

Two Cases of Solitary Renal Transplant Associated Shellfish Sensitization from the Same Allergic Donor

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Case Report

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Abstract

Background

Since the first case of transplant-acquired food allergy (TAFA) reported in the 1990s, TAFA has been increasingly recognized in solid organ and bone marrow transplantation, especially in pediatric liver transplant recipients. Due to the concern of allergic reactions, including anaphylaxis, food allergies can significantly impact patients' lives. While IgE-mediated allergy transmission has been documented across multiple organ types, TAFA following solitary renal transplantation remains rare. The mechanisms underlying TAFA and the impact of donor allergy, immunosuppressive therapy, and recipient-specific factors remain incompletely understood.

Case Presentation:

We report two cases of TAFA following solitary renal transplantation from the same donor with documented severe shellfish allergy. Both recipients underwent renal transplantation for end-stage diabetic nephropathy and were maintained on identical post-transplant immunosuppressive regimens including tacrolimus, prednisone, and mycophenolate mofetil. Following transplantation, both recipients avoided consumption of shellfish until they were evaluated in the allergy clinic. Neither recipient had a prior shellfish allergy; one had prior dust-mite sensitization with no clinical symptoms, while the other had no history of allergy. Despite their shared variables, the recipients showed markedly different sensitization profiles: both had positive skin prick testing to shrimp, but one showed a large immediate and delayed-phase reaction (wheal over 80 mm) while the other exhibited a comparatively modest reaction. Over a 9-month period, both patients showed progressive attenuation of their sensitization, with a decrease in wheal size; therefore, supervised oral challenge was successfully performed. Both were initially prescribed an epinephrine autoinjector and advised not to consume shellfish until a successful oral challenge could be completed.

Conclusion

Based on the paucity of published cases, the incidence of TAFA in solitary renal transplantation is exceedingly rare, and the long-term outcomes remain poorly defined. In our cases, both recipients received organs from the same allergic donor and identical immunosuppression regimens, yet demonstrated markedly different sensitization patterns, suggesting that TAFA cannot be explained by donor allergy or immunosuppression alone and highlighting the role of recipient-specific immune factors. Notably, the unusually large size of the wheal occurred in the mite-sensitized recipient despite regular crustacean consumption prior to the transplant. The gradual diminution with repeated testing raises questions about transient sensitization, the duration of TAFA, and the sensitivity and specificity of post-transplant skin testing. Due to the serious consequences of allergic reactions, these findings reinforce the importance of donor allergy disclosure during transplant screening, patient counselling,

precautionary avoidance, and support a cautious longitudinal approach of close follow-ups to reduce the risk to these recipients.

Background

New food allergies post-transplant are described as transplant-acquired food allergy (TAFA).¹ TAFA was first reported in the 1990s in a patient after liver and kidney transplantation.^{1,2} Since then, there has been increasing awareness of TAFA in other solid organs such as the lung, heart, intestine, and pancreas.^{1,3} The mechanism and pathophysiology of TAFA have not been elucidated, and there are currently many theories proposed as to the etiology of TAFA, including the use of specific primary immunosuppressants and passive transfer of donor allergen-specific B or T cells.⁴ Interestingly, there have been many cases of IgE-mediated food allergy transmission post-solid organ transplant, predominantly in pediatric liver transplant recipients.^{3,5-7} Therefore, most of these proposed mechanisms have been derived from liver transplantation cases. Despite renal transplant surgery being the most commonly performed transplantation surgery in the world, many retrospective studies have reported a relative absence of TAFA in cases of renal transplantation.^{2-5,8,9} As the mechanism of TAFA is still largely unclear, unique cases should be accumulated in order to provide a better understanding of TAFA. Here, we report two rare cases of transfer of shellfish allergy from an allergic donor to an anergic recipient.

