Symmetrical Acrokeratoderma: A Case Report in Thailand

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ABSTRACT:

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Symmetrical acrokeratoderma is a newly recognized skin disease, mostly affecting young and middle-aged males of Chinese descent. We report the first case of symmetrical acrokeratoderma in Thailand. Our case was a young Thai man presenting with asymptomatic brown to black hyperkeratotic patches distributed symmetrically on the volar side of the wrists, lateral aspect of the hands and dorsum of the fingers, ankles and feet without lesions on the palmoplantar side. After his hands were immersed in water, whitish-grayish maceration was observed. He was treated with a 10% salicylic acid cream, advised to avoid aggravating factors. The lesions persisted with mild improvement in wintertime.

Key words: Symmetrical acrokeratoderma, pigmented carpotarsal hyperkeratosis, hyperkeratosis nigricans carpi et tarsi, aquagenic response

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Introduction

Symmetrical acrokeratoderma or symmetrical acral keratoderma is a recently recognized skin disease, mostly reported from China, characterized by brown to black hyperkeratotic patches, symmetrically distributed on the acral regions without palmoplantar involvement. Water contact results in the lesion changing into whitish-grayish maceration and returning to its original shade after drying. The disease was exacerbated in summer and alleviated in winter.

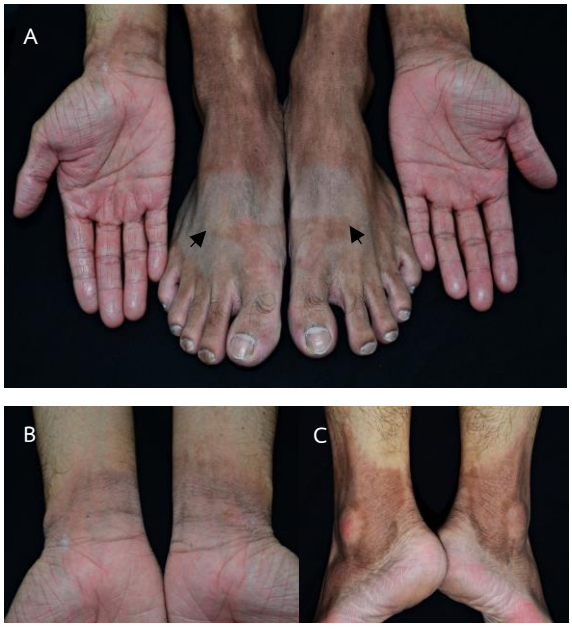

Figure 1 Symmetrical ill-defined brown to black hyperkeratotic patches on the dorsum of feet (A), volar side of the wrists (B) and ankles without lesions on the plantar side of feet (C); after sweating, lesions immediately become whitish to grayish maceration, as indicated by the black arrow in picture A

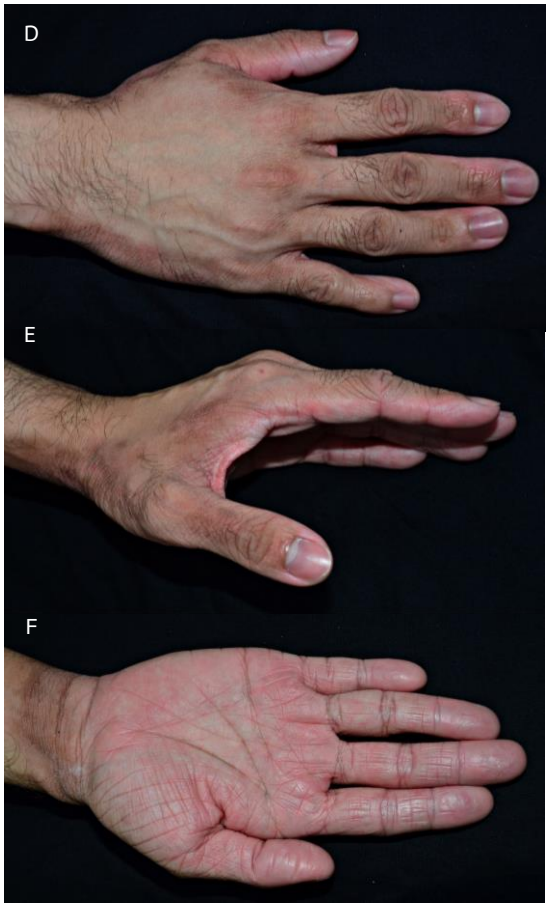

Figure 2 Ill-defined brown to black hyperkeratotic patches on the dorsum of fingers (D), lateral aspect of hands, and volar side of the wrists (E) without lesions on the palmar side of the hand (F)

Case Presentation

A 26-year-old Thai man has a three-year history of asymptomatic skin lesions involving the wrists, ankles, hands and feet. After immersion in water or sweating, the lesions immediately become whitish to grayish. He noticed that the lesions were exacerbated in summer and became milder in winter. He had no history of exposure or

contact to any irritating chemical agents. Nor was there any medical or family history of skin disease.

