

R.S. BUMBACEA^{1,2}, I. GHIORDANESCU¹

Atopic dermatitis induced by systemic immunosuppression with tacrolimus—case report

¹Department of Allergology, University Emergency Elias Hospital, Bucharest, Romania - E-mail: roxana.bumbacea@gmail.com

²University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

KEY WORDS

Atopic dermatitis, eosinophilia, hepatic transplantation, IgE, tacrolimus

Corresponding author

roxana.bumbacea@gmail.com
a.dumitru@imperial.ac.uk

SUMMARY

Type I hypersensitivity reactions have been described after solid organ transplantation despite T cell targeted immunosuppressive therapy. There are several reports of food allergy, asthma and eosinophilic colitis in pediatric transplant recipients under Tacrolimus immunosuppression, but not Cyclosporine A. We present the case of a 6 year old patient that developed de novo atopic dermatitis, eosinophilia and high levels of total IgE under systemic treatment with tacrolimus.

Introduction

Tacrolimus is one of the first macrolide immunosuppressant discovered and has been indicated for the prophylaxis of organ rejection in pediatric patients receiving allogeneic liver transplantation. It also complements existing treatment options for atopic dermatitis and has been accepted as a first-line treatment for inflammation. Type I hypersensitivity reactions have been reported after solid organ transplantation despite associated T cell targeted immunosuppressive therapy (1). There are several reports of food allergy, asthma and eosinophilic colitis developed by pediatric transplant recipients following immunosuppression with Tacrolimus, but not with Cyclosporine A (2, 3). Therefore, a causal relationship between allergic reactions and tacrolimus has been suggested. (1, 4).

In this report, we present the case of a 6-year-old male patient, with Alagille syndrome, an autosomal dominant disorder associated with abnormalities of the liver, heart, kidney, and other systems. He underwent hepatic trans-

plantation from a parental living donor (the father) in 2006 followed by long-term immunosuppression with tacrolimus. In 2008 he developed a skin condition which was suggestive for atopic dermatitis according to Hanifin and Rajka diagnostic criteria. It manifested with pruritus, flexural eczema, chronic and chronically relapsing dermatitis, cheilitis, itch when sweating, orbital darkening, recurrent conjunctivitis, xerosis, keratosis pilaris. The patient is not known with family history of allergic diseases. Laboratory finding showed elevated levels of total IgE (306 UI/L) and eosinophils (1760/mm³; 19.2 %) which had been normal before transplantation. Specific IgE (FEIA) to common allergens including Cow's milk, Dermatophagoides pteronyssinus, Dermatophagoides Farinae and Pollen Allergens (C. Dactylon, L. Perenae, S. Halepense, B. Inermis, H. Ianata) were less than 0.35 UI/mL (normal). Tacrolimus blood level ranged between 4-4.2 ng/mL. Skin prick-test could not be performed as the patient was under treatment with H1- antihistamines and systemic immunosuppression.

His treatment consisted of topical corticosteroids, emollients and H1-antihistamines. His parents would not consider topical therapy with tacrolimus as they were concerned about the increased skin absorption of this medication in skin barrier disorders, as atopic dermatitis. The patient's clinical progression under the above treatment was favorable but his pruritus persisted.

Atopic dermatitis is characterized by a Th2 immune pattern. Cyclosporine A and tacrolimus are both calcineurin inhibitors and have been extensively used as immunosuppressive therapy in pediatric liver transplant recipients. They share a similar mechanism of action by inhibiting the cytokine gene transcription, primarily interleukin-2 synthesis in Th1 lymphocytes.

