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# Circumscribed acral hypokeratosis

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**Background:** Circumscribed acral hypokeratosis (CAH) is an idiopathic condition that typically presents as an acquired, solitary, asymptomatic, well-defined, depressed, flat-based deformity, with a slightly raised border on the palm or, rarely, the sole. Histologically, the lesional epidermis is depressed with a characteristic, abrupt, hyperkeratotic, slightly-raised ridge at the transition from normal skin.

**Objective:** We sought to present 3 additional cases of CAH.

**Methods:** A review of 3 cases of CAH was performed. Liquid phase polymerase chain reaction (PCR) was conducted to evaluate for human papillomavirus (HPV).

**Results:** Three cases of CAH were reviewed. One patient had a history of a burn at the site prior to developing the disorder while another patient, as a child, had a history of verruca plantaris in the same location. Lesions were solitary, involving the palm or sole, in 2 cases and in one case they were multiple involving both the palms and the soles. HPV testing detected HPV type 6 in the lesion of one patient who previously was treated for warts in the same location. Topical fluorouracil, calcipotriol ointment under occlusion, and clobetasol ointment under occlusion were unsuccessful in one patient.

**Limitations:** In case 2, we were pathology consultants and unable to evaluate the clinical appearance of the lesion.

**Conclusions:** CAH may involve palms and/or soles. Lesions may be solitary or multiple, and vary widely in size. We believe that CAH most likely represents a reaction pattern developing in response to various stimuli, including trauma, HPV, or both. (J Am Acad Dermatol 2007;57:292-6.)

Circumscribed acral hypokeratosis (CAH), also known as circumscribed palmar or plantar hypokeratosis, is a recently described, idiopathic condition.<sup>1</sup> Patients are typically middle-aged to elderly women with a long-standing, acquired, solitary, asymptomatic, sharply marginated, flat-based deformity on the palm (thenar or hypothenar eminences) or rarely the sole, often with a slightly

#### Abbreviations used:

CAH: circumscribed acral hypokeratosis  
HPV: human papillomavirus  
PCR: polymerase chain reaction

raised border. Of the cases reported,<sup>1-12</sup> only two have had plantar lesions<sup>1,10</sup> and only 4 cases had multiple lesions.<sup>2,6,7</sup> Histologically, there is a characteristic, abrupt step-down in the cornified layer.

The origin of CAH remains elusive. Perez et al<sup>1</sup> believed that it was an acquired epidermal malformation, whereas Resnik and DiLeonardo<sup>6</sup> believed that it was a result of repetitive minor trauma. Recently, Böer and Falk<sup>8</sup> suggested that lesions may be induced by human papillomavirus (HPV), based on the detection of HPV-4 in the lesion of one patient by liquid phase polymerase chain reaction (PCR) and sequencing.

Here, we describe 3 new cases of CAH, including one case that was particularly unusual in the number and linear arrangement of lesions. Liquid phase PCR detected HPV-6 in one case. Our series expands on