Case Presentation

Case 1

A 61-year-old female with previously known dust mite sensitization without allergic reactions, type 1 diabetes, hypothyroidism, and end-stage renal disease secondary to diabetic nephropathy was seen in the adult allergy and immunology clinic following a renal transplant two months earlier for evaluation of possible shellfish allergy. She had been on peritoneal dialysis for a year and a half prior to her successful renal transplant and had been started on immunosuppressants to prevent rejection with Tacrolimus, Mycophenolate Mofetil, and prednisone. Crustaceans were a regular aspect of her diet, and she had no allergic reaction prior to her transplant. After the transplant, it was disclosed to her that the donor had a serious shellfish allergy and a question was raised about whether the allergy could be transferred to the recipient. Out of an abundance of caution, she was asked to avoid all shellfish and was referred to the allergy clinic for further investigation. At two months post-transplant, she had positive skin prick testing (SPT) to crustacean extracts with wheal diameters of 5mm to crab, 5mm to lobster, and 6 mm to shrimp. SPT testing to molluscs (clam and oyster) was negative. SPT done at the same time showed a 7 mm wheal to *Dermatophagoides pteronyssinus* and a 6 mm wheal to *Dermatophagoides farinae*. Further testing revealed elevated IgE levels against shrimp, crab, and lobster at 0.9 kU/L, 0.7 kU/L, and 0.8 kU/L, respectively. She was seen again in the clinic three months post-transplant for a possible oral challenge; however, SPT to fresh shrimp revealed an immediate, large positive reaction with a wheal diameter of 12mm (histamine 6mm, saline 0mm), and the delayed reading done at home revealed a wheal diameter

greater than 80mm. After discussion of risks and benefits, she did not wish to pursue an oral challenge at the time; therefore, an epinephrine autoinjector was prescribed with a recommendation to strictly avoid crustaceans given the large positive SPT.

She was seen again in the adult allergy and immunology clinic 6 months post-transplant for a repeat SPT to fresh shrimp. It revealed an even larger immediate positive reaction with a wheal diameter of 30 mm and a delayed reaction with a wheal diameter of 80 mm; therefore, oral challenge was not pursued (Fig. 1). She had adequate positive and negative controls to validate results. Skin prick testing to scallop at the same time revealed a small 5mm wheal; therefore, a graded oral challenge to scallop was pursued in the clinic and was successful with 59g of cooked scallop. 9 months post-renal transplant, she was seen again for follow-up, and a repeat SPT was performed to fresh shrimp, which resulted in an immediate positive reaction with a wheal of 11x10mm and a delayed reaction with a wheal of 37x53mm, suggesting possible waning of the reaction (Table 1, Fig. 2). Therefore, a supervised graded oral challenge was performed using a total of 36g of freshly cooked shrimp and was successful, with no allergic reactions. She was asked to continue avoiding lobster and crab until an oral food challenge could be pursued in the clinic.

Table 1
Clinical and
Demographic
Characteristics
of Case 1

Timeline	Skin Prick Testing wheal size in millimeters	Serum specific IgE (Ku/L)	Oral Challenge
2 months post transplant	Crab 5 Lobster 5 Shrimp 6 Clam 0 Oyster 0 <i>Dermatophagoides pteronyssinus</i> 7 <i>Dermatophagoides farinae</i> 6	Crab 0.7 Lobster 0.8 Shrimp 0.9 Clam < 0.35	
3 months post transplant	Fresh Shrimp 19x11 (at 20 min), Fresh Shrimp 80 (at 12 hours) Histamine 6		
6 months post transplant	Fresh Shrimp 30 (at 20 min), Fresh Shrimp 80x60 (at 12 hours) <i>Dermatophagoides pteronyssinus</i> 6 <i>Dermatophagoides farinae</i> 9 Clam 7 Crab 7 Lobster 10 Oyster 2 Fresh scallop 5 Histamine 4 Saline 0		Fresh Scallop (59 grams ingested, in total) - no reaction
9 months post Transplant	Fresh Shrimp 11x10 (at 20 min) Fresh Shrimp 37x 53 (at 2.5 hours)		Fresh Shrimp (36 grams ingested, in total)- no reaction

