

Severe occupational protein contact dermatitis caused by fish in 2 patients with filaggrin mutations

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doi:10.1111/cod.12031

Key words: filaggrin gene mutation; hand eczema; occupational contact urticaria; protein contact dermatitis.

Protein contact dermatitis, a frequent disorder among patients who professionally handle foods (1), causes burning, stinging, and itching, seconds to minutes following skin contact with certain foods (2). Overall, protein contact dermatitis is observed in ~20% of Danish patients with occupational skin disease who are referred to a tertiary clinic (1). The underlying immunological mechanisms have not yet been fully elucidated, although immediate hypersensitivity reactions characterized by elevated IgE levels are involved in some cases (2).

Filaggrin proteins are crucial for epidermal skin barrier functions (3). Filaggrin gene (*FLG*) mutations are common in people of European descent, and increase the risk of allergic diseases, including atopic dermatitis, asthma, rhinitis, and food sensitization (4). It is currently

unknown whether *FLG* mutations affect the risk and severity of protein contact dermatitis. Here, we present 2 patients with occupational protein contact dermatitis caused by fish and who carry *FLG* null mutations (5). We find them to be of particular interest, as both patients developed severe hand eczema and systemic allergic reactions to fish, forcing them to leave their profession.

Case 1

A 38-year-old woman with severe atopic dermatitis since birth, as well as asthma and allergic rhinitis since adulthood, was referred with severe hand eczema and asthma following contact with raw fish. She also had a history of oral food allergies to fish since childhood. Hand eczema developed within the first 3 months of her working as a sandwich-maker, in which job she continuously handled raw fish. This additionally resulted in malaise and flu-like symptoms. Because the symptoms gradually worsened, she was forced to resign from her job within 1 month. At follow-up, she still experienced immediate aggravation of her skin condition and systemic symptoms when handling fish, or when staying in a room where

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Conflicts of interest: The authors declare that they have no conflict of interest.

Funding sources: No funding source.

fish was prepared. Prick testing showed positive reactions to cod, pollen, pet fur, sagebrush, mould, oatmeal, wheat flour, rye flour, soya beans, orange, lemon, apple, salad, potato, celery, cress, watercress, chives, parsley, carrot, endive, and pineapple. She had an elevated total serum IgE level.

Case 2

A 37-year-old female cook, with a history of atopic dermatitis since birth, was referred with hand eczema and immediate-type hypersensitivity symptoms. Atopic dermatitis had cleared before puberty. Before working as a cook, she had no asthma or skin symptoms apart from xerosis. After 3 years in the profession, she developed severe vesicular hand eczema, as well as severe asthma and rhinitis, when handling raw fish, especially cod. Years later, the symptoms worsened, as she experienced airborne facial and chest contact urticaria, and systemic reactions, including malaise and flu-like symptoms, when staying in a room where raw fish was prepared. Owing to the severity of asthma, she was treated with high-dose oral corticosteroids (prednisolone 5–25 mg daily) for a year, before she had to resign from her job and was retrained in service management. At follow-up, she still experienced aggravation of the skin symptoms when handling fish or when staying in a room where fish was prepared. Prick testing with rare meat and fish products showed strong positive test reactions to cod, halibut, herring, plaice, and boiled prawns. She had elevated serum levels of IgE specific for tuna, cod, and salmon.

Discussion

We present two *FLG* mutation carriers with occupational protein contact dermatitis on the hands caused by fish exposure, and who developed severe asthma and malaise when exposed to fish. In the first patient, sensitization to cod was likely to have occurred in childhood. In the second patient, sensitization probably occurred while she was working as a cook. The impaired skin barrier in *FLG* mutation carriers, owing to low levels of filaggrin proteins and their metabolites (3), may increase the penetration of allergens. In favour of this assumption are both animal (6) and clinical studies (7) showing elevated specific IgE levels. A strongly increased risk of peanut allergy was reported among *FLG* mutation carriers (8). Also, adult *FLG* mutation carriers with dermatitis had five-fold increased levels of contact sensitization as compared with controls (JP Thyssen, manuscript in preparation 2013). *FLG* mutations increase the risk of nickel sensitization (9), probably as a result of low histidine levels in the skin, allowing nickel ions to penetrate. Skin inflammation downregulates filaggrin expression, further reducing skin protection against allergen penetration (6). On the basis of the 2 cases presented here, as well as our clinical experience with other patients suffering from protein contact dermatitis, we propose that individuals with an inherited barrier abnormality such as that resulting from *FLG* mutations may potentially have an increased risk of developing protein contact dermatitis, and may also have a more severe course, resulting in systemic symptoms and asthma following secondary airway exposure to the protein allergen.

References

- 1 Vester L, Thyssen JP, Menné T, Johansen JD. Occupational food-related hand dermatoses seen over a 10-year period. *Contact Dermatitis* 2012; **66**: 264–270.
- 2 Menné T, Johansen JD, Sommerlund M, Veien N K. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. *Contact Dermatitis* 2011; **65**: 3–12.
- 3 Irvine A D, McLean W H I, Leung D Y M. Filaggrin mutations associated with skin and allergic diseases. *N Engl J Med* 2011; **365**: 1315–1327.
- 4 van den Oord R A, Sheikh A. Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systematic review and meta-analysis. *BMJ* 2009; **339**: b2433.
- 5 Meldgaard M, Szecsi P B, Carlsen B C et al. A novel multiplex analysis of filaggrin polymorphisms: a universally applicable method for genotyping. *Clin Chim Acta* 2012; **413**: 1488–1492.
- 6 Scharschmidt T C, Man M Q, Hatano Y et al. Filaggrin deficiency confers a paracellular barrier abnormality that reduces inflammatory thresholds to irritants and haptens. *J Allergy Clin Immunol* 2009; **124**: 496–506.
- 7 Weidinger S, O'Sullivan M, Illig T et al. Filaggrin mutations, atopic eczema, hay fever, and asthma in children. *J Allergy Clin Immunol* 2008; **121**: 1203–1209.
- 8 Brown S J, Asai Y, Cordell H J et al. Loss-of-function variants in the filaggrin gene are a significant risk factor for peanut allergy. *J Allergy Clin Immunol* 2011; **127**: 661–667.
- 9 Novak N, Baurecht H, Schafer T et al. Loss-of-function mutations in the filaggrin gene and allergic contact sensitization to nickel. *J Invest Dermatol* 2008; **128**: 1430–1435.