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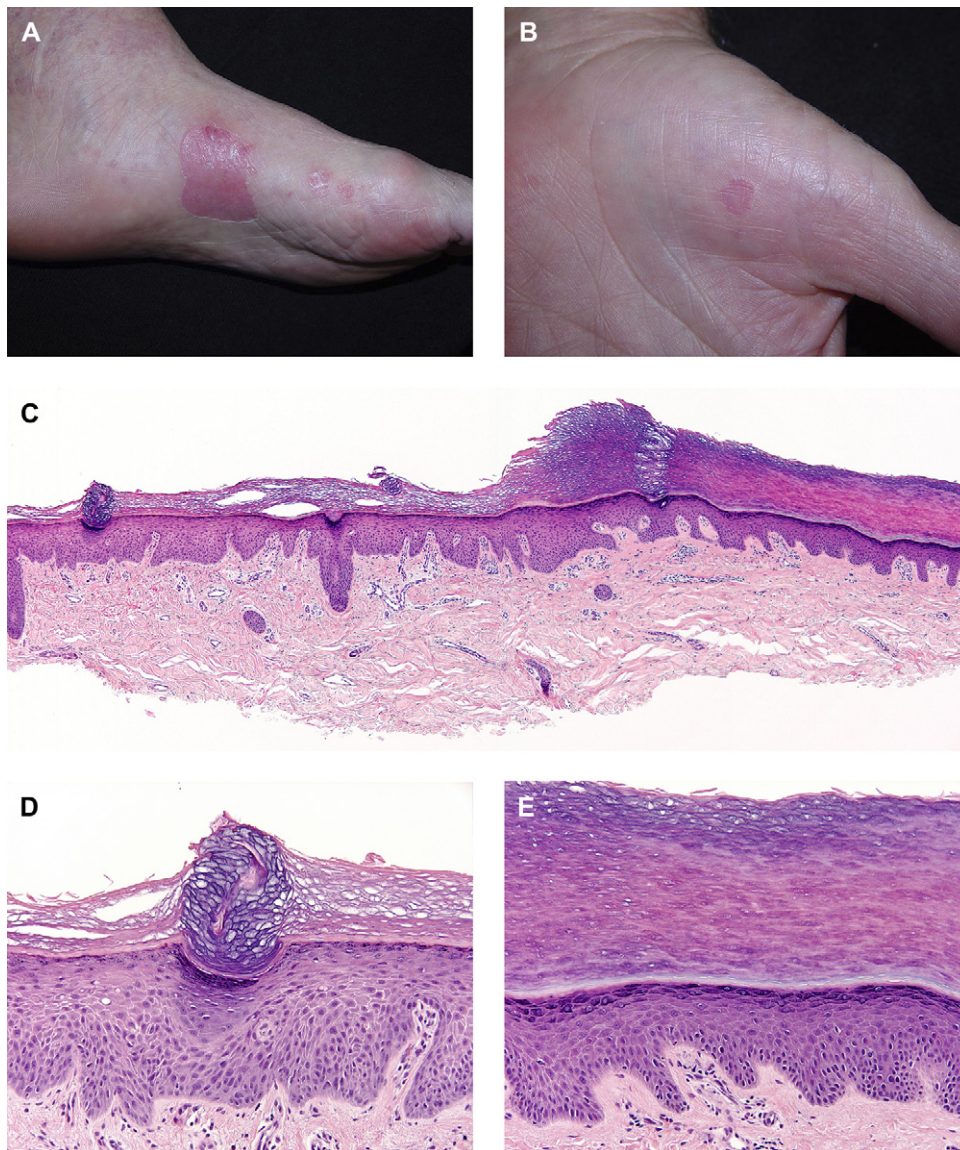
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**Fig 1.** Left medial plantar surface with multiple 0.2- to 4-cm well-circumscribed, erythematous, rounded, depressed lesions (A) and left palmar surface with 0.9-cm well-circumscribed, erythematous, depressed lesion (B) (case 1). Shave biopsy specimen from case 1 demonstrates abrupt transition from normal to depressed zone of cornification (C). Hypokeratotic cornified zone is mostly orthokeratotic, pink, and devoid of lamina lucida (D), in contrast with more compressed, control zone of cornification, which contains blue lamina lucida, pink central cornified zone, and blue superficial cornified zone (E). In lesional zone, granular layer is somewhat accentuated and there is more spongiosis than in control zone. Nuclear size and quantity of cytoplasm of keratocytes in lesional zone is subtly larger than in control areas, but there is no pleomorphism. (C to E, Hematoxylin-eosin stain; original magnifications: C,  $\times 2$ ; D and E,  $\times 10$ .)