Case 2 Presentation:

A 58-year-old male with no prior allergic history was seen in the adult allergy and immunology clinic eight months following a solitary renal transplant from a known allergic donor. He was seen by a different allergist at a different academic hospital site. He had a past medical history of diabetes leading to several complications, including retinopathy, neuropathy and end-stage renal disease leading to the transplant. Mycophenolate mofetil, Tacrolimus and prednisone were used as immunosuppressants to prevent rejection. Unlike the other recipient, he had no prior dust-mite sensitization or allergy history. He also did not enjoy shellfish, and it was not a regular part of his diet. He was asked to avoid shellfish as the deceased donor had a severe shellfish allergy. He was referred to the adult allergy clinic 8 months post-solitary renal transplant for testing. Upon presentation, he denied having any accidental exposure to any shellfish and consented to skin prick testing. Skin prick testing done at 8 months showed an immediate positive result to shrimp with a wheal of 8mm and *D. farinae* with a wheal of 6mm (Table 2). He had adequate positive and negative control with histamine (6mm) and saline, which did not result in any wheal (Fig. 3). He was given a laboratory requisition for a serum tryptase level to be performed in case he has any accidental exposure. He was also given a lab requisition for serum allergen-specific IgE levels to shrimp, crab, lobster, and dust mites (*Der. f.*, *Der. p.*) to be done at his convenience. He was prescribed an epinephrine autoinjector with a recommendation to avoid all shellfish until he can undergo a supervised, graded oral challenge in the clinic. He was also asked to monitor his skin prick test site for any delayed reaction, given the other recipient's history of large delayed skin test positivity.

The patient was seen again in the clinic 18 months post-transplant for a repeat skin prick test. He had been strictly avoiding all crustaceans and had no accidental exposure. He also did not have any history of unexplained anaphylaxis. He was motivated to undergo an oral food challenge to delabel against his shellfish allergy. Skin prick test done prior to the oral challenge showed adequate positive and negative controls: histamine at 6.5mm and saline at 0.5mm, with no flare. Skin prick test to fresh shrimp showed a 1mm wheal with no flare. He subsequently underwent a successful oral challenge with 75g of fresh shrimp, given in 6 divided doses over a 3-hour period in the clinic. He had no concerning features of anaphylaxis during the challenge and was discharged home following 1 hour of monitoring.

Table 2
Clinical and Demographic Characteristics of Case 2

Timeline	Skin Prick Testing (mm)	Oral Challenge
8 months post transplant	Histamine 6	
	Saline 0	
	Clam 0	
	Crab 0	
	Lobster 4	
	Oyster 4	
	Scallop 5	
	Shrimp 8	
	<i>Dermatophagoides pteronyssinus</i> 5	
	<i>Dermatophagoides farinae</i> 6	
18 months post-transplant	Histamine 6 Saline 0.5 Fresh Shrimp 1	Fresh Shrimp (75 grams ingested, in total)-No reaction

Discussion and Conclusions

Gel and Coombs type 1 allergies are mainly mediated by IgE antibodies. When one becomes sensitized to an allergen, IgE antibodies are generated by B lymphocytes in response to specific antigenic stimuli.¹⁰ Under sustained antigenic stimuli, Th0 cells differentiate into different subsets of T cells, such as Th1 and Th2 cells.¹⁰ Th1 mainly stimulates the cellular immune response by secreting IFN- γ and IL-2.¹⁰ Th1 is also involved in type 4 delayed reaction, while Th2 is involved in secreting IL-4, IL-5, and IL-6, promoting differentiation of B cells and humoral immune response to antigen.¹⁰ Much like traditional food allergy, TAFA leads to elevated IgE levels to a specific allergen, although the initiating mechanisms of these immunologic pathways remain incompletely understood.

