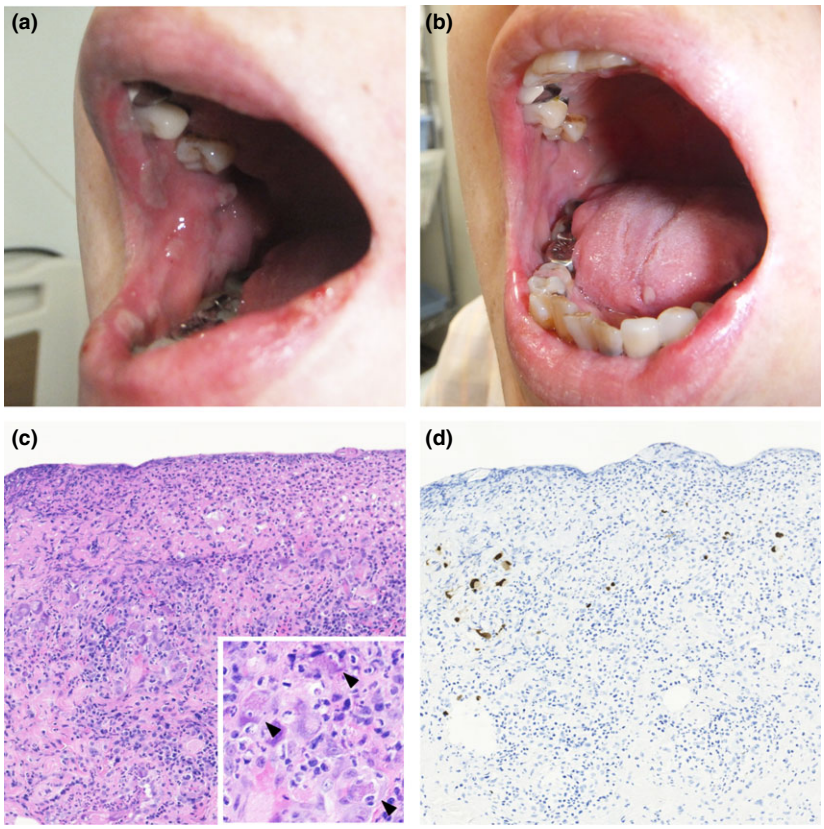

Figure 2 (a) Multiple ulcers on the lip and buccal mucosa; (b) appearance after 6 weeks of systemic administration of ganciclovir. (c) Mucosal ulcer with infiltration of neutrophils, lymphocytes, and plasma cells and (inset) owl's eye appearance (arrowheads). Haematoxylin and eosin, original magnification (c) × 10; (inset) × 40). (d) Immunohistochemical staining for cytomegalovirus antigen; a strong positive reaction was observed in the mucosal ulcer (original magnification × 10).

the blood. CMV viraemia can lead to visceral lesions, such as pneumonia, hepatitis, and enterocolitis, which can result in death. In the present case, the rapid diagnosis of CMV infection helped to prevent a fatal CMV infection.

BP patients are often elderly and immunocompromised. Although mucous lesions are not a rare symptom in patients with autoimmune bullous disease, oral ulcers should raise the suspicion of CMV infection.

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Hyper-IgE syndrome with a novel mutation of the *STAT3* gene

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Hyper-IgE syndrome (HIES) is a primary immune deficiency characterized by atopic dermatitis (AD)-like skin lesions, extremely high serum IgE levels, and increased susceptibility to bacterial and fungal infections.[1] Recent studies have revealed that most cases of HIES are caused by mutations in the signal transduction and activation of

