

Malignant circumscribed acral hypokeratosis



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Key words: Bowen disease; CAH; circumscribed acral hypokeratosis; circumscribed palmoplantar hypokeratosis; circumscribed plantar hypokeratosis; malignant transformation; squamous cell carcinoma in situ.

INTRODUCTION

Circumscribed acral hypokeratosis (CAH) is a rarely reported, idiopathic condition typically identified as a well-demarcated, depressed patch of erythematous skin, most commonly affecting the palmar aspect of the hand and, rarely, the plantar surface of the foot. The first report of CAH in the literature was in 2002 by Pérez et al.¹ It is identified by its distinct clinical and histopathologic features. It has a predilection for middle-aged to elderly women, and the lesion is most often solitary, long-standing, and asymptomatic.¹ Less commonly, reports have described multiple lesions.^{2,3} The etiology of CAH is unknown, with various hypotheses suggested to date, including epidermal malformation,¹ localized repetitive trauma,² induction by human papillomavirus,^{4,5} alteration of keratinocyte proliferation or keratin maturation,⁶ and abnormal cytokeratin expression.⁷

The first suggestion of a potential for malignant transformation with CAH was reported by Kanitakis et al,⁸ who presented a case of CAH with histologic features of actinic keratosis within the zone of hypokeratinization. Further support for malignant potential was described by Nakai et al,³ who identified a case of multiple Bowen disease lesions on the palms with CAH-like changes, and suggested a link to arsenic exposure or previous actinic keratoses. We report a novel case of CAH identified clinically, with subsequent biopsy revealing squamous cell carcinoma in situ within the lesion. To our knowledge, there have been no previous published reports of biopsy-proven malignancy in association with CAH on the plantar foot.

Abbreviation used:

CAH: circumscribed acral hypokeratosis

CASE REPORT

A 61-year-old woman presented for follow-up evaluation of a lesion on the lateral plantar surface of her left foot that had been present for many years and had increased in size. The lesion was described as “sensitive” but without pain or pruritus. Treatment was originally attempted with topical fluorouracil 5% cream applied daily to the area for 6 weeks, but there was no improvement in the size or appearance of the lesion 3 months after treatment conclusion. On examination, the primary lesion was a well-demarcated, erythematous patch with a thin peripheral hyperkeratotic border surrounding a central area of atrophy and focal crusting (Fig 1). The patch measured 4.5 × 2.4 cm. There was a smaller, secondary patch of erythematous depressed skin with central crusting to the periphery of the primary lesion. The patient did not recall any history of trauma to the area and denied a history of cutaneous or genital warts.

Microscopic evaluation of sections of a shave biopsy from the edge of the primary lesion revealed a region of normal acral epidermis with orthokeratosis before a significant, abrupt decline in the thickness of the stratum corneum, correlating with the hyperkeratotic rim of the lesion observed clinically. A frayed edge of stratum corneum was identified at the distinct transition point (Fig 2). The subsequent depressed region of hypokeratosis

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Funding sources: None.

Conflicts of interest: None disclosed.

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JAAD Case Reports 2020;6:214-6.
 2352-5126

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<https://doi.org/10.1016/j.jidcr.2020.01.006>



Fig 1. Circumscribed acral hypokeratosis. A well-demarcated, erythematous patch with a peripheral hyperkeratotic border surrounding a central area of atrophy and focal crusting. To the periphery of the primary lesion is a secondary patch of erythematous depressed skin with central crusting.

revealed parakeratosis with a decreased thickness of the granular layer of the epidermis. There was full-thickness keratinocyte atypia and loss of maturation of the keratinocytes that extended just beyond the hypokeratotic zone, consistent with squamous cell carcinoma in situ (Bowen disease) (Fig 3). Human papillomavirus viral cytopathic changes were not identified. There was a mild lymphocytic infiltrate present in the superficial papillary dermis, and cornoid lamella was not present. In situ hybridization results for high-risk human papillomavirus types 16/18 and 31/33 were negative.

After the identification of squamous cell carcinoma in situ superimposed on CAH, treatment was attempted with topical imiquimod 5% cream applied daily to the affected area 5 days per week (Monday through Friday) for 8 weeks; however, the lesion failed to resolve. The patient subsequently elected to undergo Mohs micrographic surgery for excision of the entire lesion of CAH. The procedure was successful, without recurrence at 2 years.

