

index finger of a healthy woman showing intraepidermal blisters [5]. Histopathologically, the lesion shows intraepidermal blisters containing degenerated keratinocytes and multinucleated giant cells. Another case is herpetic syco-sis without epidermal damage in a Burkitt lymphoma patient [6]. In our case, atypical herpes zoster presented as a solitary vesicular lesion, and histopathologically, VZV infection was observed both in epithelial cells and hair follicles. It was also interesting that the skin lesion in our case was persistent in spite of antiviral treatment and that the anti-VZV antibody titer was not elevated. Hematopoietic disorder and anti-CD20 antibody therapy might be the reason why such an atypical lesion occurred in this case. ■

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## Patch-type granuloma annulare

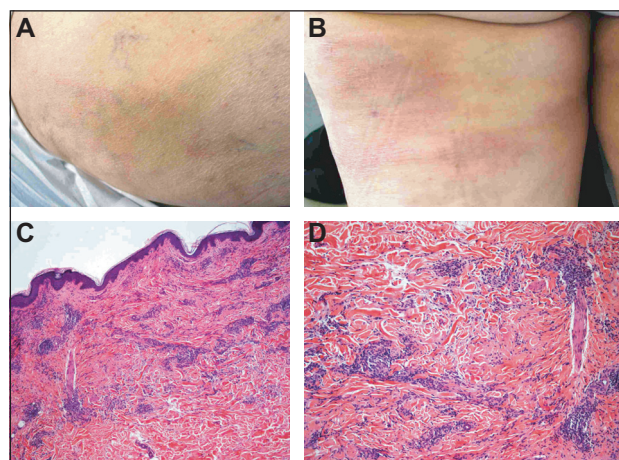
A 74-year-old white woman was referred to our department with a 1-year history of four large asymptomatic lesions on her thighs. The lesions began as small erythematous patches and subsequently increased in diameter. She had a history of arthritis, treated for the preceding 3 years with naproxen.

Examination of the posterior thighs revealed four large (between 3 × 2 cm and 17 × 14 cm) erythematous, minimally scaly, oval patches, with no induration. One of the lesions had light central clearing (*figure 1*). Physical examination was otherwise unremarkable. The initial clinical impression was parapsoriasis, and a biopsy specimen was obtained. Histopathological examination revealed a moderate superficial and mid-dermal interstitial infiltrate of lymphocytes and histiocytes, and mucin between collagen fibers; these findings are consistent with the interstitial variant of granuloma annulare. Further investigations were unremarkable. The diagnosis of patch-type granuloma

annulare was made, and the patient was treated with betamethasone ointment twice daily for 4 weeks with no improvement. We did not find any regression of the lesion after biopsy. Because the lesions were asymptomatic and caused no anxiety to the patient, topical medication was discontinued.

Granuloma annulare is a benign, self-limited condition; the cause is unknown and the pathogenesis is poorly understood. There are several clinical variants of granuloma annulare: localized, generalized, subcutaneous, perforating, linear, and patch types. There is an overlap between variants, and more than one morphological type may exist in the same patient. This patient had a rare, recently described granuloma annular variant named *patch granuloma annulare* [1]. It appears as asymptomatic erythematous to brown patches, with or without minimal scale, that may have an annular configuration on the trunk or proximal extremities. There is no evidence of papules, scales, or induration [2]. As with other forms of granuloma annulare, there is a female predominance. There is also a possible association with drug reaction (which may have been present in our patient) [1-3].

A high index of suspicion is necessary to make the diagnosis. The differential diagnosis of patch-type granuloma annulare includes morphea, erythema annulare centrifugum, and parapsoriasis. Pathologically, this entity is characterized by an interstitial pattern of mononuclear cellular infiltration with scattered histiocytes between collagen fibers; there is mucin deposition between collagen bundles that can be highlighted by Alcian blue and colloidal iron stains [4]. Necrobiotic areas are usually absent. In cases related to drug reactions, eosinophils and some lichenoid changes at the dermal-epidermal interface are present. Histological differential diagnosis includes necrobiosis lipoidica and interstitial granulomatous dermatitis. Systemic therapy is unnecessary because of the relatively limited involvement and asymptomatic nature of the lesions. It is reported that patch granuloma annulare will respond to the same therapy as other types of granuloma annulare: cryotherapy, topical and intralesional corticosteroids for



**Figure 1.** A) One oval lesion on the lateral portion of the right thigh. B) Three oval violaceous patches on the posterior left thigh. C-D) Superficial and mid-dermal interstitial infiltrate of lymphocytes and histiocytes; there is mucin deposition between collagen bundles. HE × 50 (C), HE × 100 (D).

localized disease, and photochemotherapy, isotretinoin, dapsone, or antimalarials for generalized disease. Resolution of patch-type granuloma annulare after biopsy has been reported [5].