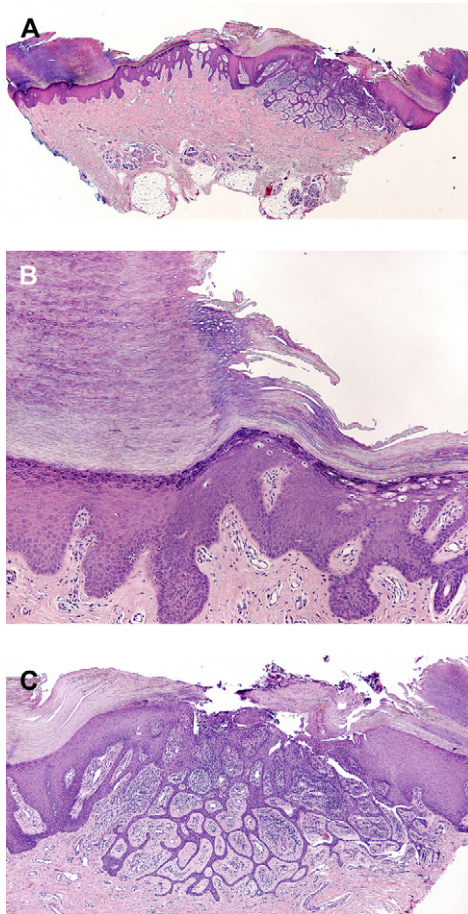
the spectrum of clinical, histopathologic, and molecular diagnostic findings for this condition.

## CASE REPORTS

### Case 1

A 75-year-old, right-handed woman presented with a 10-year history of asymptomatic, depressed,

left plantar and palmar lesions that were refractory to topical fluorouracil. Medical history included actinic keratoses and hypertension. She denied manipulating the lesions. Examination of her left medial sole revealed 13 linear, well-circumscribed, rounded, erythematous, flat-based, shallow depressions, ranging from 0.2 to 4 cm in size and arranged in a linear



**Fig 2.** Excision from case 2 demonstrates approximately 1.25-mm cornified layer peripherally (control) and thinner, approximately 0.06-mm cornified layer centrally (lesional) with abrupt drop-off at transition (**A**). Epidermis under thin cornified layer contains some clear keratocytes with moderate hypergranulosis at transition zone between thickened and thinned cornified zones (**B**). Deeper cuts reveal features of eccrine syringofibroadenoma (**C**). (**A** to **C**, Hematoxylin-eosin stain; original magnifications: **A**,  $\times 2$ ; **B** and **C**,  $\times 10$ .)

pattern (Fig 1, A). A 0.9-cm well-circumscribed, erythematous, shallow, depressed lesion was also present on the left palm (Fig 1, B). Her physical examination otherwise revealed normal findings.

Biopsy specimen showed (Fig 1, C) an abrupt transition from the normal to the depressed zone of cornification. The hypokeratotic cornified zone was mostly orthokeratotic, pink, devoid of a stratum lucidum (Fig 1, D), and approximately 0.1-mm thick. This was in contrast to the 0.3-mm thickness of the control zone of cornification (Fig 1, E) that contained a blue stratum lucidum, followed by a pink center cornified zone, and ending in a blue superficial zone of cornification. The control cornification pattern was orthokeratotic, but more compressed, than the

