

A CASE REPORT OF TRANSPLANT-ACQUIRED ALLERGY IN A CHILD POST LIVER TRANSPLANT

Debbie A White,¹ MBBCh, FCPaed(SA), MMed (Paed), DipAllergy(SA), Cert Pulm(SA) Paed

Susan Klugman,¹ MBBCh, DCH, FCPaed(SA)

Ronit Weil,¹ MBBCh, DCH, DipAllergy(SA)

Suvarna Buldeo,² MBChB, DTMH, FCPaath(SA), MMed (ClinPath)

Nikki Bouwer,² MBChB

Cecil Levy,³ MBBCh, FCPaed(SA), Cert Nephro(SA) Paed

1 Division of Paediatric Pulmonology, Department of Paediatrics and Child Health, Charlotte Maxeke Johannesburg Academic Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

2 Department of Molecular Medicine and Haematology, National Health Laboratory Services, Charlotte Maxeke Johannesburg Academic Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

3 Division of Paediatric Nephrology, Department of Paediatrics and Child Health, Charlotte Maxeke Johannesburg Academic Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

Correspondence:

Debbie White, email: Debbie.White@wits.ac.za

ABSTRACT

Transplant-acquired allergy (TAA), previously described as transplant-acquired food allergy (TAFA), is an infrequent but potentially serious complication of organ transplantation. It has been described mainly after liver transplantation, but also after bone marrow, intestinal, lung and heart transplantations. The onset of the allergic symptoms starts many months after the transplant and ranges from symptomatic eosinophilic gastrointestinal inflammation to life threatening anaphylaxis. The pathogenesis is still not understood but appears to be a complex interplay between multiple factors including donor and recipient factors, the type of organ transplanted as well as the type of post-transplant immunosuppressive therapy protocol. We report on an 8 year old girl who developed de novo severe multiple food allergies, debilitating eczema and anaphylaxis 18 months after undergoing a liver transplant. She responded well to supportive management and a targeted elimination diet.

CASE

An eight and a half year old little girl was referred to our Allergy Clinic at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) with a history of a new onset of severe multiple food allergies and anaphylaxis, 18 months after undergoing a liver transplant. She also suffered from severe debilitating eczema, asthma and allergic rhinitis. She was born in Dublin, Ireland at term weighing 2.8kg. She developed jaundice at 5 weeks of age and was diagnosed with biliary atresia, and underwent a Kasai procedure at 6 weeks of age. Her jaundice did not settle and her diagnosis was subsequently reviewed as chronic cholestatic liver disease of unknown origin. She deteriorated progressively and was referred to King's College in London for assessment, where she underwent an orthotopic liver transplant at three and a half years of age in 2007. Her mother is South African, and relocated with the child, to Soweto, Johannesburg in January 2012 when she was eight years and five months old.

ALLERGY/ATOPY HISTORY

She had demonstrated no allergic symptoms until 18 months post her liver transplant, specifically no eczema and no known food allergies prior to the transplant. She complained of immediate symptoms including angio-oedema of the lips and tongue, swollen eyes, a tight feeling in her throat sometimes associated with wheeze and urticaria upon eating beef, mutton, pork, chicken, nuts, eggs and fish. In addition to the acute symptoms mentioned above, she complained of delayed non-specific gastrointestinal symptoms including nausea, cramping and bloating, which her mom attributed to the ingestion of meat products, a few days after ingesting them. Other allergic symptoms, which all seemed to start at the same time, included a sneezy, blocked nose, intermittent red watery eyes, intermittent wheeze, and extensive itchy eczema over most of her body. She would vomit immediately after eating dairy products followed by worsening of her eczema within 24 hours. There was a significant family history of atopy in

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that her mother had asthma as a child, her father suffered from sinusitis and eczema and her brother had asthma. Her diet consisted mainly of cereal, fruit, bread, vegetables and fried potato chips.