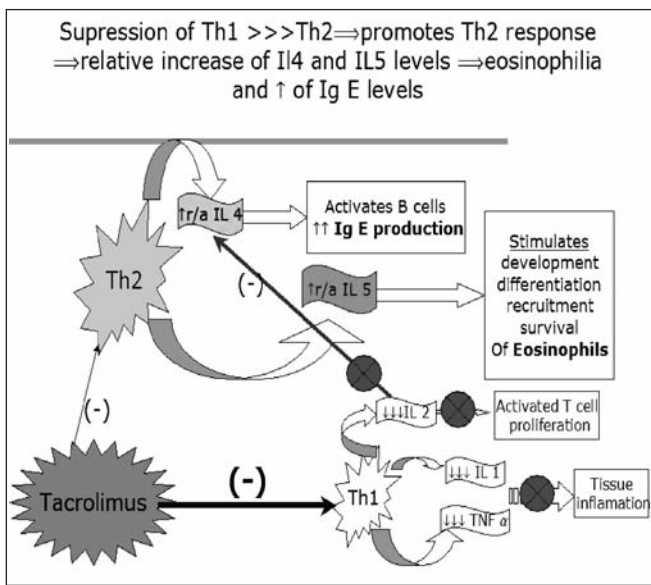
Selective suppression of Th1 lymphocytes by tacrolimus could deviate the immune response towards a Th2 phenotype; therefore it could promote an allergic immune response in these patients (Fig 1). Increased number of eosinophils has been found in up to 50% of children and adolescents following immunosuppression with tacrolimus. Most of these patients have associated high levels of total and specific IgE antibodies, particularly against food allergens. In many cases, the patients remain asymptomatic and do not present with food allergy or asthma (5). Reports have shown that once tacrolimus was

replaced with cyclosporine A in cases of associated food allergy, the number of eosinophils returned to normal, and consequently reintroduction of food allergens became possible (6). Thus, a similar mechanism could be involved in atopic dermatitis induced by an enhanced Th2 type immune response as a result of Th1 suppression with tacrolimus.

This report presents a case of a 6 year old patient that developed de novo atopic dermatitis, eosinophilia and high levels of total IgE following systemic treatment with tacrolimus. Although partly successful, the management of atopic dermatitis in this particular case has been difficult due to the lack of alternative options for his treatment. The patient presented persistent pruritus despite of combination between H1- antihistamines and steroid therapy.

We believe that systemic immunosuppression with tacrolimus induced the skin allergic condition by a mechanism similar to that encountered in other types of Th2 driven immune reactions. Nonetheless, more studies are needed to identify the prevalence of similar findings amongst other transplantation recipients.

Figure 1 - Tacrolimus inhibits primarily Th 1 response: reduces the levels of IL2 ⇒ 1) inhibits activated T cells proliferation and 2) up-regulates IL4 production; reduces the levels of IL1 and TNF α ⇒ antiinflammatory effect. Relative increase in IL4 and IL 5 production ⇒ eosinophilia, high levels of IgE.



References

1. S. Gruber, K. Tiringler, E. Dehlink, T. Eiwegger, E. Mayer, H. Konstantin, Z. Kikic, A. Graf, Z. Szépfalus, Allergic sensitization in kidney-transplanted patients prevails under tacrolimus treatment, *Clinical and Experimental Allergy*, 4 MAY 2011, DOI: 10.1111/j.1365-2222.2011.03761.
2. C. Arıkan, M. Kılıc, Y. Tokat, S. Aydogdu, Allergic disease after pediatric liver transplantation with systemic tacrolimus and cyclosporine a therapy, *Transplantation Proceedings*, Vol. 35, Issue 8, December 2003, Pages 3039 – 30412.
3. Jee Hyun Lee, Hwa Young Park, Yon Ho Choe, Suk-Koo Lee, Sang Il Lee, The development of eosinophilic colitis after liver transplantation in children, *Pediatric Transplantation*, Volume 11, Issue5, pages 518–523, August 2007, first published 16 MAR 2007, DOI: 10.1111/j.1399-3046.2007.00693.x
4. Öner Özdemir, Annie Arrey-Mensah, Ricardo U. Sorensen Development of multiple food allergies in children taking tacrolimus after heart and liver transplantation, *Pediatric Transplantation* Volume 10, Issue 3, pages 380–383, May 2006
5. E. Grano, E. Jakobovich, R. Bardenstein Tacrolimus immunosuppression – An association with asymptomatic eosinophilia and elevated total and specific IgE levels, *Pediatric Transplantation* Volume 10, Issue 6, pages 690–693, September 2006
6. Lykavieris Panayotis; Frauger Elisabeth; Habes Dalila; Bernard Olivier; Debray Dominique, Angioedema in pediatric liver transplant recipients under tacrolimus immunosuppression, *Transplantation*: 15 January 2003 - Volume 75 - Issue 1 - pp 152-155, Brief Communications: Clinical Transplantation