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Elderly-Onset Generalized Pustular Psoriasis without a Previous History of Psoriasis Vulgaris

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Key Words

IL36RN · CARD14 · Pustulosis · Aging

Abstract

Generalized pustular psoriasis (GPP) is characterized by sudden fever and extensive erythema with pustules and occurs in patients with or without preceding psoriasis vulgaris. We report an 83-year-old man showing irregularly shaped erythema with pustules on the trunk and extremities. He initially had no fever and came to our clinic a few days after the onset of the skin lesions because of high fever and general malaise. We found an extension and new development of erythema and pustules on the whole body. The patient also manifested night delirium. Histological examination revealed neutrophil infiltration into the upper epidermis, which formed a spongiform pustule of Kogoj. Pustular fluid cultures were negative for bacteria. We diagnosed GPP without preceding psoriasis vulgaris. Mutation analysis revealed no significant mutations in *IL36RN* and *CARD14*. Previous reports indicated that onset of GPP at the age of 83 years is definitely rare. In older individuals, general disease characteristics include an atypical clinical course, an especially slow appearance and cure, and mental disorder. Our case also revealed such characteristics. Thus, it is necessary to be aware of the clinical course and mental problems in elderly patients with GPP.

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Introduction

Generalized pustular psoriasis (GPP) is a rare severe psoriasis characterized by the presence of variable numbers of sterile pustules appearing in erythematous and scaly lesions. It can be lethal without proper treatment, especially in the elderly population. Mutations in *IL36RN* have been identified in familial GPP and in sporadic cases of GPP [1, 2]. Cases with *IL36RN* mutations have been delineated as psoriasis with a deficiency of IL36RN (DITRA) [1]. Recently, the gene *CARD14* has also been found to be responsible for GPP [3]. Herein, we report our recent experience with an 83-year-old man with GPP without a previous history of psoriasis vulgaris in whom we examined mutations in *IL36RN* and *CARD14*.

Case Presentation

An 83-year-old man with a 7-day history of erythematous eruption on the trunk and extremities was referred to our clinic. His history showed bronchial asthma, hypertension, atrial fibrillation, and postoperative colon carcinoma. He had never been previously diagnosed with psoriasis vulgaris. Physical examination revealed irregularly shaped erythema with scales and small pustules on the trunk and extremities (fig. 1). He had no fever. The blood test revealed a white blood cell count of 12,530/ μ l (segment 87.8%, lymphocytes 6.7%, monocytes 4.9%, eosinophils 0.5%, and basophils 0.1%) and a C-reactive protein level of 2.2 mg/dl.

We suspected pustular psoriasis and took a skin biopsy from an abdominal lesion. Since the patient had no fever, we started to treat him with oral antihistamine and topical steroid.

However, after 4 days, the patient came to our clinic because of high fever and general malaise. We found an extension and new development of erythema and pustules on the whole body (fig. 2). Coalescence of pustules resulted in lakes of pus. The blood test showed a white blood cell count of 18,920/ μ l (segment 88.4%, lymphocytes 65.0%, monocytes 6.3%, eosinophils 0.2%, and basophils 0.1%) and a C-reactive protein level of 20.171 mg/dl.

The patient was immediately admitted to our hospital ward. Although the results of pustular fluid culture and histopathology were not yet submitted, we started 60 mg/day of oral etretinate, and pustule formation decreased (fig. 3). However, erythema continued to expand, and consequently the lesions became erythrodermic. In addition, a decrease in serum albumin caused general edema, and night delirium appeared. Afterwards, erythema gradually decreased, and we tapered the dose of etretinate. Administration of diuretic furosemide was effective for general edema. The delirium gradually disappeared.

Later, histological examination revealed neutrophil infiltration into the upper epidermis, which formed a spongiform pustule of Kogoj (fig. 4). Direct immunofluorescence showed no significant deposits of immunoglobulins. Pustular fluid cultures were negative for bacteria. We performed mutation analysis, which detected no significant mutations in *IL36RN* and *CARD14*.

Discussion

GPP is characterized by sudden fever and extensive erythema with pustules and occurs in patients with or without psoriasis vulgaris. Since this case showed pustule formation on the whole body and no history of psoriasis vulgaris, the differential diagnosis initially included GPP, subcorneal pustular dermatosis, acute generalized exanthematous pustulosis,

and intercellular immunoglobulin IgA dermatosis. However, clinical, histological, and immunofluorescence findings, in conjunction with a lack of recent administration of causative drugs, resulted in a final diagnosis of GPP.

