

# Circumscribed Acral Hypokeratosis: A Report of 2 Cases and a Brief Review of the Literature

Emel Erkek, MD; Emel Dikicioğlu Çetin, MD; Engin Sezer, MD; Sedef Şahin, MD

## Practice Points

- Circumscribed acral hypokeratosis (CAH) is a novel, recently described, acquired dermatosis affecting acral skin sites.
- Circumscribed acral hypokeratosis has a predilection for middle-aged to elderly women.
- Clinically, CAH is characterized by round, circumscribed, depressed, erythematous patches with elevated and ridged borders, usually located on the palmar or plantar skin.
- Topical treatment modalities for CAH generally are either ineffective or require long-term application for a positive therapeutic outcome.

*Circumscribed acral hypokeratosis (CAH) is characterized by solitary or multiple circular, depressed, slightly erythematous patches on the palms or soles. Keratinization defects on acral sites or prior trauma to the affected area have been considered as potential triggers of CAH. Although affected patients typically present with a long-term history of the disease and characteristic cutaneous lesions, CAH is not well known by dermatologists. In this article, we describe 2 patients with CAH. From a clinical point of view, we emphasize its unique cutaneous expression, and from a histologic perspective, we speculate on protracted or repetitive blunt trauma in the elicitation of this dermatosis, perhaps only in patients with a genetic predisposition.*

*Cutis.* 2014;93:97-101.

---

From Acıbadem University School of Medicine, Istanbul, Turkey. Drs. Erkek, Sezer, and Şahin are from the Department of Dermatology. Dr. Çetin is from the Department of Pathology. The authors report no conflict of interest. Correspondence: Emel Erkek, MD, Acıbadem Maslak Hospital, Büyükdere Caddesi 40, Maslak Sarıyer 34457, İstanbul, Turkey (emelerkek@yahoo.com).

Circumscribed acral hypokeratosis (CAH) is an acquired, distinctive, localized dermatosis affecting the palmar or plantar skin.<sup>1-3</sup> The disorder initially was reported as a distinct entity by Pérez et al<sup>2</sup> in 2002. To our knowledge, approximately 50 cases of CAH have been reported in the literature.<sup>1,4-10</sup> We report 2 cases of CAH in elderly patients.

## Case Reports

**Patient 1**—A 74-year-old man presented with an asymptomatic red lesion on the left palm of 30 years' duration. The patient reported that the lesion initially had developed after trauma to the area with a hammer. His medical history was remarkable for coronary heart disease and hypertension, and he previously had surgery for colon carcinoma. He currently was in good health and no cancer recurrence was reported.

Dermatologic examination revealed a red, circumscribed, 1-cm, depressed, oval-shaped patch on the thenar eminence of the left palm (Figure 1). Histopathologic examination of a punch biopsy specimen from the lesion border revealed a stair-like frayed decrease in the thickness of the stratum corneum. In the lesional skin, a parakeratotic layer with alternating thickness overlying compact



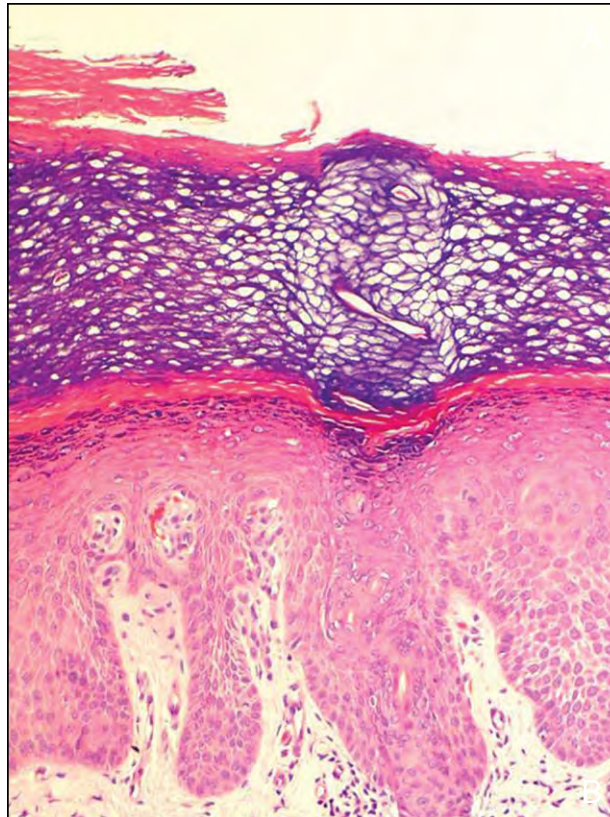
**Figure 1.** A red, depressed, oval-shaped patch on the thenar eminence of the left palm.

