Familial Spiny Keratoderma: A Case Report

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ABSTRACT:
We report a rare case of familial spiny keratoderma. A 51-year-old female complained of sensations of roughness in the palms for 6 months. She had no underlying disease. She denied exposure to arsenic, herbal medicines, and other chemicals. Physical examination revealed multiple tiny, spiny, whitish papules on the palms and soles. Other systems were unremarkable. The histopathological study was consistent with spiny keratoderma. The hereditary type is most likely in our patient because of the similar lesions on her father's palms and soles.
Key words: Music box spine keratosis, Palmoplantar filiform hyperkeratosis, Spiny keratoderma

A 51-year-old Thai female complained of sensations of roughness in the palms for 6 months. The lesions gradually increase in number. She had no underlying medical conditions and worked as an administrator for a jewelry company. She denied exposure to arsenic, herbal remedies, and other chemicals. Physical examination revealed multiple tiny, spiny, whitish papules on the palms and soles. (Figure 1 and 2) Other systems were unremarkable.

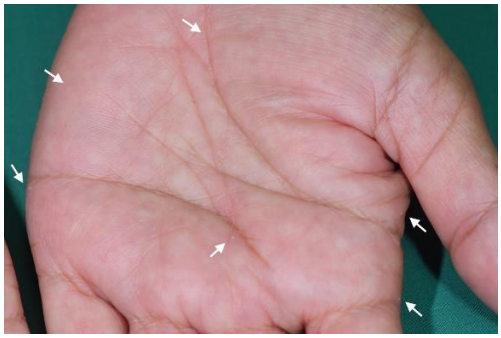

Figure 1 Multiple tiny, spine-like whitish papules on the palm (close-up view)

Her 71-year-old father has had similar lesions on the palms and soles with uncertain onset, but they were larger, thicker, and more hyperpigmented than the index case. (Figure 3) His medical background consisted of hypertension and Alzheimer disease. He had no prior history of malignancies.

The clinical differential diagnosis included spiny keratoderma, punctate porokeratosis, porokeratosis palmaris et plantaris disseminata, arsenical keratosis, and verruca filiformis.

A punch biopsy taken from the sole shows focally thick hyperkeratosis with parakeratosis without dyskeratosis or features of koilocyte. There is obvious hypogranulosis corresponding with the column of parakeratosis. (Figure 4) While clinically and histologically comparable to punctate porokeratosis, spiny keratoderma is a distinct diagnosis that exhibits similar columns of parakeratosis but usually lacks the dyskeratotic keratinocytes, whereas punctate porokeratosis is seen.

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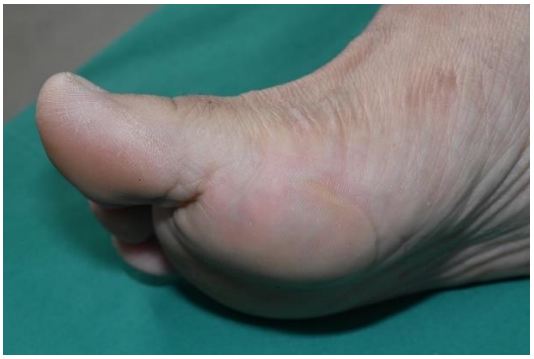

Figure 2 Multiple pinhead-sized, white, keratotic papules on the right sole

Figure 3 Numerous small, spiny, white, and hyperpigmented keratotic papules on the palm. (Father)

Hereditary spiny keratoderma could be the diagnosis for this patient because of the clinicopathological correlation and similar lesions of her father.

Our patient had experienced topical treatments with 10% urea cream, 0.05% tretinoin cream, and 20% salicylic acid ointment with little improvement. She had a previous routine annual checkup with no serious conditions. Although there is positive family history, the clinical onset is quite late. We recommend that she and her father do age-appropriate malignancy screening and clinical imaging studies.

