

CORRESPONDENCE

No filaggrin gene mutation in a patient with a combination of atopic dermatitis, alopecia areata and food allergy

Atopic dermatitis (AD) is a common chronic skin disease with high heritability. Skin barrier defect in AD can be a risk factor for developing food sensitization [1]. In addition, an association of AD and alopecia areata (AA) has previously been reported [2]. Recent meta-analyses have confirmed that mutations in filaggrin (*FLG*), which encodes an epidermal protein abundantly expressed in the outer layers of the epidermis, are strong risk factors for AD [3]. Intriguingly, it has been reported that *FLG* mutations might be related to comorbidity of atopic diseases and AA, with a more severe outcome in AA [2]. In addition, a recent report has indicated that peanut allergy is associated with *FLG* mutations [3], demonstrating that the skin and oral mucosa, which both express *FLG*, could be sites of allergic sensitization to food allergens [5]. Thus, to examine whether *FLG* mutations are involved in the association of AD, AA, and food allergy, is an intriguing issue. We report a rare case with a combination of AD, AA, and food allergy to multiple fish. An underlying barrier defect caused by *FLG* mutations was considered but the patient had no mutation, contrary to our expectation.

A 31-year-old woman presented at our hospital for investigation for fish allergy. She had experienced an uncomfortable oropharyngeal itching sensation, difficulty in breathing and generalized urticaria after intake of a filet of white fish. At the emergency department, her blood pressure was 70/40mmHg, which recovered soon after an intramuscular epinephrine injection. She had no food allergies and had previously tolerated all kinds of fish. She had suffered from AD (the SCORAD (scoring atopic dermatitis) index on arrival was 21) since childhood and severe alopecia universalis for one year (*figure 1*), which was resistant to

conventional treatments, including topical corticosteroids, intravenous steroid pulse (methylprednisolone 500 mg per day for three days) or contact immunotherapy with squaric acid dibutylester.

Skin prick tests with extracts of prawns, squid, scallops, tuna, mackerel, sardine, yellowtail, sea bream, and salmon were all positive (a wheal at least 3 mm in diameter, or larger than the diluent control is considered positive). Total IgE was 460 U/mL (control, <173 U/mL), and specific IgE levels (normal, <0.34 UA/mL) were positive for tuna (1.30 UA/mL), sardine (2.86 UA/mL), salmon (4.71 UA/mL), mackerel (1.28 UA/mL), Japanese horse mackerel (4.11 UA/mL), and devilfish (0.42 UA/mL). Although oral food challenges were not performed, we considered that the patient exhibited multiple fish allergy. Investigations with mutational analysis using genomic DNA, after obtaining informed consent, for an underlying constitutional abnormality that might explain the combination of AD, AA and fish allergy, did not detect any *FLG* mutation.

A previous report has shown that *FLG* mutations play a critical role in impairment of the skin barrier function, enhanced cutaneous allergen absorption and systemic allergen sensitization, which leads to initiation of food allergy [4]. We previously presented a case of multiple food sensitizations that might have arisen from *FLG* mutation-induced skin barrier dysfunction, but not from a gut barrier dysfunction [5]. In our case, a combination of AD, food allergy against multiple kinds of fish and AA was suggestive of an underlying barrier defect caused by *FLG* mutations, but the patient had no mutation, contrary to our expectations. Recent meta-analyses have demonstrated that three SNPs in *OVOL1*, *ACTL9* and *KIF3A* genes, associated with both epidermal barrier function and immune regulation, influence AD [6]. These new discoveries can be related to enhanced allergen absorption through the skin that may increase the responses to food allergens. Another study indicated that reduced expression of the tight junction, claudin, in the skin of patients with AD, is of particular interest, given the association of AD with food allergy [4]. Our case indicates the possibility of undetermined potent gene dysfunctions other than *FLG* mutations, even in a case with a combination of AD, AA and food allergy to multiple fish. ■

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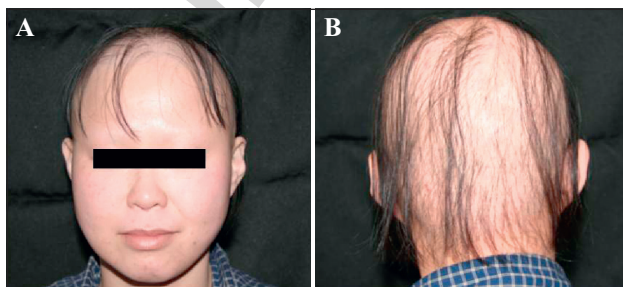


Figure 1. Clinical pictures of the patient with alopecia universalis.

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