orthokeratosis, prominent protrusion of orthokeratotic acrosyringal corneocytes above the parakeratotic layer, and psoriasiform acanthosis without atypia were noted. Cornoid lamella was absent. The granular layer was slightly diminished, excluding the acrosyringia. There were dilated blood vessels and perivascular, slight lymphocytic infiltration in the papillary dermis (Figures 2 and 3). Periodic acid–Schiff and Alcian blue stains did not demonstrate a specific abnormality. Polymerase chain reaction (PCR) analysis for pan–human papillomavirus (HPV) DNA in a paraffin-embedded biopsy sample yielded negative results.

A combination of calcipotriene ointment 0.005% applied once in the morning and tazarotene gel 0.1% at night was initiated for treatment of the residual lesion. On follow-up examination 3 months later, there was no change in the appearance of the remnant lesion.

*Patient 2*—An 83-year-old woman presented with a persistent red lesion on the right palm of 25 years' duration. She had no other concerns, but her daughter assumed the lesion was skin cancer. The patient denied prior chemical or physical trauma to the area. Her medical history was notable for hypertension and diabetes mellitus.

Dermatologic examination revealed a circumscribed, 0.5-cm, depressed, slightly erythematous patch on the thenar eminence of the right palm (Figure 4). The lesion was completely excised at the request of the patient's daughter. Histopathologic examination showed a sharp step off from the thick stratum corneum of normal acral skin to a thin stratum corneum in the lesional skin. The abrupt thinning of the orthokeratotic stratum corneum was coupled with mild hypogranulosis and acanthosis without epidermal atypia (Figure 5). Cornoid lamella



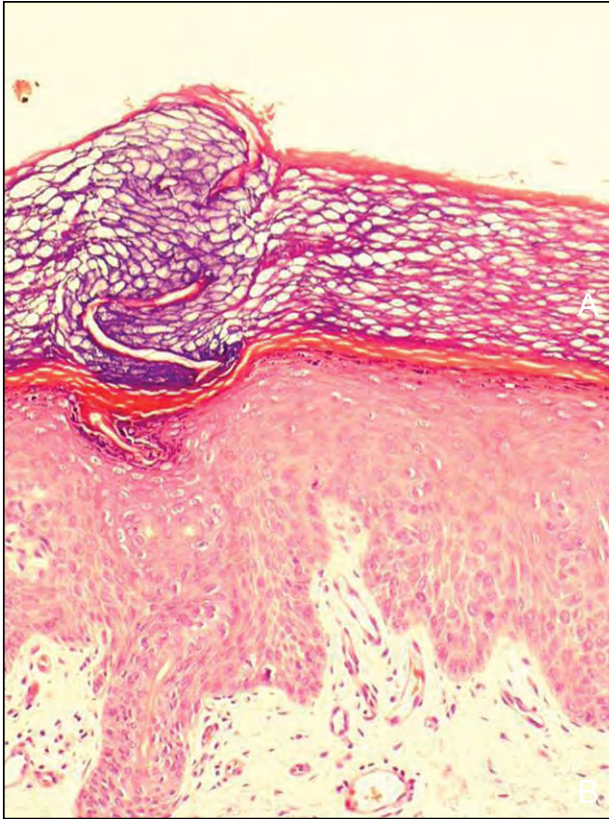
**Figure 2.** A stairlike frayed decrease in the thickness of the stratum corneum was noted at the lesion border. In the zone of hypokeratosis, acrosyringal corneocytes protruded above the parakeratotic layer and the granular layer was slightly diminished (H&E, original magnification  $\times 200$ ).

was absent. Dermal alterations were not significant. Periodic acid–Schiff and Alcian blue staining were nonspecific, and PCR analysis of the biopsy specimen for pan-HPV DNA yielded negative results.