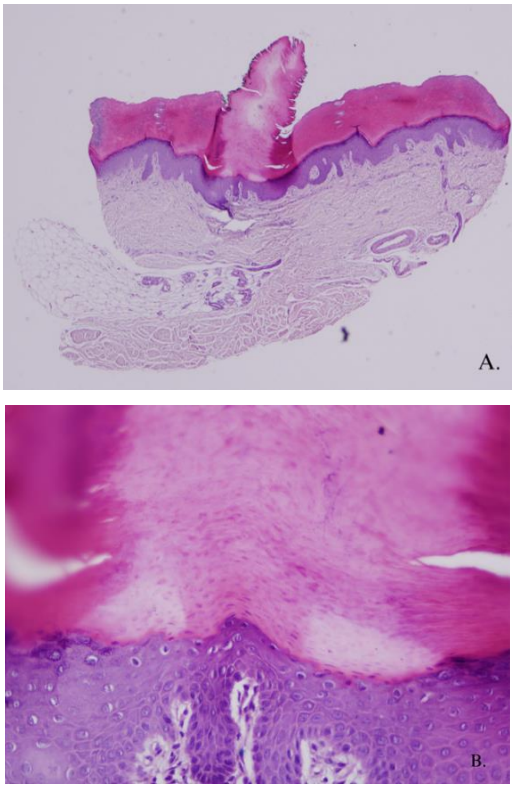

Figure 4 Column of thick parakeratotic hyperkeratosis and hypogranulosis without dyskeratosis or koilocyte **(**A; hematoxylin and eosin (H&E) X4, B; H&E, X40)

Discussion

Spiny keratoderma is a rare condition with unknown etiology, characterized by numerous spine-like keratotic papules on the palms and/or soles[1,2,3]. Various terminology has been used to describe the condition of horny projections on the palms and feet, including music box spine keratoderma, palmoplantar filiform hyperkeratosis, and multiple minute palmoplantar digitate hyperkeratosis. However, spiny keratoderma is preferred, as explained by the compatible clinicopathological characteristics[1,3].

Table 1 Differential diagnosis of spiny papules on the palms and soles

Disease	Etiology	Onset	Clinical characteristics	Histopathology
Spiny keratoderma	Unknown	Nonhereditary form: the late-onset average age of 50 and 60 Hereditary form: onset between the ages of 12 and 50	Numerous small spiny keratotic plugs limited on the palms and soles	Focal columns of parakeratosis or orthokeratosis over a hypo- or hypergranular epidermis without dyskeratosis and vacuolar changes.
Punctate porokeratosis	Concomitant occurrence with other forms of porokeratosis	Onset in childhood or adolescence	Numerous punctate 1- to 2-mm seed-like keratotic plugs limited to the palms and soles, without tendency to centrifugal enlargement	Columns of parakeratosis with underlying hypogranulosis, and scattered vacuolated dyskeratotic keratinocytes
Porokeratosis palmaris et plantaris disseminate	Autosomal dominant/ sporadic The exact etiology is unknown.	In childhood or early adolescence	Keratotic papules on the palms and soles with subsequent generalization to other areas of the body	Cornoid lamella; a column of parakeratosis arising from an invagination of the epidermis with underlying dyskeratosis and vacuolated keratinocytes in the epidermis
Punctate keratoderma type 1	Autosomal dominant Mutation of *AAGAB* gene and *COL14A1*	Onset at the first or second decades of life	Multiple hyperkeratotic, centrally indented, yellow to brown papules distributed irregularly over the palmoplantar skin. They increase in size and number with advancing age and coalescence into more confluent plaques, particularly on pressure-bearing areas of plantar skin.	Marked hyperkeratosis and acanthosis with epidermal invagination associated with focal parakeratosis, hyper- or hypogranulosis, and overlying orthokeratosis
Arsenical keratoses of the palms and soles	Chronic arsenic ingestion	Minimal latent period between the beginning of arsenic intake and the onset of arsenical keratoses of the palms and soles was 2.5 years, and the average latent period 6 years	Indurated, gritty millimeter palmoplantar papules to yellow, verrucous papules and plaques	Compact hyperkeratosis and acanthosis with or without evidence of nuclear atypia
Verruca filiformis	Human papilloma viruses type 1, 2, 4, 27, 29	All age	Long, narrow projection papule that extend from the skin, common on the face	Columns of parakeratosis with more extreme delicate papillomatosis and koilocytes.

