International Journal of Research in Dermatology
Iftikhar S et al. Int J Res Dermatol. 2024 May;10(3):132-137
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20240971

Case Series

Symmetrical acrokeratoderma: a case series

Swale Iftikhar, Anil Kumar Gupta, Rajkumar, Urjasweta Singh*

Department of Dermatology Venereology and Leprology, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh, India

Received: 04 February 2024
Revised: 04 March 2024
Accepted: 11 March 2024

***Correspondence:**
Dr. Urjasweta Singh,
E-mail: sweta5319@gmail.com

ABSTRACT

Symmetrical acrokeratoderma is rare keratinization disorder which is characterized by symmetrical acral brown to black hyperpigmented keratotic plaques. In this case series, all three patients presented with asymptomatic symmetrical thick raised dark brown skin lesions with rough surface on flexural surface of wrists and dorsum of hands and feet. Palms and soles were spared in all three patients. White maceration and swelling of skin lesions were noticed after soaking in water. All Patients showed good response to oral acitretin and patients were asked for regular follow up every 4 weekly.

Keywords: Symmetrical acrokeratoderma, White maceration, Aqua-exacerbated symmetrical acral hyperkeratosis

INTRODUCTION

Symmetrical acrokeratoderma (SAK) is a rare and recently described acquired keratotic skin disease. This condition is common in young Asian males.[1-5] It is characterised by asymptomatic brownish-black plaques distributed symmetrically over dorsum of hand and flexural surface of wrist. There is varying involvement of feet, ankle, knee and elbow.[1-4] SAK does not involve palms and soles. White maceration of lesions after contact with water is remarkable feature of SAK.[1-4] Worsening of skin lesions is noticed during summer with complete remission in winter.[1,4] SAK has emerged as new entity during last few years. Many names like pigmented aqua-exacerbated symmetrical acral hyperkeratosis, pigmented carpotarsal hyperkeratosis and hyperkeratosis nigricans carpi et tarsi have been suggested for symmetrical acrokeratoderma by different authors. Only few cases of symmetrical acrokeratoderma have been reported due to misdiagnosis because of similarity in its clinical features with other acral hyperkeratotic dermatosis. Therefore, it should be considered as one of the differential diagnosis in patient with history of white maceration of hyperkeratotic acral skin lesions after washing with water. Here we report three cases of symmetrical acrokeratoderma.

CASE SERIES

Case 1

A 22 years old male presented with asymptomatic sharply demarcated brownish-black lesions distributed symmetrically on the dorsum of the hands and flexural surface of wrist (Figure 1) for 2 years with history of exacerbation of lesions in summer and spontaneous resolution in winters. Previously he had been diagnosed with allergic contact dermatitis and had received topical corticosteroids without any benefit. There were no lesions present on the dorsum of feet, knee and elbow at the time

of examination but patient gave history of bilateral symmetrical involvement of dorsum of feet and knees during peak of summer. He observed that the lesions became white and swollen immediately after washing hands. The lesions were completely asymptomatic without any complaint of itching, burning sensation and pain. Family history was not contributory. The patient had no history of systemic disease and had no history of medication. On clinical examination, well defined hyperpigmented hyperkeratotic plaques present symmetrically over dorsum of the hands and flexural surface of wrist were noticed without involvement of palms and soles. The lesions developed white maceration immediately after washing of hand but lesions came back to their original condition after drying. Palmar erythema was absent after immersion in water. Classical symptoms of palmoplantar keratoderma were not seen. Features of atopic dermatitis, palmoplantar hyperhidrosis and ichthyosis vulgaris were absent. This patient had no other abnormalities related to skin, mucosa, hair and nails.

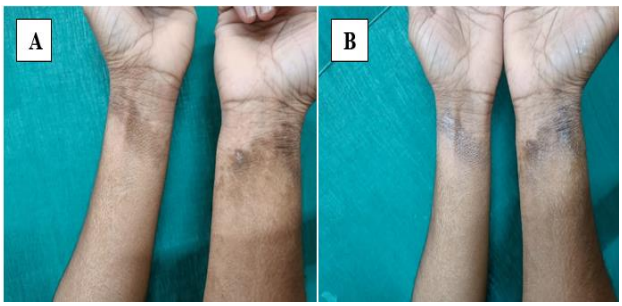

Figure 1: (A) Symmetrical Brownish black hyperkeratotic plaques on wrist (flexures), (B) White maceration of lesions after immersion in water for 5 minutes.