MEDICATIONS

Her list of current medications included the following:

- Prednisone 2.5mg daily po
- Tacrolimus 1mg BD po
- Budeflam 100mcg MDI (PRN)
- Asthavent 100mcg MDI (PRN)
- Inflanase nasal spray 1 BD
- Emulsifying ointment to the skin twice daily
- Advantan fatty ointment to her skin twice daily
- Protopic 0.1% twice daily to face (PRN)
- Wet wraps to legs and ankles (PRN)
- Emergency kit: epipen (adrenaline) and antihistamines

ON EXAMINATION

She was an alert and co-operative child. She was well grown with a weight 27 kg (z-score 0) and a height 123 cm (z-score -1). She had no obvious dysmorphic features but had the typical 'allergic facies' including bilateral allergic shiners, enlarged congested turbinates, open mouth breathing and dental malocclusion. Her ears, throat, chest and cardiovascular examinations were normal. Her abdomen was mildly distended with a transverse laparotomy scar and a midline hepatomegaly of 4 cm (Figure 1). Her skin revealed generalised xerosis with altered pigmentation, scarring and lichenification diffusely over her neck, wrists, ankles, trunk and back (Figures 2-3).

INVESTIGATIONS

Table I shows the relevant investigations performed.



Figure 1. Distended abdomen with transverse laparotomy scar and generalised xerosis of the skin.

DISCUSSION

The acquisition of new food allergy after transplantation, previously referred to as transplant-acquired food allergy (TAFA) and now more recently as transplant-acquired allergy (TAA)¹, is now a well described phenomenon, mainly reported in children.² Eosinophilic mucosal inflammation post paediatric liver transplant was first reported in 1997 by Dhawan et al.³ and transfer of allergy from a food allergic solid organ donor such as a liver donor to a previously non-allergic transplant recipient was first reported in the 1990's.¹ The picture is complicated by numerous case reports of TAFA after receiving liver grafts from donors

Table I: Relevant investigations

St Michael's Hospital, Ireland, Nov 2011	CMJAH, March 2012
Total IgE 8170 kU/l	Total IgE > 1000.00 kU/l
Cow's milk IgE > 100.00 kU/l	Chicken IgE > 100.00 kU/l
Peanut IgE > 100.00 kU/l	Pork IgE 9.26 kU/l
Egg white IgE 63.30 kU/l	Mutton IgE 4.17 kU/l
Cod fish IgE 49.5 kU/l	Beef IgE 1.49 kU/l
Soya IgE 16.5 kU/l	Anti-tissue transglutaminase IgA 0.2 U/ml, IgG 0.7 U/ml
Wheat IgE 9.16 kU/l	Anti-gliadin IgA < 1.0 U/ml, IgG 21.0 U/ml
HDM > 100.00 kU/l	
Grass pollen > 100.00 kU/l	



Figure 2. Eczema over ankles showing altered pigmentation, thickened skin and scarring.



Figure 3. Eczema over medial aspect of the wrist showing lichenification and scarring.

with no documented history of food allergy.¹ The estimated prevalence of TAAFA among young children in the literature has been documented in various studies and ranges from 6% - 57%.¹ It has been described following bone marrow and solid organ transplants; mainly liver but also in combined kidney and liver, intestine, lung and heart transplants.

The onset of allergic symptoms starts many months after the transplant; 33 ± 19 months in 7 patients following liver transplant in one study,⁴ seven months post liver transplant in another study² and 12 months post heart transplant.² The spectrum of allergic disease is quite vast and ranges from symptomatic eosinophilic gastrointestinal

inflammation resulting in chronic diarrhoea with or without occult bleeding and anaemia, angio-oedema, urticaria, eczema, stridor and wheeze to life-threatening anaphylaxis. In most of these post-transplant patients, the timing of the food-related allergic reactions is consistent with an IgE-mediated process and patients have high eosinophil counts and elevated total and specific IgE levels.⁵ Eosinophilic gastroenterocolitis is also common after transplantation and should be considered in all children with gastrointestinal symptoms.¹ In a study by Wisniewski J et al., 11 out of 15 (73%) food allergic patients post liver transplant who underwent endoscopy, had eosinophilic infiltrates in multiple segments of the oesophagus alone or in combination with other bowel segments. Food IgE sensitisation was confirmed in 9/11 (82%) of subjects who were following restricted food diets.⁶

PATHOGENESIS

The pathogenesis of TAA remains unclear but appears to be multifactorial, including donor and recipient factors, the type of organ transplanted as well as the type of post-transplant immunosuppressive therapy protocol.