In conclusion, we present a rare and recently described variant of granuloma annulare characterized by patches of erythema on the extremities and trunk that lack the usual clinical findings but display the classic histopathological findings of interstitial granuloma annulare. ■

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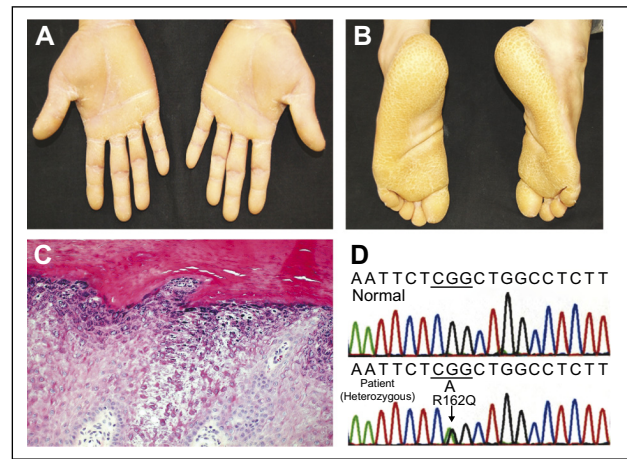
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## A missense mutation in exon 1 of the keratin 9 gene in a Japanese patient with “Vörner type” hereditary palmoplantar keratoderma

Epidermolytic hereditary palmoplantar keratoderma (EHPPK; OMIM: 144200) or Vörner type PPK is characterized by hyperkeratotic lesions confined to the palms and soles, histological granular degeneration and mutations in keratin 9 gene (*KRT9*; NCBI: NM000226) [1-5]. Here, we report a Japanese patient with EHPPK showing a missense mutation (R162Q) in *KRT9* located in the 1A rod domain, the highly conserved helix initiation motif of keratin 9.

A 28-year-old Japanese man was referred to us for evaluation of palmar and plantar hyperkeratotic lesions. The condition had developed within the first year of life and progressed until 20 years of age. He sometimes shaved the hyperkeratotic surface of the soles, but the cornified lesion recovered within a few weeks. On examination, there was a markedly thick cornified layer on the soles and palms (figures 1A,B). The dorsal aspects of the hands and feet were not affected, and the borderline between the lesional and normal skin was clear. Hyperhidrosis was unremarkable. The patient was otherwise healthy. His one-year-old daughter had the same hyperkeratotic lesions on the bilateral palms and soles, but to a lesser degree. The family history was otherwise negative for similar disorders as his parents had no palmoplantar hyperkeratosis.



**Figure 1.** A, B) Clinical appearance. Bilateral palmoplantar hyperkeratotic lesions on the palms and soles. C) Histological findings (hematoxylin-eosin, original magnification  $\times 20$ ). The epidermis of the hyperkeratotic lesional skin shows epidermolytic hyperkeratosis with coarse keratohyaline granules. D) Sequence analysis of *KRT9* gene exon 1. Sequencing of the Vörner type EHPPK patient's PCR products demonstrates heterozygous G to A substitution at nt position 551, resulting in substitution of an arginine codon (CGG) by a codon for glutamine (CAG), a mutation designated R162Q.

A skin biopsy specimen was taken from the inner aspect of his right foot. There was epidermolytic hyperkeratosis exhibiting coarse keratohyaline granules and granular degeneration (figure 1C). Thus, we diagnosed the patient as having EHPPK.

Genomic DNA was extracted from peripheral blood leukocytes. As previously reported [6], the genomic regions of the *KRT9* gene exon 1 were amplified via polymerase chain reaction (PCR), using a forward : K9.E1F : 5'-GGAGGTGACTCTGCTCTTGG-3' and a reverse: K9.E1R : 5'-AGGTGGATTCCCTGGCTATT-3' primer pair. A direct sequencing analysis identified a G to A transversion at nucleotide (nt) position 551, resulting in the substitution of glutamine (Q) for arginine (R), in the patient, as compared with the normal sequence (figure 1D).

The R162Q missense mutation identified in our case was not novel, since the mutation was located within codon R162, in which the most common mutations, R162W and R162P, have been reported. However this is the second report of the R162Q missense mutation in Japanese patients with EHPPK. This mutation has frequently been seen in non-Japanese patients, as approximately 20% Western cases had this mutation [1-3]. The result confirms the previous reports of *KRT9* mutation underlying EHPPK and re-emphasizes the importance of codon R162 for maintenance of the intermediate keratin filament network. Since keratin 9 is confirmed to the volar skin, the abnormality of keratin 9 induces palmoplantar lesions. This dominant-negative effect on keratin network formation led to the disruption of keratin filament formation, and development of epidermolytic hyperkeratosis [4]. ■

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