



Letter

Adoptive transfer of food allergy via unrelated allogeneic bone marrow transplant

Transplant-associated allergy (TAA) or transfer of donor-specific allergy to the transplant recipient is a relatively rare phenomenon. TAA has been described in related donor bone marrow transplant (BMT); however, hereditary and environmental factors may influence development of allergy in this setting. We describe a case of allogeneic transfer of peanut allergy after a BMT from an unrelated donor for T-cell acute lymphoblastic lymphoma (T-ALL).

A 43-year-old man was referred to our facility for evaluation for allogeneic stem cell transplant for his T-ALL. He did not have any personal or family history of allergy to food products or medications. He underwent reduced intensity conditioning with fludarabine, melphalan, and total body irradiation followed by HLA-matched (10/10 with DQB1) unrelated donor allogeneic BMT. He received methotrexate and cyclosporine for graft-vs-host disease prophylaxis.

On approximately day 60, he developed progressive diarrhea, abdominal cramping, and weight loss. He did not have rash or liver function abnormalities. On peripheral blood chimerism after day 60, the CD3⁺ fraction contained approximately 95% donor DNA and approximately 5% recipient DNA. The CD33⁺ fraction contained approximately 100% donor DNA and approximately 0% recipient DNA. On endoscopic evaluation, no morphologic abnormalities were found in the esophagus, stomach, duodenum, proximal jejunum, and colon. Random biopsy specimens were obtained, which revealed mucosal infiltration by eosinophils in the esophagus, stomach, and colon, suggesting a hypersensitivity reaction (Fig 1). He was treated with oral budesonide.

On day 80 after BMT, he developed acute throat swelling, muffled voice, and stridor after consuming peanut butter. His symptoms subsided after systemic corticosteroids and antihistamines. In retrospect, his previous episode of vomiting and diarrhea had occurred after eating peanut products. He also had a transient peripheral blood eosinophil percentage up to 26% during these episodes. His serum IgE test result was strongly positive for peanut at greater than 100 kU/L (class 6 positivity) and mildly positive for hazel nut IgE at 1.13 kU/L (class 2 positive) and brazil nut IgE at 2.32 kU/L. We checked peanut IgE in pretransplant stored serum, and the result was negative. On querying bone marrow registry, his donor had reported severe allergy to peanut during preharvest evaluation. He was advised to strictly avoid peanuts. The results of skin prick testing to tree nuts were negative, and the patient was offered oral food challenge to confirm tolerance; however, he declined. His cyclosporine levels were within the therapeutic range during these episodes. He did not have any further gastrointestinal symptoms,

and he tolerated other food types well. He remained asymptomatic at the time of last follow-up at after day 100 with 100% donor chimerism of CD3 and CD33 components, and his leukemia remained in remission.

Allogeneic BMT is an established procedure in management of various hematologic disorders. It involves eradication of recipient immune system with conditioning regimen (chemotherapy with or without radiation) and replacement with donor hematopoietic stem cells. This way, it provides a unique opportunity to observe the effect of adoptive transfer of allergen specific IgE and memory B- and T-cell clones from donor to recipient.

Transfer of donor allergy to the transplant recipient is a rare phenomenon and has been described mainly in solid organ transplant and less commonly with BMT.¹ In a series of pediatric liver transplant recipients, the rate of TAA was up to 21%.² In a retrospective study, cumulative incidence of food allergy among the patients who underwent cord blood transplant was 6.6% at 1 year.³ In a series on sibling- donor BMT, a total of 18 nonallergic recipients were reported to develop allergy after BMT; however, only 5 cases had conclusive evidence of transfer of allergy from donor to recipient.¹

In a series by Agosti et al,⁴ BMT recipients had increased skin test reactivity 1 year after transplant. These patients also had increased exacerbation of allergic rhinitis and asthma. On long-term follow-up, persistence of allergen specific IgE transferred from donor to recipient was observed. There was also increased incidence of de novo allergic sensitization among the recipients.⁵ This finding suggests a possibility that recipients not only are susceptible to donor-specific allergy but they also acquire increased predisposition to develop new allergen specific IgE. Certain HLA-DR and DQ loci have been associated with allergy, which may increase the recipient's susceptibility to develop new allergies. However, HLA genes comprise only a minor subset of genes responsible for the development of allergy. This way even in HLA-matched BMT, these non-HLA genes from the donor may increase susceptibility of allergy development in the recipient. Conditioning with chemotherapy and radiation is associated with mucosal injury and increased permeability, which may increase exposure to food allergens to immune system.⁶