Case 2

A 36 years old male complained of brownish black plaques distributed over flexural surface of wrist and dorsum of hand (Figure 2) for 4 years with increase severity of lesions in summer. Patient gave history of partial improvement in lesions during winter time. The lesions initially were noticed on the wrist then gradually spread to the dorsum of both hands. Family history was negative. There were no involvement of feet, knee, elbow, palms and soles in this patient.

The patient had no history of any systemic disease and medication. He had been previously diagnosed with acanthosis nigricans, allergic contact dermatitis and frictional dermatitis. We had noticed hyperpigmented well defined plaques that were symmetrically distributed over flexural surface of wrist and dorsum of hand. The lesions were not associated with any itching and other abnormal sensation. The patient had no features of palmoplantar keratoderma, atopic dermatitis, palmoplantar hyperhidrosis and ichthyosis vulgaris. White maceration of lesions was noticed within five minutes after immersion of hand in water but the lesions restored their original presentation after drying.

Figure 2: (A) Dark brown plaques on flexural side of both wrist, (B) White maceration after immersion in water.

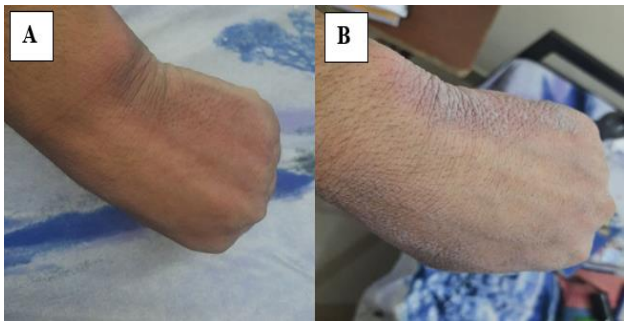

Figure 3: (A) Brownish plaque on the dorsum of hand, (B) White maceration after exposure to water for 5 minutes.

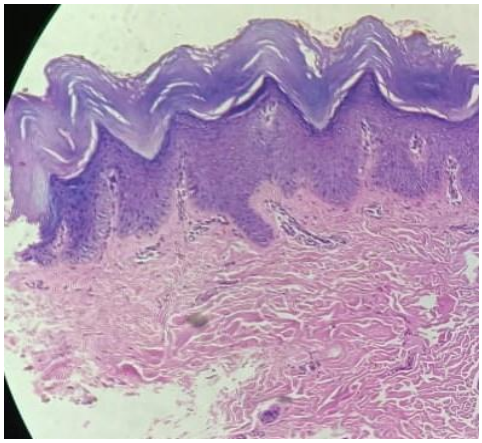

Figure 4: Histopathology show hyperkeratosis, irregular acanthosis, mild perivascular lymphocytic infiltrate.

Case 3

A 28-year-old female patient presented with asymptomatic brownish hyperpigmented plaque over dorsum of hands and feet (Figure 3) for 3 years.

Table 1: Clinical features and treatments of the patients.

Case no.	Age (years)/ sex	Total duration of disease	Sites involved	Involvement of palms and soles	Seasonal variation	Family history	Associated disease	Treatment given	Response of treatment
1.	22/M	2 years	Dorsum of the hands and flexural surface of wrist	No	Exacerbation of lesions in summer. Complete spontaneous resolution in winters.	No	No	Acitretin 25 mg/day. Urea 10%	Complete Clearance within 4 weeks
2.	36/M	4 years	Flexural surface of wrist and dorsum of hand	No	Exacerbation in summer. Partial resolution in winter	No	No	Acitretin 25 mg/day. Urea 10%	Complete Clearance within 6 weeks
3.	28/F	3 years	Dorsum of hands and feet	No	Exacerbation in summer. Complete resolution in winter	No	No	Acitretin 25 mg/day. Urea 10%	Complete Clearance within 4 weeks

Table 2: Differential diagnosis of symmetrical acrokeratoderma and distinguishing features.