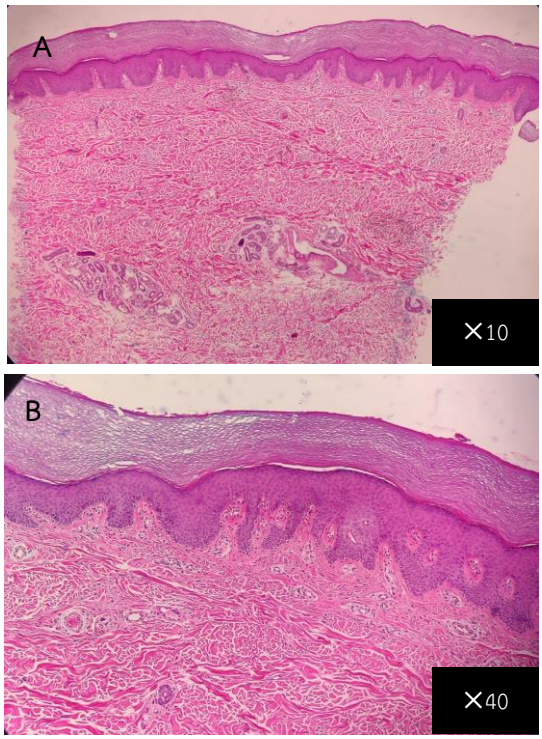

Figure 3 Histopathology, epidermal hyperkeratosis, regular acanthosis (H&E,X10), and minimal perivascular lymphocytic infiltration (H&E,X40)

Physical examination revealed symmetrical ill-defined brown to black hyperkeratotic patches on the volar side of the wrists, lateral aspect of the hands and dorsum of the fingers, ankles and feet without lesions on palmoplantar side. (Figures 1, 2) After immersing his hands in water at room temperature for five minutes, whitish-grayish maceration was observed. A skin biopsy obtained from the dorsum of the right foot revealed epidermal hyperkeratosis, regular acanthosis and minimal superficial perivascular infiltration with lymphocytes. (Figure 3) These presentations were compatible with symmetrical acrokeratoderma. He was treated with a 10% salicylic acid cream applied twice daily, and advised to avoid aggravating factors such as sweating or prolonged contact with water. One month later, the lesions persisted with mild improvement during wintertime.

Discussion

Symmetrical acrokeratoderma or symmetrical acral keratoderma is a rare and newly recognized skin disease. Almost all reported cases were from China[1], with five reported cases from India[2].

The diagnosis of symmetrical acrokeratoderma involves the following six factors[3]: including

(1) Young males are the most susceptible group to the disease.

(2) Across acral areas, hyperkeratotic patches range in color from brown to black. Typically, the patch occurs mostly on the wrists, ankles, and dorsal side of the hands and feet, but usually spares the palmoplantar area.

(3) Water immersion or sweating can turn the shade of the lesion from whitish to gray; the shade gradually returns to its original color after drying.

(4) Generally, the lesions are asymptomatic.

(5) The morphology of lesions varies due to weather conditions, worsening in summer but resolving spontaneously in wintertime, and

(6) Histopathologic property reveals hyperkeratosis in the epidermis, acanthosis and superficial perivascular lymphohistiocytic infiltration.

The differential diagnosis of such cutaneous lesions includes acral acanthosis nigricans, palmoplantar keratoderma of the Nagashima type, palmoplantar keratoderma of the Bothnia type and aquagenic palmoplantar keratoderma. Acral acanthosis nigricans is characterized by velvety and pigmented hyperkeratosis lesions that prominent over the dorsal aspects of hands and feet with knuckle hyperpigmentation, not affected by seasonal change and no whitish alteration upon water immersion. Palmoplantar keratoderma of the Nagashima type, palmoplantar keratoderma of the Bothnia type and aquagenic palmoplantar keratoderma were included in differential diagnosis due to whitish changes upon water immersion but the skin lesions of these three entities distributed mainly on the palms and soles which were not found in symmetrical acrokeratoderma.