### Comment

*Epidemiology and Clinical Presentation*—Circumscribed acral hypokeratosis is a novel entity in the dermatology literature. The typical age of onset for CAH ranges from 35 to 81 years with a predilection for middle-aged to elderly women<sup>1,2,5,7,11</sup>; however, reports of CAH occurring in men, such as patient 1, and recent reports of congenital cases disprove gender and age as distinguishing criteria.<sup>3,8,9,12,13</sup>

Clinically, CAH is characterized by a round, circumscribed, depressed, erythematous patch presenting on the palmar or plantar skin.<sup>1-3,14</sup> The border of the lesion may be slightly elevated and ridged.<sup>1,7</sup> The most commonly affected sites are the thenar or hypothenar eminences of the palms or soles, respectively.<sup>2,5,7,11,15</sup> Rarely, the fingers may

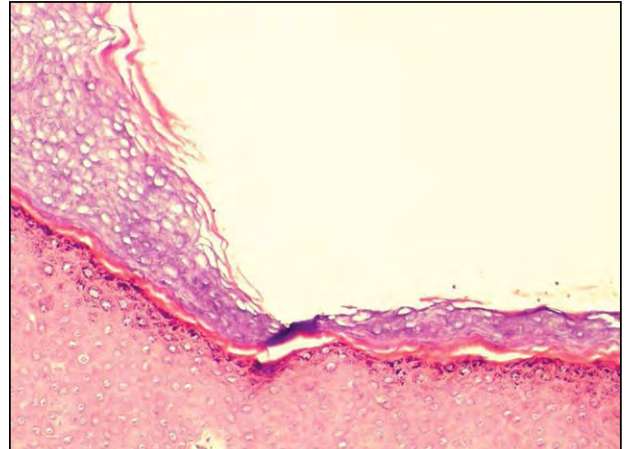


**Figure 3.** Acrosyringal corneocytes protruding above the zone of hypokeratosis were noted in the lesional area. The granular layer was slightly diminished, hypokeratotic epidermal keratinocytes showed no atypia, and there were elongated and dilated capillaries in the papillary dermis (H&E, original magnification  $\times 200$ ).



**Figure 4.** A round, 0.5-cm, circumscribed, depressed patch on the thenar eminence of the right palm.

be affected.<sup>2,7,11,16</sup> Involvement of the predominant hand has been more frequently reported.<sup>7</sup> Most patients present with a solitary lesion, though multiple lesions also have been reported.<sup>6,7,15,17,18</sup> Lesions



**Figure 5.** Histology revealed an abrupt, stairlike, frayed decrease in the thickness of the stratum corneum at the lesion border (H&E, original magnification  $\times 400$ ).

generally are asymptomatic; tenderness and burning are rare concerns.<sup>1,12,19</sup> The lesions are relatively stable with no tendency for alteration in size, shape, or color over time.<sup>1,3,12,20</sup> Spontaneous resolution may occur.<sup>11,16,17</sup> To date, there is only a single report of malignant degeneration,<sup>7</sup> and 2 cases of CAH in the setting of actinic keratosis<sup>7</sup> and disseminated superficial actinic porokeratosis<sup>21</sup> have been reported. The clinical differential diagnosis includes porokeratosis of Mibelli, squamous cell carcinoma, Bowen disease, and friction blisters.<sup>4,7,13,15,17,18,22</sup>

**Histopathology**—Histology is quite diagnostic in patients with CAH, and our cases are representative of the histologic alterations described in the literature.<sup>1-4,6,7,11,13-18,23</sup> Clinically evident redness of the lesions has been attributed to the thinning of the cornified layer and to elongated and dilated capillaries in the dermis.<sup>2-4,16,23</sup> Electron microscopy has shown decreased maturation of keratinocytes and a thinned granular cell layer.<sup>11</sup> Transmission electron microscopy has shown a reduction in keratin bundles and keratohyalin granules with an increase in lipid droplets up to the stratum corneum.<sup>18</sup>

**Treatment**—Treatment options such as topical corticosteroids, calcipotriene, retinoids, and keratolytics are constrained by futile outcomes.<sup>2,4,7,13-15,22</sup> A single case of complete resolution following a 4.5-year course of topical calcipotriene has been documented.<sup>20</sup> Topical fluorouracil cream was partially effective in one case.<sup>10</sup> Partial regression of CAH has been reported following 4 sessions of 5-aminolevulinic acid-mediated photodynamic therapy,<sup>13</sup> and cryotherapy was helpful in another case.<sup>19</sup> Excision is a last resort because it rarely is practical.<sup>1,7,14,18</sup>