Parameters	Symmetrical acrokeratoderma	Aquagenic syringeal acrokeratoderma	Acral acanthosis nigricans	Palmoplantar keratodermas
Age\sex	Young male	Adolescent female	Middle-age to elderly	Adolescent
Prevalence	Rare	Rare	Common	Common
Clinical features	Symmetrical black and brown hyperkeratotic plaques on acral areas	Whitish papules, edema, and increase wrinkling of hands and feet	Dark velvety hyperkeratosis on dorsal aspect of hands and feet. Intertriginous areas may also get involved.[1]	Thickening of palms and soles
Symptoms	Usually asymptomatic	Pain, burning sensation, itching and palmar erythema	Usually asymptomatic	Itching, burning sensation and Pain
On exposure to water and sweating	Whitish maceration of the lesions	White maceration of the lesions and wrinkling and edema increase	No effect	No effect
Seasonal variation	Yes	No	No	No
Involvement of palms and soles	No	Yes	Usually spared	Yes
Associated disorder	Atopic dermatitis, ichthyosis vulgaris, asthma and palmoplantar hyperhidrosis.	Cystic fibrosis	Diabetes mellitus, obesity and insulin resistance.[1]	Cardiac disorders or esophageal carcinoma, deafness, periodontitis.[1]

No lesions were seen on wrist, knee, and elbow at the time of examination but patient complained of bilateral involvement of elbow and knee during summer season. She noticed that the lesions were alleviated in winter. She had history of maceration of lesions after sweating. She had no history of contact to any allergic or irritating agents and had no history of any systemic disease, medication and family history of similar disease. The patients had been diagnosed with psoriasis and dermatophytes in past and had received topical corticosteroids and antifungal without any relief. Examination revealed symmetrical hyperkeratotic plaques on dorsum of hands and feet without palmoplantar involvement. After immersing her hands in water, we observed whitish maceration of the lesions without any pain, burning sensation and erythema of hands.

Histopathology of all the patients revealed similar findings of epidermal hyperkeratosis, irregular acanthosis, orthokeratosis of stratum corneum and perivascular lymphocytic infiltrate in papillary dermis (Figure 4). These findings were consistent with symmetrical acrokeratoderma. After reviewing and combining the history, clinical presentation and histopathology findings a diagnosis of symmetrical acrokeratoderma was established in all three patients. Oral acitretin 25 mg daily with 10% urea as a keratolytic agent was prescribed to all patients. All Patient showed marked improvement in skin lesions within 4 weeks of starting treatment (Figure 5). All Patients have been followed up for 16 months. Clinical features and treatments of the patients are summarized in (Table 1).

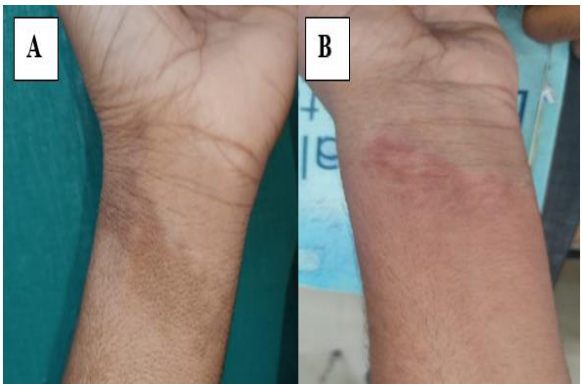

Figure 5: A) Pre-treatment, B) After 4 weeks of treatment.

DISCUSSION

Symmetrical acrokeratoderma is a recently described skin condition in young adult males of Asian origin. The first case was reported from Taiwan in 1991, where it was mistakenly misdiagnosed as acral acanthosis nigricans.[6] The first case of symmetrical acrokeratoderma in English literature was reported by Fan et al.[2] On the basis of its characteristic features, some author suggested a new term for this condition "Pigmented Aqua exacerbated symmetrical acral hyperkeratosis".[7] The diagnosis of symmetrical acrokeratoderma includes the following six features: 1) Young males with Asian ethnicity, 2) Brown to black hyperkeratotic plaques distributed over acral areas, mainly on flexural surface of wrists, dorsum of hands with varying degree of involvement of feet, ankles, elbows and knees. Peculiarly, palms and soles are spared in this condition, 3) Exacerbation of the lesions during summer with spontaneous remission of skin lesions in winter, 4) Repetitive and short-term whitish maceration of skin lesions immediately after water contact. 5) Lesions regain their original state after drying, the lesions are usually asymptomatic and 6) The typical histopathology features include epidermal hyperkeratosis, acanthosis and superficial perivascular lymphohistiocytic infiltration.[1-4]