Based on previous studies, several mechanisms of TAFA have been proposed. One hypothesis involves the role of immunosuppressive therapy, particularly tacrolimus, which has been shown to induce an imbalance between Th1 and Th2 responses.¹⁰ Tacrolimus preferentially suppresses Th1 over Th2, thereby indirectly promoting a Th2 response, leading to IgE secretion from B lymphocytes.¹⁰ In a retrospective study by Guo et al., 9 out of 79 solitary renal transplant patients developed sensitization, with the majority developing hypersensitivity to inhalants.¹⁰ It was unknown whether the donors had any allergies and whether there was transfer of such allergies to recipients post-transplant, as sensitization

was reported to be de novo post-surgery.¹⁰ Notably, 8 out of these 9 patients who developed sensitization were treated post-transplant with tacrolimus for primary immunosuppression, suggesting a potential association between tacrolimus use and TAFA.¹⁰ However, in other studies, such as Marcus et al., who conducted a cross-sectional cohort study involving pediatric patients who underwent single-organ transplant (liver, heart, kidney and visceral organ), did not show an association between types of post-transplant immunosuppressive agents and the risk of TAFA.³ Notably, the interpretation of this study is limited due to all study participants being on tacrolimus, precluding a meaningful comparison.³

In our case presentations, both recipients received identical immunosuppressive therapy consisting of tacrolimus, mycophenolate mofetil, and prednisone, yet exhibited markedly different sensitization responses. This suggests that immunosuppressive agents alone may not account for the variability in allergic responses. The controlled nature of donor exposure and immunosuppression in these cases allows for a more focused consideration of recipient-specific factors as key determinants of post-transplant sensitization.

Another proposed mechanism is the passive transfer of donor-derived allergen-specific immune cells, including allergen-specific B and T lymphocytes.⁴ This phenomenon has been most demonstrated in cases of liver transplant.⁴ The liver can act as a source of hematopoietic stem cells facilitating engraftment of donor immune cells; however, this is rare in solitary kidney transplantation.^{2,5} A case report by Berry et al presented a patient who received a kidney-pancreas combined transplant from an allergic donor. The recipient developed sensitization to peanut with normalization of peanut allergy biomarker after 6 months, suggesting transient transfer of donor Th2 lymphocytes to the recipient.¹¹ Interestingly, another recipient of the solitary kidney from the same donor did not develop sensitization to peanut, suggesting that passive transfer of such lymphocytes may be more probable if an organ other than the kidney is involved, but is unlikely in an isolated kidney transplant.¹¹

Cross-reactivity between inhalant allergens and shellfish represents an additional mechanism. Shrimp allergy has been linked to dust-mite sensitization due to homology between dust-mite and shellfish tropomyosins.¹²⁻¹⁶ Gamez et al noted differences in mite-crustacean cross-reactivity based on climate and humidity, with shrimp being the primary sensitizer in drier climates, as in western countries.¹⁶ As the patient in case one had prior known dust mite sensitization, there may be a possibility of hypersensitivity reaction to crustaceans being attributable to *Dermatophagoides pteronyssinus* (Der p 10) cross reactivity with shrimp (Pen a 1). This could contribute to the large positive reaction to crustacean serum-specific IgE and SPT post-transplant. The size of the wheal does not indicate the severity of the allergic reaction but can be correlated with the degree of sensitivity to the specific allergen.¹⁷

The most notable observation in these cases is the discordant clinical phenotype despite comparable exposure variables. Each recipient received a kidney from the same allergic donor and underwent identical immunosuppressive regimens; however, they demonstrated markedly different skin test responses and clinical trajectories. Notably, the recipient with a pre-existing atopic background, including

sensitization to house dust mite and established oral tolerance to shellfish before transplantation, exhibited the more pronounced skin prick test response. This finding raises the possibility that transplantation may have been associated with a breakdown of pre-existing tolerance, thereby contributing to the observed sensitization and clinical phenotype. This finding challenges a simplified model in which atopy or known cross-reactivity predicts post-transplant food allergy risk. Furthermore, the impressive size and delayed test results suggest a T-cell mediated process.