Recently, mutations in *IL36RN* and *CARD14* have been found to be responsible for GPP [1, 2]. The IL36RN protein is primarily expressed in the skin and is an antagonist of three cytokines that belong to the interleukin-1 family: interleukin-36 α , interleukin-36 β , and interleukin-36 γ , which are also known as interleukin-1F6, interleukin-1F8, and interleukin-1F9, respectively [4]. These cytokines activate several proinflammatory signaling pathways, such as the nuclear factor- κ B and mitogen-activated protein kinase pathways [4]. Therefore, loss of function of IL36RN may cause GPP. Tominaga et al. [5] reported that a 78-year-old woman with GPP and a previous history of psoriasis vulgaris had causative mutations in the *IL36RN* gene. Since it was possible that our patient might have had mutations in *IL36RN* or *CARD14*, we performed mutation analysis. However, we were unable to find any of the known mutations.

An interesting point of this case is that the onset of GPP occurred at an older age. The age of onset in Japanese patients recently reported in reliable English-language papers was 2–78 years in 31 cases [6], 36–71 years in 3 cases [7], 16–74 years in 14 cases [8], and 21–64 years in 3 cases [9]. In addition, the age of onset in a recent report from Malaysia was 21–81 years in 102 cases [10]. These reports suggest that the age of onset in the present case (at 83 years) is definitely rare. In older individuals, general disease characteristics include an atypical clinical course, an especially slow appearance, a slow cure, and mental disorder. In our case, we were initially unable to recognize the severity of the disease because of the lack of fever and a low C-reactive protein level. Three days after his first visit, however, sudden fever and extension of the skin lesions were detected, and he reported night delirium. This illustrates the need to be aware of the clinical course and mental problems in elderly patients with GPP.

Statement of Ethics

The authors state that the patient gave his informed consent, and the informed consent was in accordance with the guidelines approved by Hirosaki University Graduate School of Medicine.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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Fig. 1. Clinical findings at his first visit. Irregularly shaped erythema with scales and small pustules on the trunk and extremities. The patient had no fever. **a** Trunk. **b, c** Upper extremities. **d, e** Thighs.

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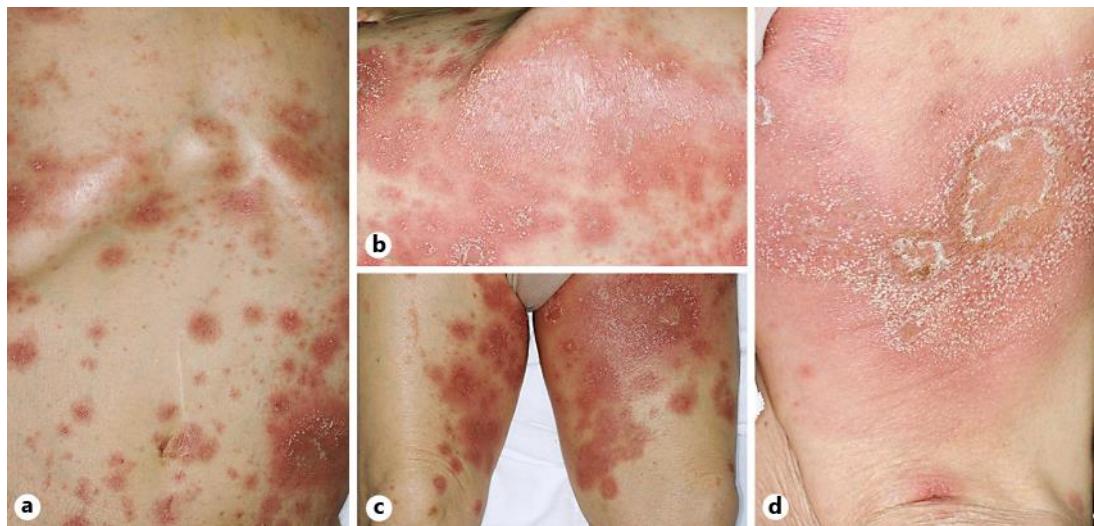


Fig. 2. Clinical findings at his second visit. The patient came to our clinic because of high fever and general malaise. We found an extension and new development of erythema and pustules on the whole body. **a** Abdomen. **b** Buttock. **c, d** Thighs.