Calcineurin inhibitors, such as tacrolimus and cyclosporine, are known to induce T_H2-type T-cell responses and a cytokine environment to promote allograft tolerance. T_H2 response is known to promote allergic reaction by promoting interleukin 4 and interleukin 5 cytokines and IgE production.⁷ It is also known to increase intestinal permeability by inhibiting energy production in endothelial cells, which may lead to increased exposure to allergenic proteins. There is no direct comparison between different

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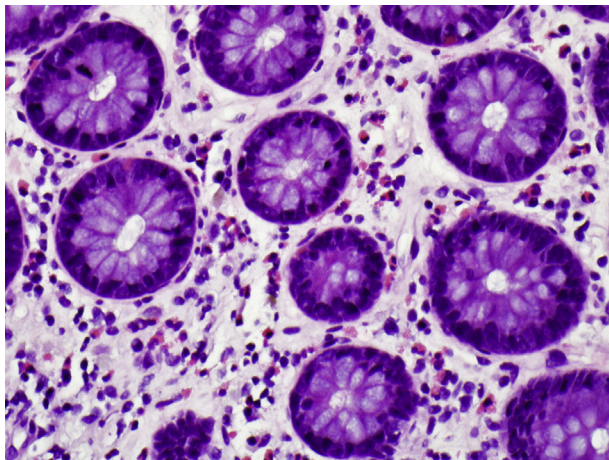


Figure 1. Colon mucosal biopsy specimens showing increased eosinophils at 85 per high-power field (hematoxylin-eosin; original magnification $\times 40$).

immunosuppressive drugs and incidence of allergic sensitization. In 1 study of kidney transplant recipients, the rate of clinically relevant allergy in patients receiving tacrolimus was twice that in patients receiving cyclosporine (15% vs 8%).⁸

Presentation of TAA is variable, and delayed onset of clinical symptoms up to 2 years after BMT has been described. Skin prick testing and detection of allergen specific IgE by radioallergosorbent assay testing may help with detecting specific causative allergens. Management is strict avoidance of identified food allergens and symptomatic treatment with epinephrine. Switching the immunosuppressive regimen from tacrolimus to cyclosporine may help based on reports of patients undergoing solid organ transplant.⁹

Transfer of donor allergy to BMT recipient can cause life-threatening anaphylactic reactions. Pretransplant donor screening for common allergens and preemptive avoidance in recipients after BMT is an option. This case is important because it reveals that transfer of allergy is possible even in an unrelated donor BMT compared with previous reports of sibling-matched BMT in which

genetic and environmental factors may confound susceptibility of recipient to TAA.

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References

- [1] Khan F, Hallstrand TS, Geddes MN, Henderson WR Jr, Storek J. Is allergic disease curable or transferable with allogeneic hematopoietic cell transplantation? *Blood*. 2009;113:279–290.
- [2] Ozbek OY, Ozcay F, Avci Z, Haberal A, Haberal M. Food allergy after liver transplantation in children: a prospective study. *Pediatr Allergy Immunol*. 2009;20:741–747.
- [3] Mori T, Kato J, Sakurai M, et al. New-onset food allergy following cord blood transplantation in adult patients. *Bone Marrow Transplant*. 2016;51:295–296.
- [4] Agosti JM, Sprenger JD, Lum LG, et al. Transfer of allergen-specific IgE-mediated hypersensitivity with allogeneic bone marrow transplantation. *N Engl J Med*. 1988;319:1623–1628.
- [5] Hallstrand TS, Sprenger JD, Agosti JM, Longton GM, Witherspoon RP, Henderson WR Jr. Long-term acquisition of allergen-specific IgE and asthma following allogeneic bone marrow transplantation from allergic donors. *Blood*. 2004;104:3086–3090.
- [6] Ozdemir O. New developments in transplant-acquired allergies. *World J Transplant*. 2013;3:30–35.
- [7] Durham SR, Till SJ. Immunologic changes associated with allergen immunotherapy. *J Allergy Clin Immunol*. 1998;102:157–164.
- [8] Gruber S, Tiringier K, Dehlink E, et al. Allergic sensitization in kidney-transplanted patients prevails under tacrolimus treatment. *Clin Exp Allergy*. 2011;41:1125–1132.
- [9] Lykavieris P, Frauger E, Habes D, Bernard O, Debray D. Angioedema in pediatric liver transplant recipients under tacrolimus immunosuppression. *Transplantation*. 2003;75:152–155.