For our patient in case one, it is interesting that she had both a large immediate and delayed reaction to fresh shrimp that waned after months of observation, leading to successful completion of an oral challenge to fresh shrimp. It would have been interesting to perform an oral challenge to shrimp earlier on; however, the patient was understandably reluctant at the time, given the large SPT result, and it would have been unethical to pursue such a test without consent. Similarly, the patient in the second case was found to have dust-mite sensitization along with sensitization to mollusks and crustaceans. It is possible that there is cross-reactivity with dust-mite tropomyosin; however, this cross-reactivity would not explain sensitization to mollusks. The SPT result for the second patient also showed waning of sensitization, with a successful oral challenge at the end, as has been described in cases of TAFA. Unfortunately, we do not have Component-resolved diagnostics available locally for further diagnostic clarity.

In summary, these cases highlight that TAFA in renal transplantation is likely multifactorial and cannot be explained alone by immunosuppressive regimen, donor allergy, pre-existing food tolerance, or pre-existing atopic status. Despite identical donor exposure and immunosuppression, the two recipients exhibited markedly different patterns of sensitization, with unexpectedly more pronounced early reactivity in the non-atopic individual and transient, waning sensitization in both cases. Notably, the most pronounced sensitization occurred in the recipient with baseline atopy who was regularly consuming crustaceans pre-transplant. While inhalant sensitization and tropomyosin-mediated cross-reactivity may contribute in selected patients, they likely do not fully account for the variability observed. These findings underscore the importance of recipient-specific immune factors in modulating post-transplant allergic responses and highlight the need for careful pre-transplant screening and patient education regarding the possibility of TAFA. They also highlight gaps in the literature regarding optimal diagnostic strategies, including the utility, timing, and interpretation of post-transplant allergy testing, as well as the duration of sensitization. Overall, these cases support a cautious interpretation of early post-transplant testing, with longitudinal reassessment and a supervised oral food challenge, and underscore the need for further studies to better define mechanisms and guide clinical management.

Abbreviations

TAFA

Transplant Acquired Food Allergy

SPT

Skin Prick test

Der. f

Dermatophagoides farinae

Der. p

Dermatophagoides pteronyssinus

Declarations

Ethics Approval and consent to participate:

Ethics approval was obtained for this case report from the Health Research Ethics Board – Bannatyne Campus, University of Manitoba

Consent for publication:

Written informed consent was obtained from both patients for the publication of this case report

Competing Interest:

None are relevant to this publication

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None

Author Contribution

JH collected the data and drafted the initial manuscript. LM and CB provided patient data, clinical guidance and revision. NT provided critical edits to the manuscript. All authors read and approved the final manuscript

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Availability of data and materials:

Not applicable

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Figures

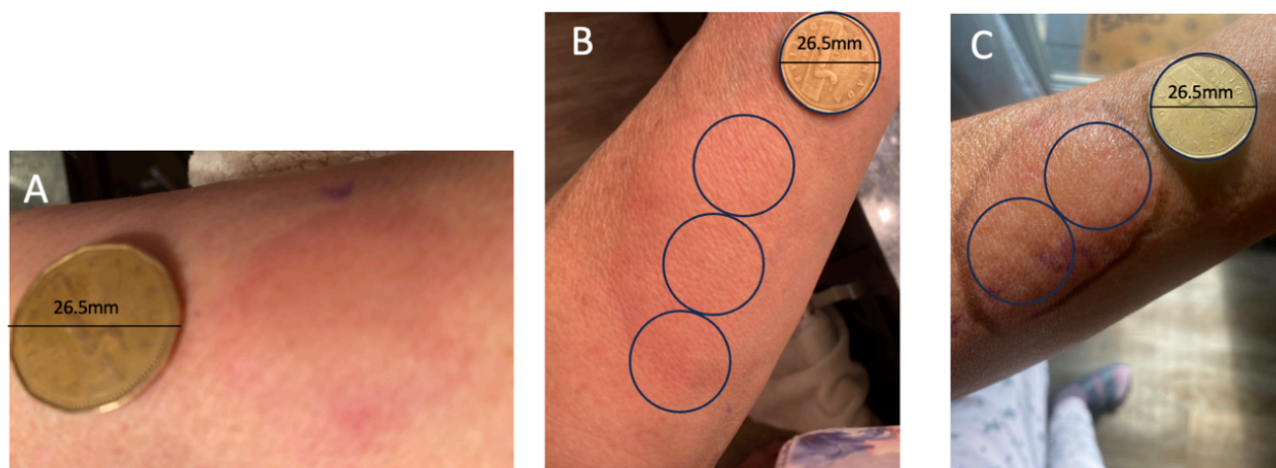


Figure 1. A) Skin testing done with Fresh shrimp 6 months post transplant in case one shows immediate positive reaction that is >30mm (compared to Looney). B) Skin testing done with Fresh shrimp 6 months post renal transplant in case one shows increase in diameter of the wheal >80mm 12 hours later. C) Skin testing done with Fresh shrimp 9 months post renal transplant in case one shows wheal diameter of 37x 53mm 2 hour and 30min later

Figure 1

See image above for figure legend.

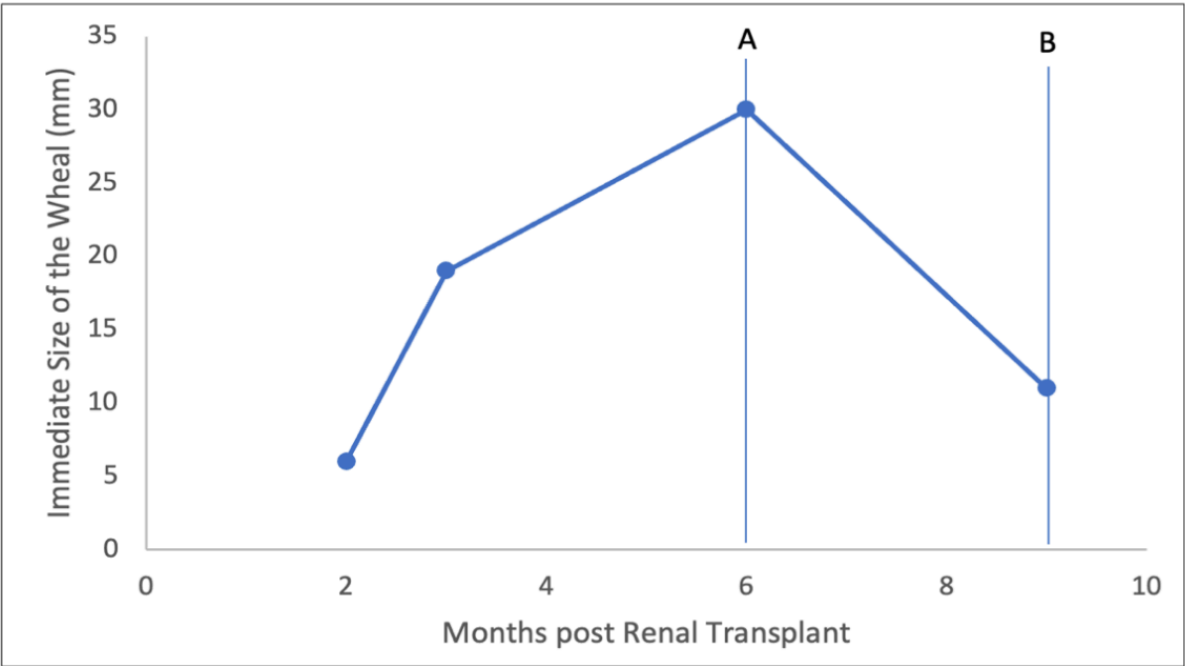


Figure 2. Waning of the immediate size of the wheal to fresh shrimp over 9 months period for case one
A) Negative oral challenge to Mollusks 6 months post Renal Transplant, B) Negative oral challenge to fresh shrimp 9 months post Renal Transplant

Figure 2

See image above for figure legend.