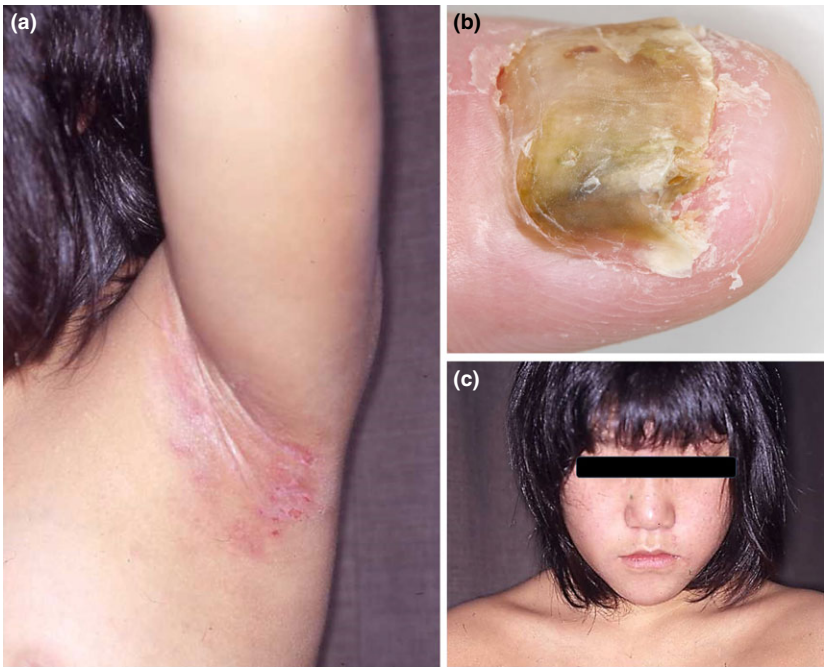

Figure 1 (a) Erythematous skin lesions on the bilateral axillae, with dry skin on the chest and the limbs; (b) bacterial paronychia on the finger; and (c) the characteristic leonine face of hyper-IgE syndrome.

transcription 3 gene (*STAT3*).[1] We report a patient with HIES manifesting intractable eczematous eruptions with xerosis, who had a novel mutation in the *STAT3* gene.

An 11-year-old Japanese girl presented with erythematous skin eruptions. Reddish papules and pustules were noted on both axillae (Fig. 1a), and the scalp was covered with scaly erythematous plaques. Paronychia and fingernail deformities were seen (Fig. 1b), and severe xerosis was noted over the whole body.

The skin eruption had first been noted when the child was 1 month of age. At 3 months of age, she had been admitted to hospital with pyoderma and measles, and histology had shown pulmonary infiltration with eosinophilia. Since then, the patient had repeatedly experienced lung abscesses, phlegmon and otitis media.

Laboratory investigations showed that T-cell counts, numbers of CD4-positive and CD8-positive cells, and CD4/CD48 ratios were normal. Analysis of the patient's peripheral blood using flow cytometry revealed slightly raised B cell counts. Serum IgE levels were also raised (6700–8800 U/mL; normal range < 170 U/mL).

HIES was considered because of the combination of raised IgE levels, eosinophilia (3–22%; normal range 0–10%), recurrent cutaneous abscess formation, infection, pneumonia with pneumatocele formation, and progressive coarsening of the facial features (Fig. 1c).

We carried out a genetic study on the patient. The study was approved by the ethics review committee of Nagoya University School of Medicine and all participants (or guardians) gave fully informed consent.

We performed mutation analysis of *STAT3* to confirm the diagnosis, and detected a novel pathogenic mutation, c.1397A>T (p.N466S). We also searched for mutations of the filaggrin gene (*FLG*), which are important predisposing factors for AD. We screened for almost all the *FLG* mutations that are specific to the Japanese population,[2] but no population-specific mutations were noted in this case.

The patient was treated with hydrocortisone cream and antimycotic drugs, but minimal improvement was obtained, and the eczema and intense (possibly fungal) infection continued. Linezolid was then administered, which produced an excellent response of the fingernail deformities.

Dominant-negative mutations in *STAT3* account for the majority of autosomal and sporadic HIES cases.[1] Because the STAT3 protein plays an important role in signal transduction induced by many cytokines, including interleukin (IL)-6, IL-10, IL-17, IL-21 and IL-22, its deficiency results in upregulation and downregulation of pro-inflammatory and anti-inflammatory responses, leading to characteristic immunological abnormalities and infections.[3] However, the molecular mechanisms of these phenotypes have not been clarified completely.