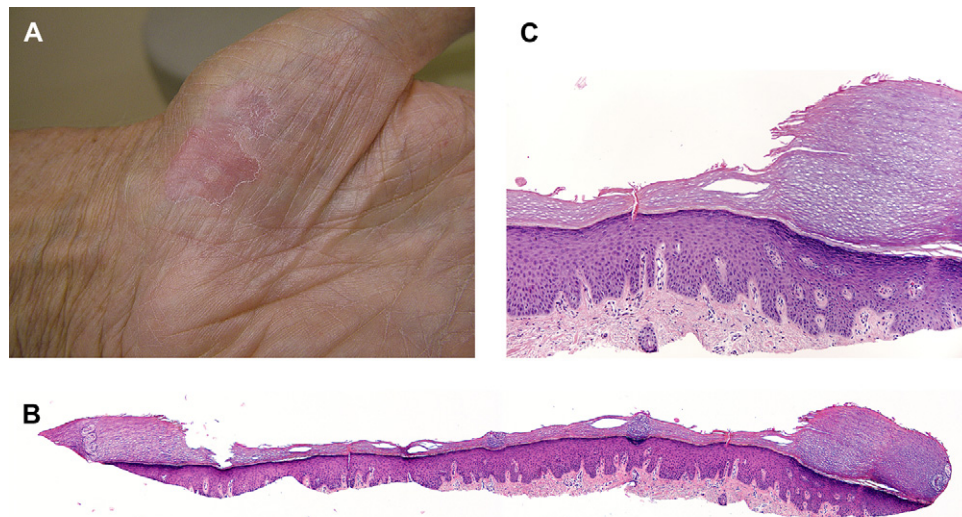
hypokeratotic zone. The granular layer was somewhat accentuated in the hypokeratotic zone, its quality being subtly different from the adjacent control areas owing to slightly larger granules and greater variation in spacing of them compared with control. The epidermis within the lesional zone was slightly acanthotic compared with control. It contained periodically spaced, small funnels of blue orthokeratotic cornification (Fig 1, D) present in vertical columns; these were the funnels of the intracorneal eccrine ducts. The keratocytes were not pleomorphic but they were separated from each other by a minor degree of spongiosis, which was not found in the adjacent control. The nuclear size of the keratocytes in the lesional zone were subtly larger than in the control areas, and the cytoplasm of the lesional keratocytes was also slightly increased in amount; some of these findings may have resulted from an optical illusion as a result of the spongiosis in the lesional area. No cornoid lamellae were present. Liquid phase PCR did not detect HPV.

A trial of calcipotriol ointment twice daily under occlusion was initiated. After 6 weeks, she experienced crusting and pain. Calcipotriol was discontinued and replaced by clobetasol ointment twice daily, with intermittent occlusion. When seen at follow-up 3 months later, the lesions were not changed significantly from their initial presentation.

## Case 2

In this case, the authors were involved only as pathology consultants and did not have the opportunity to assess the clinical appearance of the lesion. A 49-year-old Caucasian female nurse with a history of hypothyroidism presented to a podiatrist with a 10-year history of a left lateral plantar lesion that had recently become pruritic. As a child, she had a history of verruca plantaris at that location that had been "treated with a laser." She otherwise denied trauma to the area. When seen by the podiatrist, physical examination revealed a 1.5-cm slightly erythematous patch on the left sole. The podiatrist's differential diagnosis included dermatitis and tinea pedis. The podiatrist prescribed fluocinonide ointment, which the patient used twice daily for the next 5 months before presenting for follow-up. At re-examination by the podiatrist, the lesion had become partially ulcerated, depressed, and more erythematous. A total excision was performed by the podiatrist to exclude a malignancy.

Microscopic examination (Fig 2, A) revealed an approximately 1.25-mm cornified layer peripherally (control) and a thinner, approximately 0.06-mm cornified layer centrally (lesional) with an abrupt drop-off at the transition. The epidermis under the



**Fig 3.** Left thenar eminence (A) with 3- × 2-cm pink plaque with raised borders (case 3). Shave biopsy specimen from case 3 demonstrates normal palmar cornification, ranging from 0.3- to 0.45-mm thick, up to one edge, with abrupt transition to hypocornification, measuring approximately 0.7-mm thick (B). There is sharp depression between normal cornified zone and more thinly cornified central zone (C). (B and C, Hematoxylin-eosin stain; original magnifications: B, ×2; C, ×10.)

thin cornified layer contained some clear keratocytes with moderate hypergranulosis noted at the transition zone between thickened and thinned areas of cornification (Fig 2, B). In the deeper cuts, features of (presumed reactive) eccrine syringofibroadenoma were identified (Fig 2, C). Liquid phase PCR detected HPV-6. She reported no persistence 5 months after excision.