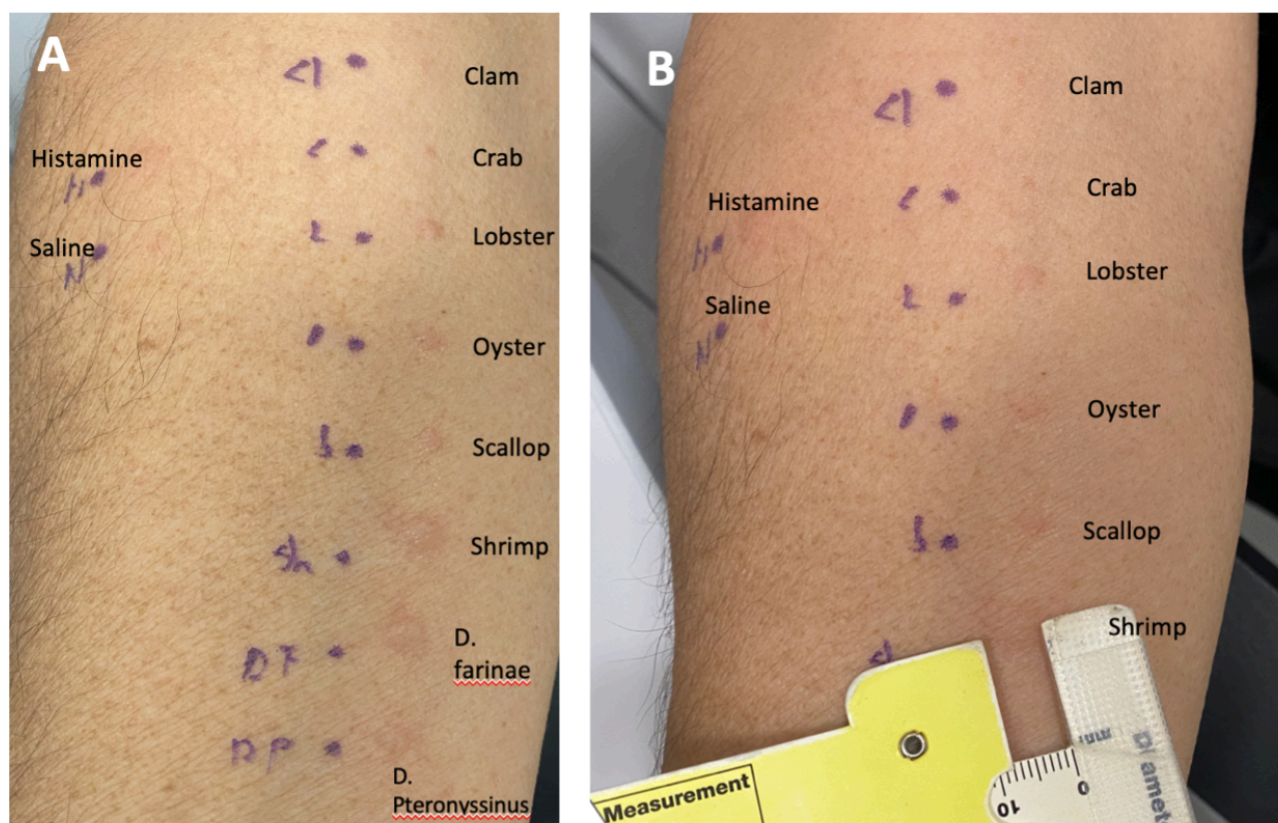


Figure 3. A) Skin prick testing done to crustacean and dust mite 8 months post transplant in case two shows immediate positive reaction to shrimp and *D. farinae*. B) Skin prick testing done to crustacean and dust mite in case two 8 months post renal transplant with measurement of wheal for shrimp

Figure 3

See image above for figure legend.