bone marrow transplantation,⁵ where it was well documented in 4 transplant recipients.⁶⁻⁸ It has also been reported after solid organ transplantation. The first case of food allergy transfer following organ transplantation was described by Legendre et al.⁹ It occurred in a 35-year-old man after liver and right kidney transplantation from a 22-year-old man who died from an allergic response to peanut antigens. The recipient's peanut allergies were conclusively documented following skin testing and positive basophil degranulation tests. Three other cases of food allergy transfer have been reported: 2 after liver transplantation^{10,11} and 1 after lung transplantation.¹² Table 2 summarizes the clinical and immunologic features of the 4 reported cases of transferred food allergy responses following solid organ transplantation, including data from the present case report. In only 2 cases was there documentation of the donor's food allergy status with specific IgE titer data. In contrast, assessment of food allergies in donors described in the other case reports could be made only from respective clinical histories, owing to the difficulty associated with obtaining more specific allergy response data from the donors for ethical reasons.

The median age of the donors at the time of death was 18.6 years. With the exception of the case reported here, all of the other donors died from anaphylaxis. In our case, the tryptase assay was not performed to eliminate allergic

Table 1. Atopic Status and Demographic Data of the Organ Recipients from the Same Donor with Peanut Allergy

Transplanted Organ	Pre-Tx Recipient Atopic Status	Pre-Tx Recipient Allergic Data	Immunosuppressive Therapy	Post-Tx Recipient Allergic Reaction	Post-Tx Recipient Allergic Data
Heart	No history	No data	Cyclosporine corticosteroids	No symptoms	No data
Lung	No history	IgE Ara–	Anti-IL-2, FK506, MMF, corticosteroids	Urticaria, angioedema after peanut ingestion	IgE Ara + SPT Ara +
Right kidney	No history	No data	Anti-IL-2, FK505, MMF	No symptoms	IgE Ara– SPT Ara–
Left kidney	No history	No data	Anti-IL-2, Cyclosporine azathioprine, corticosteroids	No symptoms	IgE Ara– SPT Ara–
Liver	No data	No data	No data	Anaphylaxis after peanut ingestion?	No data
Pancreas	No data	No data	FK506-everolimus	Urticaria	IgE Ara–

Abbreviations: Tx, transplantation; IL, interleukin; FK506, tacrolimus; MMF, mycophenolate mofetil.

Table 2. Reported Cases of Food Allergies Resulting from Solid Organ Transplantation

Case Report	Legendre et al, 1997 ⁹	Phan et al, 2003 ¹⁰	Khalid et al, 2008 ¹²	Vagefi et al, 2009 ¹¹	Current Report
Donor (gender, age)	M, 22 y	M, 15 y	Unknown, 12 y	F, 24 y	M, 20 y
Atopic status	IgE Ara+	IgE Ara, cash nuts, sesame+	History of peanut allergy	History of food allergy (nuts, kiwi)	History of peanut allergy
Cause of death	Anaphylaxis	Anaphylaxis	Anaphylaxis	Anaphylaxis	Brain hemorrhage
Recipient (gender, age)	M, 35 y	M, 60 y	F, 42 y	M, 54 y	F, 54 y
Atopic status	No history of allergy	No history of allergy	No history of allergy	No history of allergy	No history of allergy
Pre-Tx allergic data	IgE Ara–	No data	No data	No data	IgE Ara, Ara h 1,2,3–
Tx organ	Liver and kidney	Liver	Lung	Liver	Lung
Immunosuppressive therapy	OKT3, cyclosporine, azathioprine, corticosteroids	FK506, azathioprine, corticosteroids	cyclosporine, azathioprine, corticosteroids	FK505, azathioprine, corticosteroids	Anti-IL-2, FK506, MMF, corticosteroids
Allergic symptoms	Skin rash, laryngeal dyspnea	Laryngeal dyspnea, vomiting, diarrhea	Asthma, urticaria, dizziness	Laryngeal edema, asthma, urticaria, abdominal pain	Urticaria, asthma
Post-Tx time	3 months	25 days	4 days	8 days	3 months
Allergen	Peanut	Cashew nut	Peanut	Unknown	Peanut
Post-Tx recipient atopic data	IgE Ara +	SPT cashew nut +, peanut, sesame	SPT peanut +	SPT and IgE Walnut –, oral challenge walnut +	SPT peanut + IgE Ara, Ara h1,2,3 +

Abbreviations as in Table 1

disease as the cause of death. The recipient's median age at transplantation time was 49 years. None of the recipients had a history of allergy before transplantation; however, with the exception of the case reported by Legendre *et al*⁹ and the present case, the recipient's atopic status before transplantation had not been established by SPTs or specific IgE antibody responses.