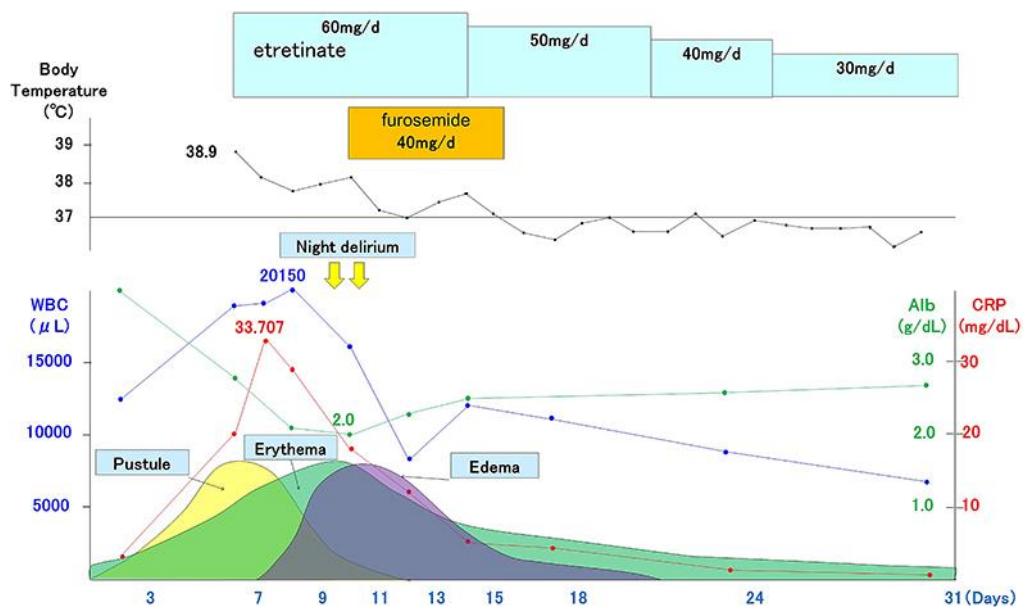


Fig. 3. Clinical course and treatments.

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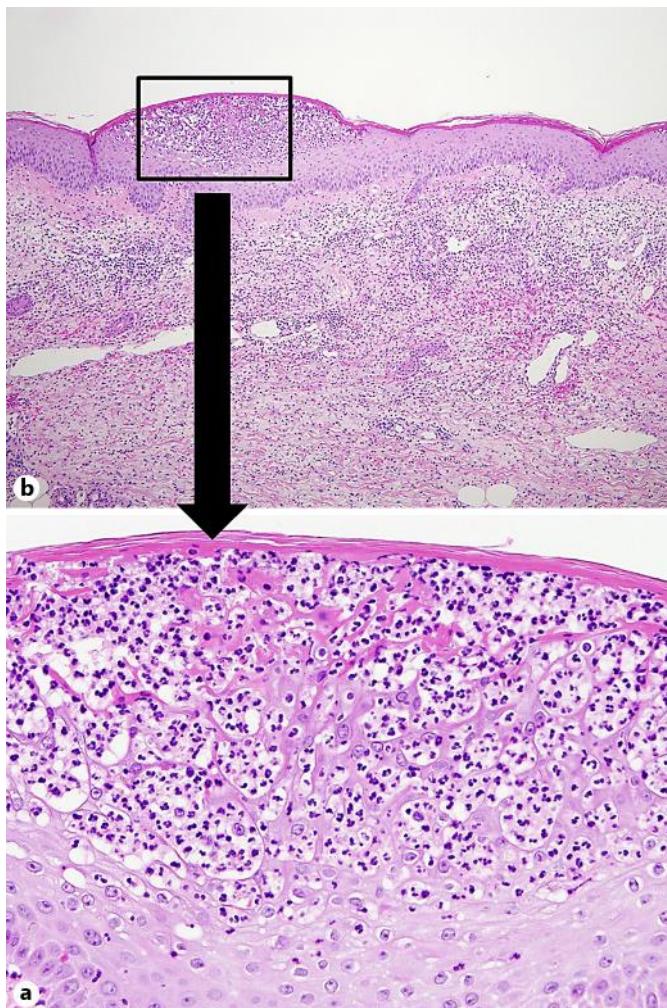


Fig. 4. **a, b** Histopathological findings. Neutrophil infiltration into the upper epidermis, which formed a spongiform pustule of Kogoj. **b** An enlarged photo of a part of **a**. **a** $\times 40$. **b** $\times 200$.