

Brown Plaque in the Axilla Following Immobilization of the Arm

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A 62-year-old woman presented to our clinic for evaluation of a brown plaque in the left axilla of 2 weeks' duration. She had a history of a rotator cuff injury and adhesive capsulitis several months prior that required immobilization of the left arm in a shoulder orthosis for several months. After the sling was removed, she noticed the lesion and reported mild cutaneous pain. Physical examination revealed a 1.5-cm, verrucous, red-brown plaque in the left axillary vault. A shave biopsy of the plaque was performed.

WHAT'S YOUR DIAGNOSIS?

- Fox-Fordyce disease
- granular parakeratosis
- Hailey-Hailey disease
- inverse lichen planus
- seborrheic keratoses

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The authors report no conflict of interest.

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THE DIAGNOSIS: Granular Parakeratosis

Histopathology demonstrated diffuse parakeratosis with retention of keratohyalin granules throughout the stratum corneum consistent with a diagnosis of granular parakeratosis (Figure), a rare benign cutaneous condition that is thought to occur due to a defect in epidermal differentiation. The lesion resolved without additional treatment.

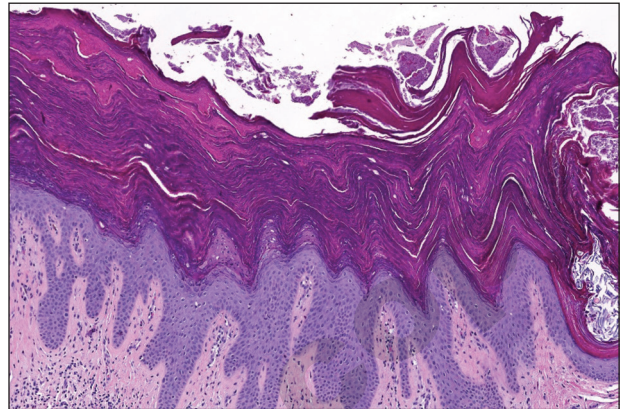
The pathogenesis of granular parakeratosis is unclear, but a reactive process in which locoregional irritation or occlusion prompts increased cell turnover and prevention of profilaggrin breakdown has been proposed.^{1,2} The diagnosis is linked to various precipitating agents, most commonly topical products (eg, zinc oxide, antiperspirants) and products with benzalkonium chloride (eg, laundry rinses). These agents are thought to cause retention of keratohyalin granules in the stratum corneum during epidermal differentiation.^{1,2}

Most affected patients are middle-aged women (mean age at diagnosis, 37.8 years).² Patients present with eruptions of erythematous, brown, hyperkeratotic patches and papules that coalesce into plaques.^{1,2} These lesions can be pruritic and painful or asymptomatic. They often manifest bilaterally in intertriginous sites, most commonly the axillae, groin, or inguinal folds.^{1,2}

Treatment involves identification and removal of potential triggers including changing antiperspirants, limiting use of irritating agents (eg, topical products with strong fragrances), and reducing heat and moisture in the affected areas. If the lesion persists, stepwise treatment can be initiated with topical agents (eg, corticosteroids, vitamin D analogues, retinoids, keratolytics, calcineurin inhibitors) followed by systemic medications (eg, antibiotics, isotretinoin, antifungals, dexamethasone) and procedures (eg, botulinum toxin injections, surgery, laser, cryotherapy).^{1,2}

Unilateral granular parakeratosis, as seen in our patient, is an uncommon manifestation. Our case supports the theory that occlusion is a precipitating factor for this condition, given persistent axillary exposure to heat, sweat, and friction in the setting of limb immobilization.³

Granular parakeratosis is a challenge to diagnose due to clinical overlap with several other cutaneous conditions; histopathologic confirmation is required. Fox-Fordyce disease is a rare condition that is thought to result from keratin buildup or occlusion of apocrine or apoecrine sweat ducts leading to duct rupture and surrounding inflammation.⁴ Common triggers include laser hair removal, hormonal changes, and living conditions that promote hot and humid environments.⁵ It can manifest similarly to granular parakeratosis, with eruptions of multiple red-violet papules that appear bilaterally in



Histopathology revealed diffuse parakeratosis with retention of keratohyalin granules throughout the stratum corneum consistent with a diagnosis of granular parakeratosis (H&E, original magnification $\times 100$).

apocrine gland-rich areas, including the axillae and less commonly the genital, periareolar, thoracic, abdominal, and facial areas.^{4,5} However, most patients with Fox-Fordyce disease tend to be younger females (aged 13–35 years) with severely pruritic lesions,^{4,5} unlike our patient. In addition, histopathology shows hyperkeratosis, hair follicle plugging, and sweat gland and duct dilation.⁴

Seborrheic keratoses are common benign epidermal tumors caused by an overproliferation of immature keratinocytes.^{6,7} Similar to granular parakeratosis, they commonly manifest in older adults as hyperpigmented, well-demarcated, verrucous plaques with a hyperkeratotic surface.⁶ However, they are more common on the face, neck, trunk, and extremities, and they tend to be asymptomatic, differentiating them from granular parakeratosis.⁶ Histopathology demonstrates a papillomatous epidermal surface, large capillaries in the dermal papillae, and intraepidermal and pseudohorn epidermal cysts.⁷

Inverse lichen planus, a variant of lichen planus, is a rare inflammatory condition that involves the lysis of basal keratinocytes by CD8⁺ lymphocytes.⁸ Similar to granular parakeratosis, lichen planus commonly affects middle-aged women (aged 30–60 years), and this particular variant manifests with asymptomatic or mildly pruritic, hyperpigmented patches and plaques in intertriginous areas. Although it also shows hyperkeratosis on histopathology, it can be differentiated from granular parakeratosis by the additional findings of epidermal hypergranulosis, sawtooth acanthosis of rete ridges, apoptotic keratinocytes in the dermoepidermal junction, and lymphocytic infiltrate in the upper dermis.⁸

Hailey-Hailey disease (also known as familial benign pemphigus) is a rare condition caused by an autosomal-dominant mutation affecting intracellular calcium signaling that impairs keratinocyte adhesion.⁹ Similar to granular parakeratosis, it is most common in middle-aged adults (aged 30–40 years) and manifests as pruritic and burning lesions in symmetric intertriginous areas that also can be triggered by heat and sweating. However, patients present with recurrent blistering and vesicular lesions that may lead to erosions and secondary infections, which reduced clinical suspicion for this diagnosis in our patient. Histopathology shows suprabasilar and intraepidermal clefts, full-thickness acantholysis, protruding dermal papillae, and a perivascular lymphocytic infiltrate in the superficial dermis.⁹

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