Liver transplantations are most commonly associated with the transfer of food allergies (3/5), and allergic responses to peanut antigens are the most common (3/5). Food allergy symptoms occurred at a median time of 43.4 days after transplantation. The symptoms were less severe than those presenting in the respective donors (anaphylaxis), probably owing to the recipient's immunosuppressive drug regimen. Immunosuppressive treatments included tacrolimus in 3, cyclosporine in 2, azathioprine in 3, and mycophenolate mofetil in 1 case. All patients had been on corticosteroid treatment, and 2 had received induction therapy: one anti-interleukin(IL)2 and the other OKT3.

The underlying mechanisms associated with the transfer of type I food hypersensitivity between donors and recipients are at present unknown. The persistence of antigen-specific donor IgE has been proposed as a mechanism of passive allergy transfer following blood transfusions.¹³ There are significant amounts of blood present in transplanted organs, potentially explaining a passive transfer of TAFA. This is even more likely to occur in cases where the donor has high titers of specific IgE, resulting in the presentation of allergic reactions shortly after transplantation. The half-life of serum IgE is ~2–4 days, but specific IgE could remain bound to high-affinity receptors present on circulating basophils and tissue mast cells for several months.¹⁴ This may explain why sensitization decreased

over time and disappeared in the liver recipient a few months after transplantation. However, passive transfer of allergen-specific IgE is unlikely to be responsible for the atopic response described in this case report, because skin sensitization to nut allergens other than those associated with peanuts developed 12 months after lung transplantation. Therefore, it is likely that other mechanisms may be involved and that longer-lived sensitization after solid organ transplantation may be more likely due to adoptive transfer of food allergen-specific T lymphocytes than from the acquisition of allergen-specific IgE. In mouse models, ovalbumin-triggered allergic asthma has been successfully transferred from ovalbumin-allergic to nonallergic mice with allergen-specific CD4⁺ T cells.¹⁵ Antigen specific T cells have been isolated from children with peanut allergies.¹⁶ therefore, passive transfer of allergen-specific T cells present in transplanted organs is a likely possibility. Transfer of allergen specific IgE-producing donor-derived B cells may be associated with the delayed onset of sensitization, but these mechanisms have not yet been elucidated.

In contrast to allergy transfer, the occurrence of food allergies following organ transplantation from a nonallergic donor occurs primarily in young children. In 2009, Ozbeck *et al*¹⁷ performed a prospective study identifying 6/28 children with orthotopic liver transplantations who also developed multiple food allergies. The mean age of the 6 children who developed food allergies was less than that of the other organ recipients (10.2 months vs 68.9 mo). A younger patient age suggested that the immune response of immature infants with limited exposure to food allergens could play an important role in their predisposition to allergic disease. In most other retrospective studies, it is difficult to link the cause of the food allergy to the transplant procedure, owing to the

lack of information regarding the atopic status of the donor and recipient before transplantation.

New-onset allergy following solid organ transplantation has been most often described with liver transplantation but also after small bowel¹⁸ and heart¹⁹ transplantation. The time to clinical symptoms of food allergy after solid organ transplantation varies from 9.3 months to 3.75 years depending on the report.^{2,17} Food allergy typically involves multiple allergens common to the diets of children, including milk, eggs, and wheat.¹⁷ Several authors have suggested that liver TAAFA represents an adverse effect associated with tacrolimus therapy,² because this drug is known to impair intestinal permeability, resulting in increased exposure to antigens. Another underlying immunologic mechanism could be a tacrolimus-induced T_H1 to T_H2 switch resulting in an inhibition of IL-2 synthesis²⁰ or facilitation of IgE production and secretion as well as augmentation of eosinophil-promoting cytokines (eg, IL-13 and IL-5, respectively). The levels associated with tacrolimus were greater than those induced by cyclosporine,²¹ ie, some investigators have reported a resolution of food allergy symptoms in patients with liver TAAFA who were switched from tacrolimus to cyclosporine.²

The present case report, together with those reported in the literature, suggests that TAAFA, particularly peanut allergies, could represent a life-threatening condition in solid organ transplant recipients. Therefore, we suggest that the allergic status of organ donors be thoroughly defined and the risk of allergy transfer be described in reports to the transplant team. Preventive strategies in organ recipients at risk should include systematic avoidance of foods containing potential allergens and repeated allergen testing (SPTs and specific IgE levels) before allowing allergens to be reintroduced into the recipient's diet.

In conclusion, we report a food allergy transfer case that developed after lung transplantation with documentation of pre- and posttransplantation IgE levels. Transfer of food allergies after solid organ transplantation are rare, having been reported only after liver and lung cases. The main risk factor associated with the development of food allergies after transfer is donor death from anaphylaxis. The recipient's history of allergic disease or tacrolimus therapy seem to not predispose to allergy transfer. The TAAFA reported in the present case was different from the TAAFA present in recipients who develop atopy following transplantation from nonallergic donors, where risk factors included recipient age (<1 y), liver transplantation, and the use of tacrolimus immunosuppressive therapy. Donor food allergy status should be taken into account when introducing posttransplantation diets to recipients. One should carefully assess the allergic profile of every potential organ donor.

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