The exact prevalence of symmetrical acrokeratoderma is still unknown. Over 248 cases have been reported, mostly among the young and middle-aged Chinese male population[4]. Associated diseases, including endocrine disorders, atopic dermatitis, obesity and ichthyosis have been described, although any precise relationship remains unclear[1]. No associated diseases were identified in our case. Although about 10% of the patients reported a history of similar skin lesions among family members, any definite hereditary pattern remains to be identified[1]. A recent genetic report studying four-generations in one Chinese family showed a missense mutation, encoding a c.85C>A alteration (p.Pro29Thr) in the first exon of the transcription factor 4 (TCF4) in all four affected individuals, suggesting an autosomal dominant inheritance[4]. TCF4 is the downstream effector of the Wnt/β-catenin signaling pathway. In the skin, this pathway normally plays a role in regulating and maintaining epithelial stem cells[1,4]. After TCF4 mutated, the result was an overexpression of differentiation genes in keratinocytes, including KRT1, KRT14, loricrin and involucrin, causing hyperkeratosis in the clinical phenotype[4].

The typical histopathologic features of symmetrical acrokeratoderma include epidermal hyperkeratosis; normal or thin granular layer, acanthosis and papillary dermal perivascular infiltrate of lymphohistiocytes[3]. The immersed lesion showed loosening of the stratum corneum[5].

Ultrastructural findings by electron microscopy from the case report studied by Chang-Xing Li, et al. for the non-immersed lesion

revealed remarkable clumped or aggregated keratin filaments and tonofilaments in the keratinocyte, normal desmosome and an abundance of melanin granules in basal cell layers[6]. Futhermore, Yi-Ming Fani, et al. reported spongiotic changes and a partial split of desmosomes in immersed lesions[7].

The immunohistochemistry from a cross-sectional analytic study by Yang PP, et al. demonstrated the upregulated expression of K14, K16, involucrin, filaggrin and higher expression numbers of Ki-67+, Melan-A+ cells among patients with symmetrical acrokeratoderma than normal healthy skin. These findings suggested excessive keratinocyte proliferation and abnormal differentiation, resulting in epidermal hyperplasia. On the other hand, aquaporin-3 (AQP3) expression was decreased on lesional and perilesional skin of symmetrical acrokeratoderma[8]. Normally, AQP3 is the most abundant aquaglyceroporin in the human epidermis, regulating skin hydration, keratinocyte migration and proliferation. Therefore, decrease of AQP3 expression in symmetrical acrokeratoderma should impact skin functions by reducing skin hydration, enhancing transepidermal water loss, causing epidermal hyperplasia and epidermal abnormality in symmetrical acrokeratoderma lesions[8,9].

Moreover, clinical features of symmetrical acrokeratoderma include brown to black color on skin lesions in an acral distribution, suggestive of melanocytic proliferation as demonstrated by abundant melanin granules in the entire basal layer of lesional and perilesional skin under the electron microscope, with significantly increased in Melan-A+ cells on immunohistochemistry.

There are no therapeutics specifically designed to cure the disease. Some drugs may alleviate the lesions for a short period, including topical retinoic acid (tretinoin or adapalene), keratolytic agents (salicylic acids, urea cream) and moisturizers.

In case of occasional inflammation or pruritus, topical steroids are needed to relieve the symptoms[1]. It is advisable to inform patients of noticeable improvement of the skin condition during wintertime. In order not to aggravate symptoms, patients should avoid contact with water or sweating, reside in places with average temperatures below 30°C and regularly apply skin moisturizers[3]. One case report asserted that acitretin may completely clear lesions with short term effectiveness, but long term effectiveness has not been reported[2]. So far, the natural history is intractable and might be prolonged up to 10 years[1].

In 2019, there was a proposal to change the name of the disease from symmetrical acrokeratoderma to pigmented carpotarsal hyperkeratosis or hyperkeratosis nigricans carpi et tarsi to emphasize a distribution of rashes located

only on the dorsum aspects and more relating to clinical manifestation[1].

Conclusion

We report a case of young Thai man with a unique clinical pattern including symmetrical brown to black hyperkeratotic patches on the acral parts, without palmoplantar involvement. This was diagnosed as symmetrical acrokeratoderma, a recently recognized skin disease. Pathogenesis, prognosis and treatment of symmetrical acrokeratoderma are still being investigated.

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