In our case, we found a pathogenic mutation c.1397A>T (p.N466S) in *STAT3*. Although two other mutations, c.1396A>G (p.N466D) and c.1398C>G (p.N466K) were reported previously in this residue, the present mutation in N466S is novel.[4] This residue might be crucial for the function of STAT3.

Our patient had severe xerosis and eczematous eruptions, which are also seen in patients with AD. Mutations in *FLG* are frequently found in patients with AD. Filaggrin is a major structural protein in the stratum corneum of the epidermis and plays a key role in the barrier

function of the skin.[2] The disruption of the barrier function causes severe xerosis in AD. In the present case, we searched for mutations in *FLG*, but found no population-specific mutations in our case. Therefore, the STAT3 deficiency itself might be related to expression of proteins and genes that are responsible for the barrier function of the skin. Investigation of the pathophysiology of HIES may help clarify the mechanisms of barrier dysfunction and dry skin in AD, and lead to development of new treatments.

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Generalized pustular psoriasis treated with ustekinumab

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Generalized pustular psoriasis (GPP) is a rare and severe form of psoriasis that is frequently refractory to treatment. Ustekinumab is a fully human monoclonal antibody that binds with high affinity to the p40 subunit of interleukin (IL)-12 and IL-23.[1] It has been shown to be safe and effective for the treatment of chronic plaque psoriasis.[2]

We report a case of a 90-year-old woman who initially presented in late 2009 with GPP. She had no preceding history of psoriasis and no obvious precipitating factors such as infection, drugs or recent systemic corticosteroid therapy.

Physical examination revealed widespread urticated plaques with sheets of studded pustules on the patient's trunk, arms and legs (Fig. 1). Approximately 35% of her body surface area was affected.

The patient was commenced on ciclosporin A (CsA) (Neoral©; Novartis Pharmaceuticals Ltd, Camberley, Surrey, UK) at 2.5 mg/kg and her skin dramatically improved. Three months later, methotrexate was added with an initial test dose of 2.5 mg/week and subsequently increased to 10 mg/week with folic acid supplementation. Unfortunately, the patient's psoriasis flared upon weaning of the CsA despite the dose of methotrexate being increased to 20 mg/week. After 6 months of therapy, methotrexate was discontinued because of lack of efficacy, and acitretin 30 mg was commenced in addition to the existing dosage of CsA. The psoriasis improved, allowing the CsA to be tapered off, but the patient then developed hepatic dysfunction, which required discontinuation of acitretin. The patient was restarted on CsA at 2.5 mg/kg. She subsequently developed nausea and acute kidney injury on CsA, requiring discontinuation of the drug. She was commenced on adalimumab 40 mg/week in February 2011 after initial loading doses; unfortunately, after 14 months of adalimumab therapy, she developed widespread pustulation requiring inpatient hospital care. Her skin improved with the addition of CsA at 2.5 mg/kg.

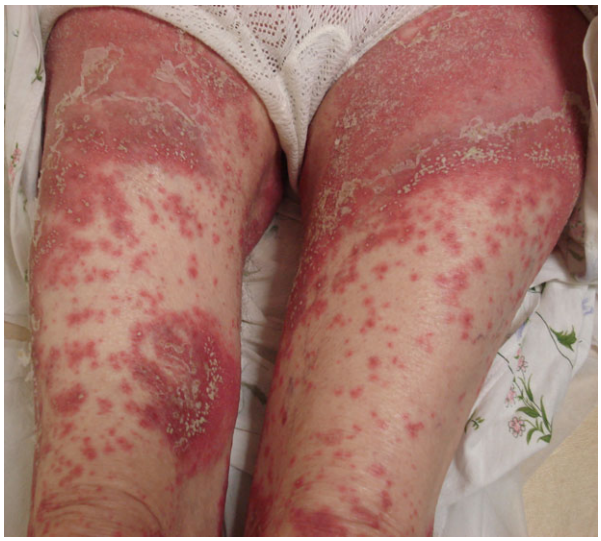

Figure 1 Widespread studded pustules on an erythematous base affecting the thighs bilaterally.