Chen et al, proposed to change the name of the disease from symmetrical acrokeratoderma to pigmented carpotarsal hyperkeratosis or hyperkeratosis nigricans carpi et tarsi based on distribution of the lesions and clinical features.[3] White macerations of the skin lesions after exposure of hands with water and sweating is not specific for symmetrical acrokeratoderma.[7,4] This postimmersion maceration is also seen in aquagenic syringeal acrokeratoderma (ASA).[8-14] There may be association of symmetrical acrokeratoderma with atopic dermatitis, ichthyosis vulgaris, asthma and palmoplantar hyperhidrosis.[3,8,9] No associated diseases were present in all the patients of this case series. Exact cause of higher incidence of symmetrical acrokeratoderma in patients with ichthyosis vulgaris, atopic dermatitis, asthma remains unclear. None of our patients had family history of similar lesions but 10% of the individuals with symmetrical acrokeratoderma may have positive family history of similar lesions without any definite hereditary pattern.[3] A missense mutation, encoding a c.85C>A alteration (p.Pro29Thr) in the first exon of the transcription factor 4 (TCF4) was found in four generations of one Chinese family. This mutation showed autosomal dominant inheritance.[10]

The exact etiology and pathogenesis of symmetrical acrokeratoderma is not fully known but a gene transcription factor 4 mutation is supposed to be responsible for the pathogenesis of symmetrical acrokeratoderma.[1,10] TCF4 mutation results in overexpression of differentiation genes in keratinocytes including KRT1, KRT14, loricrin and involucrin. Overexpression of these genes causing hyperkeratosis.[10] Patients with symmetrical acrokeratoderma show increased transepidermal water loss (TEWL) and decreased skin hydration. This is attributed to decrease expression of aquaporin-3 (AQP3) in lesional and perilesional skin of symmetrical acrokeratoderma.[1,11] AQP3 is the most abundant aquaporin in the human epidermis regulating skin hydration.[11] Fan et al observed spongiotic changes and a partial split of desmosomes in immersed lesions of symmetrical acrokeratoderma.[2]

Chinese literature suggests Malassezia as a causative agent for symmetrical acrokeratoderma but in our cases histopathology did not show any fungal element.[2,8,9] Ultrastructural features of symmetrical acrokeratoderma include clumping of keratin filament and tonofilament in perinuclear cytoplasm.[12]

Symmetrical acrokeratoderma shows marked hyperkeratosis, irregular acanthosis, mild perivascular lymphocytic infiltrate and increased pigmentation at papillary tips on histopathology. Loosening of the stratum corneum is appreciable in a biopsy from post immersion skin lesion.[1,8,9] Increase pigmentation at papillary tips is suggestive of proliferation of melanocytes and increase expression of Melan-A+cells which corresponds to brown and black colour of the lesions.

Symmetrical acrokeratoderma needs to be differentiated from other acquired/inherited palmoplantar keratoderma, acral acanthosis nigricans, and aquagenic syringeal acrokeratoderma. Acral acanthosis nigricans is characterised by dark velvety hyperkeratosis lesions mainly over the dorsum of the hands and feet, not associated with seasonal variation.

Acquired/inherited palmoplantar keratoderma is characterised by thickening of palms and soles. White maceration seen after exposure to water and recovery after drying can help in distinguishing symmetrical acrokeratoderma from other acquired/inherited palmoplantar keratoderma and acral acanthosis nigricans. Symmetrical acrokeratoderma can be distinguished from ASA by the sparing of palms and soles and absence of burning sensation and palmar erythema after water immersion whereas these findings are present in ASA.[13,14] Differential diagnosis of symmetrical acrokeratoderma and distinguishing features are summarized in (Table 2).[1,14]

There is no cure of this condition. Drugs including acitretin, topical retinoic acid, salicylic acids, and urea only give symptomatic relief. Patients should be informed about the benign nature of this condition and patients should avoid prolong contact with water and sweating and regularly use moisturizers.[8] Recently botulinum toxin A injection has been used in the treatment of symmetrical acrokeratoderma. Skin texture, thickness, pigmentation and extent of lesions were improved after five weeks therapy of botulinum toxin.[15,16]