In patient 1, a short-term trial of calcipotriene ointment 0.005% and tazarotene gel 0.1% was not effective. Patient 2 was treated with complete excision. In our experience, topical modalities may work slowly and either long-term topical treatment is necessary to achieve a positive outcome or destructive treatment modalities (eg, cryotherapy, photodynamic therapy) should be employed.

**Pathogenesis**—Currently, the etiology of CAH is unknown, but there are several theories. One hypothesis speculates that trauma can be a triggering incident.<sup>4,16,17,23</sup> Lesions have been reported to develop at sites of prior trauma or burns, supporting this theory; there is preferential involvement of the predominant hand, and involvement of the thenar and hypothenar eminences.<sup>1,7,11,13,17,19</sup> Although each patient may not recall trauma,<sup>1,3,20</sup> the long duration of the disorder may result in an unreliable patient history. Patient 1 reported prior trauma to the affected area from a hammer. It is possible that long-term, cumulative, or repetitive blunt trauma to acral skin might permanently alter the keratinization process. We believe that CAH may represent an acquired, trauma-induced, localized malformation of acral skin. Histologic findings in our case and from the literature also strongly support the trauma hypothesis. Relative sparing of acrosyringeal keratinocytes may be attributed to their different histogenesis and earlier keratinization compared with epidermal keratinocytes.

Another hypothesis suggests that CAH represents a rare morphologic forme fruste of acral verruca vulgaris.<sup>3,13,17</sup> Increased expression of proliferation markers and the tumor protein p53 gene, *TP53*, in lesional keratinocytes could be considered indirect evidence of a virus-mediated epidermal disorder.<sup>7,13</sup> Böer and Falk<sup>3</sup> demonstrated PCR amplification of HPV-4 DNA from lesional skin samples and interpreted HPV-4 as the offending agent in CAH. Likewise, Berk et al<sup>17</sup> described a case of CAH in a patient with a history of verruca plantaris at the same location and demonstrated amplification of HPV-6 from lesional skin; however, HPV cannot be demonstrated consistently in CAH<sup>11,24</sup> and its sole existence cannot be considered as proof for an etiologic role. Therefore, the premise of CAH representing a virus-mediated disorder remains skeptical. In both of our patients, HPV was not part of the diagnosis.

Other alternative hypotheses include CAH signifying either a type of keratoderma resulting from an aberrant mutant clone of epidermal cells or a type of chronic noninflammatory defect in keratinization at acral sites involving granular and horny layers or a hyperproliferative epidermal disease with

enhanced corneocyte fragility.<sup>5,6,11,20,22,24</sup> In a report of 10 patients with CAH, Pérez et al<sup>2</sup> suggested that CAH is an epidermal malformation because of the persistence of lesions and absence of antecedent trauma; however, late onset of the disorder may be evidence against a developmental anomaly hypothesis.<sup>7,14,15,19</sup> Furthermore, slow expansion of the lesions in some cases contradicts the malformation assumption, even though it may support the abnormal clonality hypothesis.<sup>5,6,24</sup> Differences in the keratin expression profiles of lesional and nonlesional skin and favorable response of CAH to long-term calcipotriene ointment 0.005% treatment in some reported cases favor an abnormal focal keratinization process.<sup>5,6,18,20,24</sup>

## Conclusion

Although it remains an underrecognized clinical entity, we believe CAH is more common than the relevant literature indicates.<sup>12</sup> It remains to be determined if CAH represents an acquired acral keratinization disorder secondary to long-term trauma arising in patients with inherent genetic susceptibility.