### Case 3

An 84-year-old Caucasian man with a medical history of basal cell carcinoma, squamous cell carcinoma, hypertension, and essential tremor presented with a 40-year history of an asymptomatic, recently enlarging left palmar lesion that developed after burning his palm on a hot motorcycle muffler. Physical examination revealed an erythematous, 3.7- × 2.0-cm, circumscribed, flat-based deformity with raised borders (Fig 3, A). The clinical differential diagnosis included squamous cell carcinoma and porokeratosis.

Shave biopsy specimen (Fig 3, B) showed normal palmar cornification, ranging from 0.3- to 0.45-mm thick, up to one edge, with an abrupt transition to hypocornification, measuring approximately 0.7-mm thick, producing a sharp depression between the normal cornified area and the more thinly cornified central portion of the lesion (Fig 3, C). No distinct cornoid lamellation was identified. No treatment was attempted. Liquid phase PCR did not detect HPV.

### DISCUSSION

Clinical and histopathologic characteristics of CAH are distinctive. Patients are usually middle-aged to elderly women. Lesions are frequently long-standing, acquired, and asymptomatic. They often appear as solitary, circumscribed, shallow, flat-based deformities on thenar or hypothenar skin. Histologically, the epidermis is depressed with a diminished cornified layer and an abrupt, hyperkeratotic ridge at the transition from normal-appearing skin. Lesions are not erosions in that the epidermis is depressed but not missing. Other features may include a diminished quality of the granular layer and dilated blood vessels in the dermal papillae. The differential diagnosis includes squamous cell carcinoma, Bowen's disease, porokeratosis, and friction blister.

Although most reports document long-standing, persistent lesions, several cases have spontaneously resolved.<sup>6</sup> Topical corticosteroids,<sup>2</sup> retinoids,<sup>2</sup> and calcipotriol<sup>5</sup> have been unsuccessfully tried. Case 1 of our series documents failure to respond to fluorouracil cream and calcipotriol and clobetasol ointments under occlusion. Case 1 was also particularly unusual in the large number, size (largest 4 cm), and linear arrangement of lesions. None of the previously reported patients have had more than two lesions. Furthermore, cases 1 and 2 are only the third and fourth reported cases with plantar lesions.

In case 2, the conjunction of CAH and eccrine syringofibroma has, to our knowledge, thus far not

been reported. Eccrine syringofibroadenoma has, historically, been described as a solitary lesion (putatively hamartomatous or, possibly, neoplastic),<sup>13,14</sup> as nevoid lesions sometimes presenting in linear patterns,<sup>15</sup> and as hyperplasias (eg, in scar sites, regressed keratoacanthoma fields, and some areas of vascular compromise, and rarely in patients with ectodermal dysplasias).<sup>16,17</sup> It is not fully clear why this association is present in case 2. We believe it probably is hyperplasia in the context presented here.

Several hypotheses have been proposed regarding the origin of CAH. Perez et al<sup>1</sup> suggested that it was an acquired epidermal malformation. Resnik and DiLeonardo<sup>6</sup> indicated that CAH was caused by repetitive minor trauma, based on known trauma in some cases, the occurrence of lesions on dominant hands of patients, and the involvement of thenar and hypothenar eminences. Although all of our patients denied repetitive trauma to their lesions, patients 2 and 3 reported distant histories of trauma.

Although Perez et al<sup>1</sup> failed to detect HPV-specific DNA by PCR in two patients, Böer and Falk<sup>8</sup> documented HPV-4 in a single lesion of CAH. Case 2 of our series is the second case to document HPV in a lesion of CAH. However, we were involved in this case only as pathology consultants and, therefore, were unable to evaluate the clinical appearance of the lesion.

CAH most likely represents a reaction pattern developing in response to various stimuli, including trauma, HPV, or both. The failure to detect HPV in lesions does not exclude the possibility that HPV was once present or originally caused the lesions. CAH may also be caused by HPV types that are not detected by current assays. The possibility that HPV positivity may be an incidental finding in lesions cannot be excluded.

Ongoing collection of cases, HPV testing, and therapeutic trials with other topical agents such as retinoids or imiquimod are needed to better define the origin and management of this condition.

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