CONCLUSION

Symmetrical acrokeratoderma is a rare type of keratotic skin condition that usually affects young Asian males. It is characterised by symmetrical dark brown hyper-keratotic plaques over acral areas. Currently, there is no definitive treatment available for symmetrical acrokeratoderma. Oral acitretin with topical retinoids and keratolytic agents provide symptomatic relief only. For better understanding of symmetrical acrokeratoderma many undiscovered areas of its pathogenesis and treatment are needed to be explored by further research.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Xiao Q, Zhou R, Li Y, Zhao L, Xiong L, Tang J, et al. Symmetrical Acrokeratoderma: A Case Report and Literature Review. Clin Cosmet Investig Dermatol. 2022;15:247-52.
2. Fan YM, Li SF, Yang YP, Chen QX, Li W. Is acquired symmetrical acrokeratoderma a new dermatosis? Two case reports and Chinese literature review. Int J Dermatol. 2010;49:647-52.
3. Chen W, Song Z, Young CC, Hao F. Symmetrical acral keratoderma revisited: proposal for a new term pigmented carpotarsal hyperkeratosis. J Eur Acad Dermatol Venereol. 2019;33:277-82.
4. Vinay K, Sawatkar GU, Saikia UN, Dogra S. Symmetrical acrokeratoderma: a case series in Indian patients. Orphanet J Rare Dis. 2016;11(1):156.
5. Nomura T, Takeda M, Jin TP. Symmetrical acral keratoderma: a waxing and waning scaly pigmented skin lesions on the acral extremities. J Dermatol. 2021;48:e151.
6. Chen SY, Liu HT, Ho JC. Acanthosis nigricans limited in acral areas-acral acanthosis nigricans. Dermatol Sinica. 1991;9:55-60.
7. Bishnoi A, Vinay K, Dogra S. Pigmented aqua-exacerbated symmetrical acral hyperkeratosis. J Eur Acad Dermatol Venereol. 2019;33:e187-229.
8. Liu Z, Zhou Y, Chen RY, Shi G, Li W, Li SJ, et al. Symmetrical acrokeratoderma: A peculiar entity in China? Clinicopathologic and immunopathologic study of 34 new cases. J Am Acad Dermatol. 2014; 70:533-8.
9. Li CX, Han CL, Zeng K, Zhang XB, Ma ZL. Clinical, demographic and histopathological features of symmetrical acral keratoderma. Br J Dermatol. 2014; 170:948-51.
10. Chen P, Sun S, Zeng K. Exome sequencing identifies a TCF4 mutation in a Chinese pedigree with symmetrical acral keratoderma. J Eur Acad Dermatol Venereol. 2018;32:1204-8.
11. Voss KE, Bollag RJ, Fussell N, By C, Sheehan DJ, Bollag WB. Abnormal aquaporin-3 protein expression in hyperproliferative skin disorders. Arch Dermatol Res. 2011;303:591-600.
12. Li CX, Wen J, Zeng K, Tian X, Li XM, Zhang XB. Ultrastructural study of symmetrical acral keratoderma. Ultrastruct Pathol. 2014;38:420-4.
13. Luo DQ, Li Y, Huang YB, Wu LC, He DY. Aquagenic syringeal acrokeratoderma in an adult man: case report and review of the literature. Clin Exp Dermatol. 2009;34:e907-9.

14. Darlenski R, Tsankov N. Aquagenic syringeal acrokeratoderma. J Dtsch Dermatol Ges. 2012;10: 198.
15. Chiang CY, Tsai TF. Botulinum toxin type A injection in the treatment of acquired symmetrical acrokeratoderma: One case report. Dermatol Ther. 2020;33(6):e14442.
16. Garayar Cantero M, Delgado Mucientes C, Muñoz Fernández-Lomana C. Use of botulinum toxin in the treatment of aquagenic keratoderma: one case report. Dermatol Ther. 2018;31:e12689.

Cite this article as: Iftikhar S, Gupta AK, Rajkumar, Singh U. Symmetrical acrokeratoderma: a case series. Int J Res Dermatol 2024;10:132-7.