## REFERENCES

1. DeBloom JR 2nd, Ting W, Stone MS, et al. Circumscribed palmar hypokeratosis. *J Am Acad Dermatol.* 2004;51:319-321.
2. Pérez A, Rütten A, Gold R, et al. Circumscribed palmar or plantar hypokeratosis: a distinctive epidermal malformation of the palms or soles. *J Am Acad Dermatol.* 2002;47:21-27.
3. Böer A, Falk TM. Circumscribed palmar hypokeratosis induced by papilloma virus type 4. *J Am Acad Dermatol.* 2006;54:908-909.
4. Jarrett P, Sutton T. Circumscribed palmar hypokeratosis. *Australas J Dermatol.* 2007;48:57-59.
5. Tanioka M, Miyagawa-Hayashino A, Manabe T, et al. Circumscribed palmo-plantar hypokeratosis: a disease with two subtypes. *J Invest Dermatol.* 2009;129:1045-1047.
6. Ishiko A, Dekio I, Fujimoto A, et al. Abnormal keratin expression in circumscribed palmar hypokeratosis. *J Am Acad Dermatol.* 2007;57:285-291.
7. Kanitakis J, Lora V, Balme B, et al. Premalignant circumscribed palmar hypokeratosis: a new form of circumscribed palmar hypokeratosis? case report and literature review. *Dermatology.* 2010;220:143-146.
8. Arbesman J, Loss LC, Helm KF, et al. A congenital case of circumscribed acral hypokeratosis. *Pediatr Dermatol.* 2012;29:485-487.
9. Santamarina-Albertos A, Noguera-Morel L, Feito-Rodríguez M, et al. Congenital circumscribed acral hypokeratosis. *Pediatr Dermatol.* 2013;30:e102-e103.

10. Wilk M, Zelger BG, Zelger B. Circumscribed palmar hypokeratosis: successful treatment with fluorouracil cream. *Dermatol Ther (Heidelb)*. 2011;1:11-14.
11. Barry CI, Glusac EJ, Kashgarian M, et al. Circumscribed palmar hypokeratosis: two cases and a review of the literature. *J Cutan Pathol*. 2008;35:484-487.
12. Burnett JW, Harvey VM. Circumscribed palmar or plantar hypokeratosis: report of two additional cases. *J Am Acad Dermatol*. 2004;51:843.
13. Benoit S, Seitz CS, Hamm H, et al. Circumscribed palmar hypokeratosis: partial remission by photodynamic therapy. *Br J Dermatol*. 2007;157:804-806.
14. Mensing CH, Schleusner VH, Sander CA, et al. Circumscribed palmar or plantar hypokeratosis: two cases of a recently described entity of unknown origin. *Am J Dermatopathol*. 2005;27:247-249.
15. Obermoser G, Zelger B. "Multifocal" circumscribed palmar hypokeratosis: malformation or not? *J Am Acad Dermatol*. 2003;49:1197-1198.
16. Resnik KS, DiLeonardo M. Circumscribed palmar hypokeratosis: new observations. *Am J Dermatopathol*. 2006;28:112-116.
17. Berk DR, Böer A, Bauschard FD, et al. Circumscribed acral hypokeratosis. *J Am Acad Dermatol*. 2007;57:292-296.
18. Lee SE, Kim YC, Kim SC. Circumscribed palmar or plantar hypokeratosis: report of a Korean case and published work review. *J Dermatol*. 2006;33:403-405.
19. Boffa MJ, Degaetano JS. Circumscribed palmar hypokeratosis: successful treatment with cryotherapy. *J Eur Acad Dermatol Venereol*. 2007;21:420-421.
20. Urbina F, Misad C, González S. Circumscribed palmar hypokeratosis: clinical evolution and ultrastructural study after prolonged treatment with topical calcipotriol. *J Eur Acad Dermatol Venereol*. 2005;19:491-494.
21. Blanco-Barrios S, Cañueto J, Santos-Briz A, et al. Circumscribed palmar hypokeratosis associated with disseminated superficial actinic porokeratosis. *Am J Dermatopathol*. 2011;33:21-23.
22. Fueyo-Casado A, Mallo-García S, Martínez-González C, et al. Circumscribed palmar hypokeratosis. *J Am Acad Dermatol*. 2009;61:1090-1091.
23. Resnik KS, DiLeonardo M. Trauma and erosion in circumscribed hypokeratosis. *J Am Acad Dermatol*. 2008;58:174.
24. Yasuda M, Abe M, Suto M, et al. Circumscribed palmar hypokeratosis on both hands: distinct keratin expression in multiple depressed lesions. *Br J Dermatol*. 2011;164:211-213.