To the Editor:
Transient reactive papulotranslucent acrokeratoderma (TRPA) is a rare disorder that also has been described using the terms aquagenic syringeal acrokeratoderma, aquagenic palmoplantar keratoderma, aquagenic acrokeratoderma, aquagenic papulotranslucent acrokeratoderma, and aquagenic wrinkling of the palms.1 It was initially described in 1996 by English and McCollough,2 and since then fewer than 100 cases have been reported.1-12

A 38-year-old man presented with prominent palmar hyperhidrosis with whitish papules on the palms of 10 days’ duration. The lesions were exacerbated following exposure to water but were asymptomatic aside from their unsightly cosmetic appearance. Dermatologic examination revealed translucent, whitish, pebbly papules confined to the central palmar creases (Figure 1) that were intensified following a 5-minute water immersion test.

Histopathologic examination of a punch biopsy specimen from the right palm revealed orthokeratotic hyperkeratosis and slight hypergranulosis in the epidermis (Figure 2). Subtle eccrine glandular

Figure 1. Whitish, pebbly papules confined to the central palmar creases in a 38-year-old man.

Figure 2. Orthokeratotic hyperkeratosis and mild hypergranulosis was noted in the epidermis (H&E, original magnification ×100).
hyperplasia was evident in the dermis (Figure 3). Periodic acid–Schiff staining was negative. Based on the clinical findings and results of the water immersion test, a diagnosis of TRPA was made. A therapeutic trial of calcipotriene ointment 0.005% twice daily was initiated and resulted in dramatic clearance of the lesions within 2 weeks (Figure 4). At 1-month follow-up, the patient was virtually free of all symptoms and no disease recurrence was noted at 5-year follow-up.

A 25-year-old woman presented with whitish plaques on the palms of 7 days’ duration. She reported frequent use of household cleansers in the month prior to presentation. The lesions were associated with prominent hyperhidrosis, pruritus, and a tingling sensation in the palms. Dermatologic examination revealed confluent, macerated, white, pavement stone–like papules with prominent puncta around the palmar flexures on both palms. Lesions were exacerbated after a 5-minute water immersion test (Figure 5).

The patient refused skin biopsy, and conservative treatment with a barrier cream and limited water exposure were of no benefit. Based on the clinical findings and results of the water immersion test, a diagnosis of TRPA was made. Due to the excellent outcome experienced in treating the previous patient, a trial of calcipotriene ointment 0.005% twice daily was initiated, and the patient reported complete resolution of signs and symptoms within the initial 2 weeks of treatment. Treatment was terminated at 1-month follow-up.

A 6-year-old boy presented with swollen, itchy palms of 2 months’ duration that the patient described as “wet” and “white.” Due to a recent epidemic of bird flu, the patient’s mother had advised him to use liquid cleansers and antiseptic gels on the hands for the past 2 months, which is when the symptoms on the palms started to develop. On dermatologic examination, whitish, cobblestonelike papules were noted near the palmar creases in association with profuse hyperhidrosis (Figure 6). Based on the clinical findings, a diagnosis of TRPA was made. Biopsy was not attempted and the patient was treated with calcipotriene ointment 0.005% twice daily. At 1-month follow-up, complete clearance of the lesions was noted.

FIGURE 3. Luminal dilatation in the eccrine glands with a prominence of glandular epithelial cells, which displayed abundant cytoplasm with a granular appearance (H&E, original magnification ×100).

FIGURE 4. Remarkable response to calcipotriene ointment 0.005%. The white punctuate scar indicates the previous punch biopsy site.