Spiny keratoderma can be divided into acquired and hereditary types. From literature reviews, the majority (70.2%) are non-hereditary, have late onset at 50-60 years of age, and can be associated with systemic diseases or malignancies, such as Darier disease, polycystic kidney disease, type IV hyperlipoproteinemia, asthma, type II diabetes, pulmonary tuberculosis, myelofibrosis, melanoma, leukemia, squamous cell carcinoma, lung cancer, esophageal cancer, multiple myeloma, breast cancer, colon cancer, and renal cell carcinoma. However, whether the correlation between spiny keratoderma and systemic diseases or a paraneoplastic phenomenon is coincidental or a true association, these have been uncertain because of the insufficient information, the limited number of reported cases, and the fact that the elderly have their own risk of malignancy[1,2,4,5].

While 29.8% of cases were hereditary and genetically transmitted in an autosomal dominant pattern. The hereditary form has a benign presentation and typically appears between the ages of 12 and 50. Interestingly, female familial spiny keratoderma cases had fewer and less noticeable keratotic plugs than affected males. No malignancy and other

systemic conditions have been correlated with these hereditary cases[1,2].

With spiny keratoderma, the lesions are typically asymptomatic, but some have reported slight pain with pressure, mild pruritus, or feeling roughness. Malignant transformation of the spiny papules has never been reported[1,2,5].

The hypotheses about etiology could be possible. 1) An ectopic hair formation based on the detection of a hair-specific antibody (AE13) in the lesion. 2) Overexpression of keratin 6 and 16 in the keratotic lesion is attributable to repeated trauma. 3) Overexpression of p63, a transcription factor that regulates the proliferation and differentiation of the keratinocytes. 4) A disruption of cholesterol synthesis with induction of epidermal hyperplasia caused by the coenzyme A reductase inhibitors[4].

The differential diagnosis included spiny keratoderma, punctate porokeratosis, porokeratosis palmaris et plantaris disseminata, punctate palmoplantar keratoderma, arsenical keratoses of the palms and soles, and verruca filiformis[1,2,3,6]. (Table 1)

Systemic workup and monitoring for internal malignancies are warranted in the cases of acquired spiny keratoderma. Tumor markers, including carcinoembryonic antigen (CEA), carcinoma antigen (CA) 125, CA 19.9, CA 15.3, alpha-fetoprotein, prostate-specific antigen, and serum electrophoresis were suggested. Computed tomography of the chest, abdomen, and pelvis should be considered. An annual age-appropriate cancer screening and thorough skin examination should be performed[2,3].

Reported treatments for spiny keratoderma included various methods: shaving, mechanical debridement by a pumice stone, topical applications including 10–20% urea cream, 5–10% salicylic acid, tacalcitol ointment, 0.05% tretinoin, 5-fluorouracil, and systemic drugs such as acitretin[1,4,7]. The lesions usually recur after cessation of treatment. In some cases, had been reported, the lesions completely regressed after successful treatment for malignancy and pulmonary tuberculosis[1,2].

Learning points

Spiny keratoderma is an uncommon disease characterized by spiny keratotic plugs causing palpable projections limited to the palms and soles. Histopathology is helpful for differential diagnosis.

Spiny keratoderma has nonhereditary and hereditary variants. In sporadic adult-onset spiny keratoderma, investigations are recommended for systemic diseases and internal malignancies.

True incidence may be underreported because the patients may not visit the dermatologists despite having the lesions.

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