DISCUSSION

CAH was previously believed to be a benign process; however, more recent reports, including the identification of actinic keratosis in association with

CAH⁸ and a case of Bowen disease with CAH-like changes on the palms,³ as well as successful treatment of lesions with fluorouracil⁹ and cryotherapy,¹⁰ support the hypothesis that the keratinocytes in the lesion of CAH may have an increased predisposition to abnormal proliferation, including premalignant or malignant transformation. The case described earlier suggests that CAH may have malignant potential. Alternatively, the clinical and histopathologic findings of CAH in our patient may have been secondary to the underlying squamous cell carcinoma in situ.

The exact etiology of CAH is uncertain, with multiple hypotheses proposed to date, including several related to abnormal keratinization.^{6,10} The mechanism responsible for potential malignant transformation within CAH is also unknown. Kanitakis et al⁸ suggested that the hypokeratotic area renders the underlying epidermis more susceptible to solar damage and photocarcinogenesis. However, this seems less plausible in our patient, given the location of the lesion on the plantar surface of the foot. The case described by Butler et al,¹⁰ whereby resolution of CAH was achieved with liquid nitrogen cryotherapy, further supports the theory that CAH is secondary to atypical keratinocyte proliferation, in which the destruction of the abnormal keratinocytes allows restoration of normal epidermal architecture. Increased proliferation of atypical keratinocytes would explain the development of CAH, as well as provide a mechanism for its possible underlying malignant potential.

The case presented here highlights the importance of recognizing CAH according to its distinct clinical features and performing further evaluation to exclude the presence of an underlying premalignant or malignant change, which, if present, would require prompt treatment. Reports of lesions that have resolved with topical fluorouracil and cryotherapy provide support that therapy for CAH is indicated, regardless of whether an existing premalignancy or malignancy is identified histopathologically, considering the possible potential for future malignant transformation. Although several treatments have been suggested without consistently successful results, if malignant transformation is identified, resolution of both the malignancy and the CAH lesion would likely be achieved with excision.

It is unknown whether the changes of CAH predispose to malignant transformation, or whether malignancy could induce the changes of CAH observed clinically. Further investigation into a possible association between CAH and malignancy is needed.

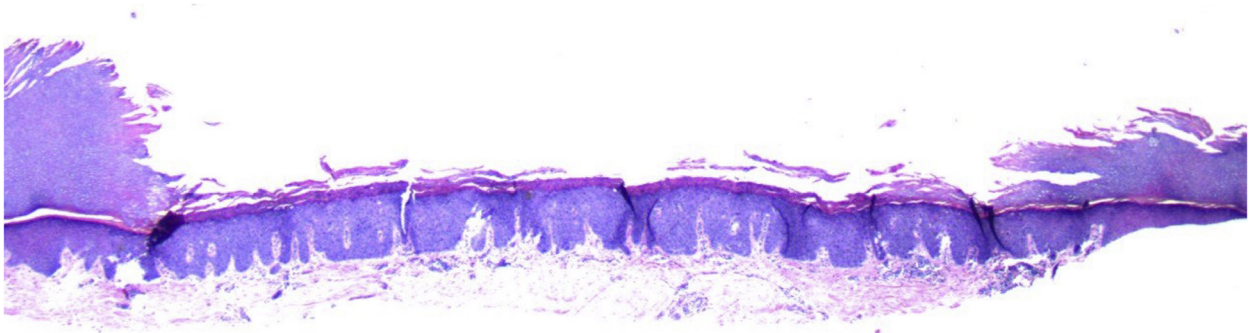


Fig 2. Circumscribed acral hypokeratosis histopathology. A region of normal acral epidermis with orthokeratosis before an abrupt decline in the thickness of the stratum corneum, with a frayed edge of stratum corneum at the distinct transition point. The subsequent depressed region revealed hypokeratosis, parakeratosis, and hypogranulosis. (Hematoxylin-eosin stain.)

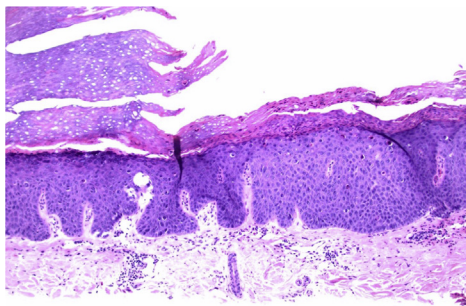


Fig 3. Squamous cell carcinoma in situ superimposed on circumscribed acral hypokeratosis. Within the zone of hypokeratosis, there is full-thickness epidermal keratinocyte atypia and loss of orderly maturation, consistent with squamous cell carcinoma in situ. (Hematoxylin-eosin stain.)

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