

were not sufficient to cause a systemic reaction after entering into the general circulation.

There has been no previous report to date of urticaria limited to the lymph flow, but the SNB procedure could conceivably lead to the urticaria distribution seen in our patient.

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Second report of *FLG* R501X mutation in Japanese patients with atopic dermatitis

Dear Editor,

Mutations in the gene encoding filaggrin have been identified as one of the important causes of atopic dermatitis (AD).¹ We report the second report of R501X *FLG* mutation, which is an European type mutation, in Japanese AD patients.

A 22-year-old Japanese man was referred to us for evaluation of his atopic eczema. He had suffered from AD and asthma since childhood and then developed allergic rhinitis. On examination, he had moderate severity of AD (SCORAD, 23.9), but did not show ichthyosis vulgaris or palmar hyperlinearity. His family histories including those of his parents were unremarkable in allergic diseases, and he had no European ancestry. The serum immunoglobulin (Ig)E level was 37 420 kU/L (normal, <160 kU/L), and eosinophil counts were 3.6%. Specific IgE levels to *Dermaphagoides pteronyssinus* and *Dermaphagoides farinae* were both class 6 (maximum value).

FLG mutation analysis was performed. Genomic DNA was extracted from peripheral blood mononuclear cells. The genomic region of *FLG* unit 1 (312 bp) was amplified with polymerase chain reaction (PCR) using a forward primer (FilH1F3, 5'-CAC-ggAAAggCTgggCTgA-3') and a reverse primer (RPT1P6, 5'-AC-CTgAgTgTCCAgACCTATT-3').² The primer pair was used in 1× Ex Taq buffer (Takara, Otsu, Japan), 4% dimethylsulfoxide, deoxyribonucleotide triphosphate, and one unit Ex Taq polymerase (Takara). Reactions were amplified under the following conditions: 94°C for 5 min, 35 cycles of 94°C for 30 s, 58°C for 45 s, 72°C for 1 min, and one cycle of 72°C for 5 min. By direct sequencing analysis with FilH1F3 primer and BigDye Terminator ver. 3.1 cycle sequencing kit (Applied Biosystems, Foster City, CA, USA), we identified a C-to-T transversion at nucleotide position 1501, which leads to the substitution of stop codon (X) for arginine (R), as compared with the normal sequence

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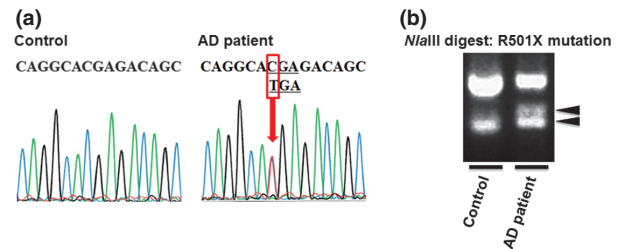


Figure 1. Sequence analysis of *FLG* gene. (a) Sequencing of the patient's polymerase chain reaction products demonstrates heterozygous C to T at position 1501, resulting in substitution of an arginine codon (CGA) by a stop codon (TGA), a mutation designed R501X. (b) Conformation of mutation R501X by *Nla*III restriction digest from patient. AD, atopic dermatitis.

(Fig. 1a). Furthermore, as referred by the previous report,² we also confirmed R501X *FLG* gene heterozygous nonsense mutation in our patient by PCR restriction fragment length polymorphism analysis with restriction enzyme, *Nla*III (Fig. 1b).

The R501X mutation in *FLG* is frequently seen in European AD patients, as this variant is carried by 9% of people of European origin.³ However, this mutation was only reported in a Japanese family, including four individuals from two generations with ichthyosis vulgaris complicated by AD.⁴ The children in the family had compound heterozygous mutations, and the father and mother were heterozygous for R501X and 2282del4, respectively. Therefore, our patient had the same mutation as did the father of the reported case. The patient had only R501X mutation, indicating no compound heterozygous *FLG* mutation regarding at least the eight known mutations.

The R501X leads to a complete loss of filaggrin peptide synthesis, because this mutation is located within the first filaggrin repeat.² Among Asian populations including Chinese, Korean, Taiwanese and Japanese, only individuals of European ancestry can possess R501X.¹ Hamada *et al.*⁴ suggested that R501X mutation may occur as a result of de novo mutation in any population regardless of their race. The second Japanese case reported herein also might be a de novo case because of the lack of family history.

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Penile lichen nitidus successfully treated with topical pimecrolimus 1% cream

Dear Editor,

Because lichen nitidus (LN) is usually asymptomatic and is not accompanied by any sequelae, most patients do not require treatment. Patients with symptomatic and persistent LN, however, require treatment. We describe a 20-year-old man with penile LN who was effectively treated with topical pimecrolimus 1% cream.

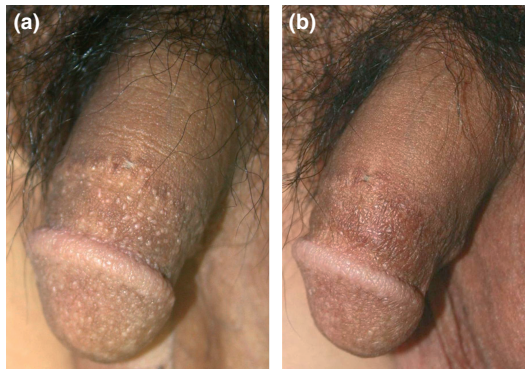


Figure 1. (a) Pretreatment photograph showing multiple, discrete, flesh-colored, glistening papules on the penile glans and shaft. (b) Photograph showing marked improvement in skin lesions after treatment with topical pimecrolimus 1% cream for 2 months.

A 20-year-old man presented with multiple, pinhead-sized papules on his penis. These lesions first appeared 10 months earlier, and had increased in number over time. A physical examination showed multiple, discrete, shiny, 1–2-mm sized, flesh-colored papules on the penile glans and shaft (Fig. 1a). There were no mucosal or nail lesions. He had no systemic problems and his medical history was unremarkable. He had not visited a medical clinic earlier because the lesions were asymptomatic. Histopathological examination of a papule on the penile shaft revealed elongated marginal rete ridges and inflammatory cell infiltration in the papillary dermis (Fig. 2a). A well-circumscribed, lichenoid, lymphohistiocytic infiltrate closely attached to the epidermis was noted (Fig. 2b). The epider-

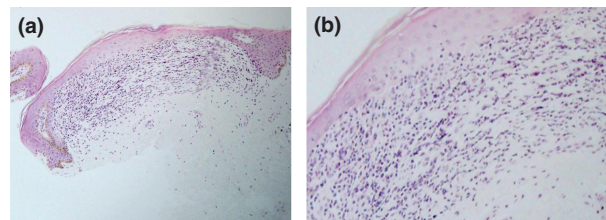


Figure 2. (a) Histopathological examination of a papule, showing a pattern resembling a “claw clutching a ball” with elongated marginal rete ridges. (b) Well-circumscribed lichenoid lymphohistiocytic infiltrate in the papillary dermis (hematoxylin–eosin, original magnifications: [a] $\times 40$; [b] $\times 200$).

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