DONOR FACTORS

New onset food allergy can arise as a consequence of passive transfer from the donor; resulting from the receipt of food-antigen-specific IgE or food-antigen-specific lymphocytes from a sensitised donor.⁷ This appears to be the main mechanism in adult transplant patients. Interestingly, transfer of allergy to nuts to the recipient of the liver has been described, but not to recipients of other transplanted organs, from the same donor.⁸

THE ORGAN TRANSPLANTED

The absence of food allergy in tacrolimus-treated kidney transplant recipients compared to liver-transplant recipients, suggests that a contributor to new-onset post-transplantation food allergy is the actual organ itself, and the role that it plays in developing immune tolerance, i.e. mainly the liver.⁹ The finding that mostly liver transplantations seem to be associated with new onset TAA suggests the pluripotential hematopoietic tissue and dendritic cells, normally resident in the liver, play a role in this phenomenon.¹ T-cell activation by antigens migrating through the portal vein occurs in the liver and some liver-resident dendritic cells and liver sinusoidal endothelial cells direct naïve CD4 T cells preferentially to Th2 differentiation.¹

IMMUNOSUPPRESSIVE PROTOCOL

Calcineurin inhibitors, cyclosporin A and the more potent

drug tacrolimus, block T-cell cytokine production are used as first-line therapy in post-transplant settings. Tacrolimus has been found to be superior to cyclosporine A for rescue therapy as well as for earlier weaning of steroids.¹ An association between tacrolimus therapy after liver transplantation and development of food allergy was first suggested by Lacaille et al. in 1997.¹⁰ Maarof et al. report food allergy after liver transplant in 4.5% and 26% of recipients with a cyclosporine- or tacrolimus-based regimen, respectively.⁴ Tacrolimus increases intestinal permeability, which may favour transport of antigens from the intestinal lumen and exposure to the immature intestinal mucosal system of children, increasing the risk of sensitisation and food allergy development.⁴ It has also been shown to induce a shift toward a Th2 cytokine profile and IgE production, and also has an effect on the pool, function, or both of regulatory forkhead box protein 3-positive T cells (T regulatory cells).⁴

RECIPIENT FACTORS

Children with chronic cholestasis, such as biliary atresia, often receive special feeding with an artificial formula and poorly diversified diet until liver transplant, and have highly altered microbial ecology that can affect the function of the regional immune system.⁴ Wisniewski J et al. showed that de novo food sensitisation and eosinophilic gastrointestinal disease were linked to transplantation at a younger age (mostly less than one year of age) and an underlying predisposition to atopic disease.⁶

MANAGEMENT

Treatment consists of elimination of the allergenic foods, administration of hypoallergenic formula, antihistamine medication and adrenaline for anaphylactic reactions.⁹ A treatment strategy involving a combination of a switch from a tacrolimus- to a cyclosporine-immunosuppressive regimen with an elimination diet has been shown to result in disappearance of clinical and biological symptoms of food allergy.⁴ Reducing the immunosuppression has also been shown to result in symptomatic improvement.^{6,11} However, these strategies need to be weighed up against the risk of graft rejection.

PROGRESS IN OUR PATIENT

Our patient responded well to management of her allergic disease with appropriate pharmacotherapy, and a strict targeted elimination diet, including elimination of cow's milk, eggs, peanuts, fish, chicken, pork and mutton. She was able to tolerate soya, wheat and small amounts of beef despite sensitisation. In consultation with our paediatric nephrologist who looks after our kidney and liver

transplant patients, we decided to continue tacrolimus as her immunosuppressive therapy, monitoring the levels closely, as she was at risk of graft rejection with a switch to cyclosporine A.

CONCLUSION

Transplant-acquired allergy (TAA) is an infrequent but potentially serious complication of organ transplantation. Recognition, symptomatic management of the allergic disease, a strict targeted elimination diet and a possible switch from a tacrolimus- to a cyclosporin-immunosuppressive regimen or a reduction in immunosuppression, appear to be the current mainstays of therapy.

DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest.

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