Symmetrical acrokeratoderma: A peculiar entity in China? Clinicopathologic and immunopathologic study of 34 new cases

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Background: Symmetrical acrokeratoderma seems to be a new disorder in China, and 138 cases have been reported in the Chinese literature.

Objective: We sought to summarize the clinicopathologic features and immunophenotyping of inflammatory cells in 34 new cases.

Methods: Clinical data of 34 patients were prospectively collected over 4 years. Histopathology and immunostaining of infiltrated cells were performed in 27 and 9 patients, respectively.

Results: Brown to black hyperkeratotic patches were symmetrically distributed over the acral regions in 33 cases and on the scalp in 1 case, with a whitish change after water contact or sweating. The condition was aggravated in summer and alleviated in winter in 33 patients. History of ichthyosis vulgaris was seen in 23 cases. The typical histopathology included epidermal hyperkeratosis, acanthosis, and papillary dermal perivascular infiltrate of lymphohistiocytes. Number of $CD3^+$, $CD4^+$, and $CD8^+$ cells increased in lesional and perilesional skin compared with normal-appearing skin. The skin lesions developed slowly but were confined to the acral predilection sites after the mean follow-up of 25.4 ± 13.8 months.

Limitations: The follow-up time was short.

Conclusion: This disorder may represent a peculiar dermatosis that is frequently associated with ichthyosis vulgaris. No specific therapy is available for the disorder. (J Am Acad Dermatol 2014;70:533-8.)

Key words: friction melanosis; histopathology; ichthyosis vulgaris; immunohistochemistry; symmetrical acrokeratoderma; terra firma-forme dermatosis.

In 2008, 27 patients with symmetrical acrokeratoderma (SAK) or pigmented SAK were reported in 2 Chinese articles.[1,2] In 2010, clinicopathologic features of 29 Chinese cases were reviewed and the term "acquired symmetrical acrokeratoderma" was proposed.[3] This disorder is characterized by symmetrical distribution of brown to black hyperkeratotic patches on the wrists and back of hands, fingers, and feet, but without palmoplantar involvement. The lesions become whitish immediately after water contact and improve generally in winter.[1-3] These clinical characteristics are not only different from other acral keratodermas such as acral acanthosis nigricans, palmoplantar keratodermas, aquagenic acrokeratoderma, and focal acral hyperkeratosis,[3] but are also distinguished from progressive symmetrical erythrokeratoderma,[4,5] terra firma-forme dermatosis,[6,7] and friction melanosis.[8,9] To date 138 cases have been documented in the Chinese literature.[1-3,10-19] However, a literature research in the MEDLINE database and the 8th edition of *Rook Textbook of*

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Supported by the Innovative Team Fund of Guangdong Medical College (grant No. TD1103) and Outstanding Master Dissertation Cultivation Fund of Affiliated Hospital of Guangdong Medical College (grant No. YS1102).
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Conflicts of interest: None declared.

Accepted for publication October 29, 2013.
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Published online January 2, 2014.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2013.10.061

Dermatology[20] demonstrates no similar dermatoses in other countries. It is curious whether this problem is a peculiar disorder in China. Its nomenclature, etiopathogenesis, treatment, and prognosis are unclear. In this study, therefore, we report 34 new cases and try to further characterize clinicopathologic features of this condition and to investigate its origin and relationship to other dermatoses.

CAPSULE SUMMARY

- Symmetrical acrokeratoderma is an uncommon condition predominantly affecting young men in China, characterized by symmetrically acral distribution of hyperkeratotic patches, whitish change after water contact, and summer aggravation.
- Histopathologic features include epidermal hyperkeratosis, acanthosis, and papillary dermal perivascular infiltrate of lymphohistiocytes.
- This disorder is frequently associated with ichthyosis vulgaris and lack of specific therapy.

METHODS

Patients

Between July 2009 and July 2013, 34 patients were enrolled in our hospital. This study was approved by the ethical committee of our hospital, and written informed consent was obtained from all patients and control subjects. Detailed medical history was taken, including onset and duration of disease; occupational exposure; aggravating factors; associated diseases such as ichthyosis vulgaris, atopic diseases (atopic dermatitis, allergic rhinitis, or allergic asthma), diabetes, acanthosis nigricans, pityriasis versicolor, and *Malassezia* folliculitis; and previous treatment.

Mycological examination

Smears of skin scrapings were observed in 10% potassium hydroxide and cultured on Sabouraud dextrose agar.

Histopathology

The samples were fixed in 10% neural formalin, embedded in paraffin, and stained with hematoxylin-eosin and periodic acid—Schiff stain.

Immunohistochemistry

Immunostaining was performed as described previously.[21] Rabbit anti-CD3 (RMA-0543), rabbit anti-CD4 (RMA-0620), mouse anti-CD8 (MAB-0021), citrate buffer (MVS-0066), Elivision plus kit (KIT-9901), and diaminobenzidine kit (DAB-2031) were purchased from Fuzhou Maixin Biotechnology Co Ltd (Fuzhou, China). The immunostained cells were counted wholly in 10 different high-power fields (at ×400 magnification) in superficial perivascular locations and papillary dermis. The results were expressed as mean and SD, and analyzed using analysis of variance with least significant difference post hoc test or Welch test with Dunnett T3 post hoc test.

RESULTS

Demographic and occupational data

Of the 34 patients, 29 were male (85.3%) and 5 were female (14.7%), and the male to female ratio was 5.8. Their age was 14 to 39 (25.4 ± 7.4) years and onset age was 7 to 37 (22.0 ± 7.4) years. Two brothers had the disorder in only 1 family. Twenty-seven patients came from Guangdong, and 7 were from Hunan, Jiangxi, Shangdong, Chongqing, and Hebei provinces. There were 10 students, 9 workers, 7 office clerks, 4 farmers, and 4 other careers, and no occupational tendency was observed.

Clinical data

Clinical data of 34 cases are shown in Table I. The onset was insidious, and 18 (52.9%) patients did not recall the initial involvement of skin lesions. Brown to black hyperkeratotic patches were symmetrically distributed over the acral regions in 33 cases, mainly on the wrists, ankles, and back of hands and feet (Fig 1, *A* to *D*). Palms and soles were spared. In addition, brown hyperkeratotic lesions were present on the forehead, temples, and vertex in a 37-year-old male civil servant with a 10-year history of androgenetic alopecia. The dirtlike lesions with accentuated skin markings were not removed by alcohol swabbing. The lesions became whitish after 5-minute water immersion or sweating (Fig 1, *E* and *F*), with epidermal peeling by gentle scraping, but recovered gradually after drying. The condition was aggravated in summer and alleviated in winter in 33 (97.1%) patients. Mild itching occurred occasionally in 7 (20.6%) cases.

Associated diseases and predisposing factors

Twenty-three (67.6%) patients had personal and/or family history of ichthyosis vulgaris, of them 2 possessed family history of allergic rhinitis or allergic asthma. One patient presented with a 10-year history of androgenetic alopecia. No cases were associated with diabetes, acanthosis nigricans, pityriasis versicolor, and *Malassezia* folliculitis. The results of complete blood count, glucose, and liver function