Transient reactive papulotranslucent acrokeratoderma is an acquired and sporadic disorder that can occur in both sexes.2,4,6-8,11 Onset generally occurs during adolescence or young adulthood.1,3,8,9 Clinically, TRPA is characterized by edema and wrinkling of the palms following 5 to 10 minutes of contact with water that typically resolves within 1 hour after cessation of exposure.2,3,6-8,10 The “hand-in-the-bucket” sign refers to accentuation of physical findings upon immersion of the hand in water.2,3,10,11 Patients frequently report itching, burning, or tingling sensations in the affected areas.2,4,6,7,9,11 Transient reactive papulotranslucent acrokeratoderma usually affects the palms in a diffuse, bilateral, and symmetrical pattern,2,4,6-10 but cases showing involvement of the soles,6,7 marginal distribution of lesions,1 unilateral involvement,1 and prominence on the dorsal fingers5 also have been reported. The natural disease course involves reactive episodes and quiescent intervals.2,7,9 Spontaneous resolution of TRPA has been reported.4,6,8
The histological characteristics described in previous reports involve compact orthohyperkeratosis with dilated acrosyringia, hyperkeratosis and hypergranulosis in the epidermis, and eccrine glandular hyperplasia. Alternatively, the skin may appear completely normal on histology.

Originally, it was proposed that TRPA is a variant of punctate keratoderma or hereditary papulotranslucent acrokeratoderma. However, its position within the keratoderma spectrum is unclear and the etiopathogenesis has not been fully elucidated. Some investigators believe that transient structural and functional alterations in the epidermal milieu prompt epidermal swelling and compensatory dilation of eccrine ducts. Other reports implicate the inherent structural weakness of eccrine duct walls or aberrations in eccrine glands. Whether the fundamental pathology lies within the epidermis, eccrine ducts, or the eccrine glands remains to be determined. Nevertheless, reports of TRPA in the setting of cystic fibrosis and its carrier state as well as the presence of hyperhidrosis in most affected patients and the accumulation of lesions along the palmar creases may implicate oversaturation of the epidermis (due to salt retention or abnormal water absorption by the stratum corneum) as the pivotal event in TRPA pathogenesis. Once the disease is expressed in susceptible individuals, episodes might be provoked by external factors such as friction, occlusion, sweating, liquid cleansers, antiseptic gels, gloves, topical preparations, and oral medications (eg, salicylic acid, cyclooxygenase 2 inhibitors).

Treatment alternatives such as hydrophilic petrolatum and glycerin, ammonium lactate, salicylic acid (with or without urea), aluminum chloride hexahydrate, and topical corticosteroids are limited by unsuccessful or temporary outcomes. Botulinum toxin injections were effective in a patient with TRPA associated with hyperhidrosis. In the cases reported here, topical calcipotriene accomplished dramatic clearance of the lesions within the initial weeks of therapy. Spontaneous resolution was unlikely in these cases, as conservative therapies had not alleviated the signs and symptoms in any of the patients. However, we cannot exclude the possibility that improvement of the skin barrier function associated with other ingredients in the calcipotriene ointment (eg, petrolatum, mineral oil, α-tocopherol) may have led to the resolution of the lesions.

Calcipotriene has demonstrated efficacy in treating cutaneous disorders characterized by epidermal hyperproliferation and impaired terminal differentiation. Immunohistochemical and molecular biological evidence has indicated that topical calcipotriene exerts...
more pronounced inhibitory effects on epidermal proliferation than on dermal inflammation. It has been proposed that the bioavailability of calcipotriene in the dermal compartment may be markedly reduced compared to its availability in the epidermal compartment \(^{13}\); therefore it can be deduced that its penetration into the dermis is low in the thick skin of palms and its effect on eccrine sweat glands is negligible. Based on these factors, the clinical benefit of calcipotriene in TRPA could be ascribed directly to its antiproliferative and prodifferentiating effects on epidermal keratinocytes. We believe the primary pathology of TRPA lies in the epidermis and that changes in eccrine ducts and glands are secondary to the epidermal changes.

It is difficult to conduct large-scale studies of TRPA due to its rare presentation. Based on our encouraging preliminary observations in 3 patients, we recommend further therapeutic trials of topical calcipotriene in the treatment of TRPA.

**REFERENCES**