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Keratoderma Hereditaria Mutilans (Vohwinkel's Syndrome): A Trial of Isotretinoin

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Abstract: An 8-year-old girl with the classic findings of keratoderma hereditaria mutilans (Vohwinkel's syndrome) was seen. Treatment with isotretinoin was instituted to decrease the hyperkeratosis and to prevent further autoamputation. After a 12-week course at 2 mg per kg per day, the patient had only minimal decrease in the amount of hyperkeratosis. Because of the well-known long-term risks of systematic retinoids and her suboptimal improvement, therapy was discontinued.

Keratoderma hereditaria mutilans (KHM) is a rare palmoplantar keratoderma syndrome initially described by Vohwinkel in 1929 (1). Onset typically begins in infancy, with diffuse honeycombed hyperkeratosis of the palmar and plantar surfaces, star-shaped keratosis located on the dorsa of the digits, and linear keratosis on the knees and elbows. The most distressing and serious component of this condition is an ainhum-like constriction of the digits, usually beginning at age 4 or 5 years. Autoamputation usually involves only the fifth toes but may occur in all digits. This process initially involves the formation of fibrous bands at the base of the digit, which reduces the blood supply and causes autoamputation. Usually the inheritance is autosomal dominant, but recessive patterns and sporadic cases have been reported. Other associated findings have included high-frequency hearing loss, deaf mutism, ichthyosis, and cicatricial alopecia (2, 3).

Until recently, the treatment of KHM has been largely unsuccessful. Although various keratolytics were somewhat helpful in softening the hyperkeratosis, they did not alleviate or prevent constriction and autoamputation of the digits. Recently, the case report (4) of significant improvement with an oral retinoid (etretinate) prompted us to institute a trial of isotretinoin (Accutane) in the treatment of a young girl with KHM.

CASE REPORT

An 8-year-old black female was first referred to the University of Michigan Department of Dermatology in January 1983. Her skin affliction began with dryness of the palms and soles at age 3 months and slowly progressed to severely thickened hyperkeratosis. Between the ages of 3 and 5 years, she developed fibrous bands circumferentially around the bases of the fourth and fifth toes bilaterally. The toes slowly became gangrenous and were surgically

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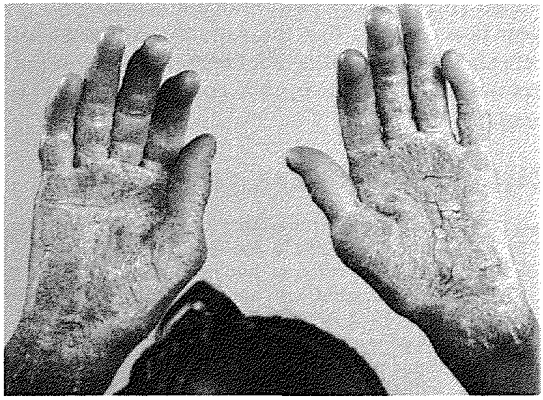


Figure 1. Honeycombed hyperkeratosis of the palms.

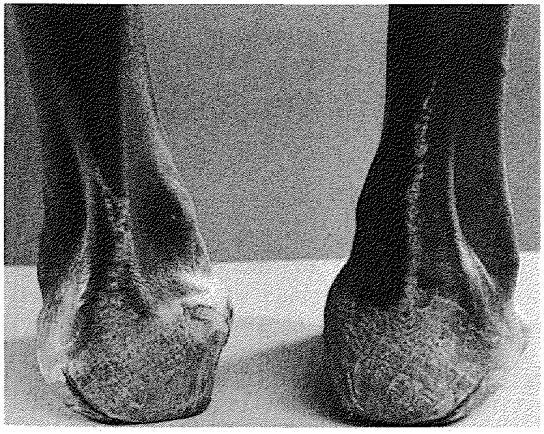
amputated. Topical salicylic acid has been used over the last two years as a keratolytic with minimal results. Recently, she developed fissures at the base of her right fifth finger, the initial sign of ainhum-like constriction. The patient was referred to us for evaluation and treatment of this disorder.

Past medical history included the presence of ectropion at birth, severe bilateral myopia, and strabismus of the right eye. Development was slow in school, with the patient being one grade behind her peers, which was felt to be secondary to her decreased vision. There was no history of decreased hearing, alopecia, or ichthyosis. She is the first-born of three children, and no other family members have a similar affliction.

On physical examination, she had marked hyperkeratosis of the palms and soles, in a honeycombed pattern (Fig. 1). Bilaterally a circumscribed hyperkeratosis extended up the Achilles tendon (Fig. 2), on the knees and elbows, as well as on the knuckles of the hands and feet (Fig. 3). Fissures were evident at the base of the right fifth finger, but a fibrous band was not present. The fourth and fifth toes were absent bilaterally (Fig. 4). All nail plates exhibited severe dystrophy. Other than the myopia and strabismus previously mentioned, the rest of the examination was within normal limits.

Results of laboratory examinations, including complete blood count, liver and renal function, urinalysis, triglyceride, and cholesterol, were within normal limits. Roentgenograms of the lateral

Figure 2. Extension of hyperkeratosis up the Achilles tendon.



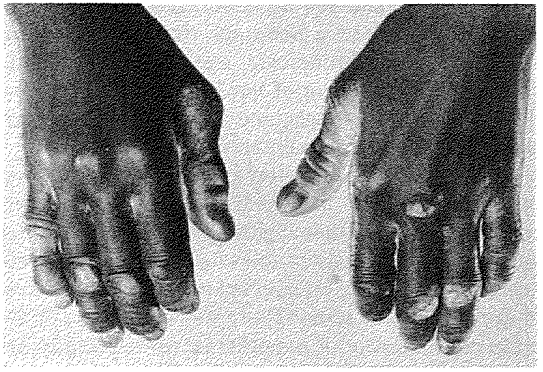
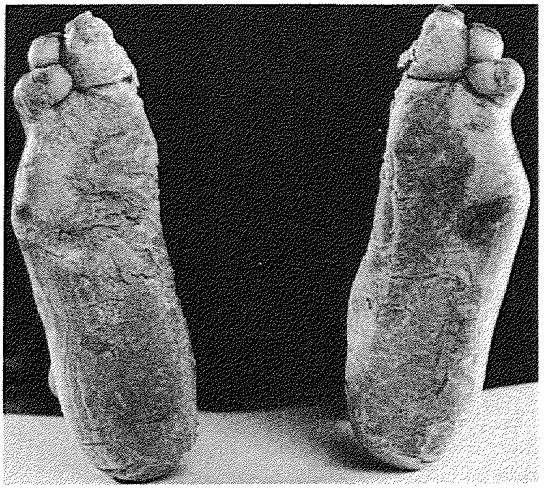


Figure 3. Hyperkeratosis involving the knuckles of the hands.

Figure 4. Absence of the fourth and fifth toes secondary to ainhum-like constriction.



thoracic spine showed no abnormalities, and hand films demonstrated a bone age that corresponded well with her chronologic age. Histopathologic examination from skin of her left sole featured orthokeratosis, acanthosis, and an increased granular layer consistent with palmoplantar keratoderma.

Isotretinoin was initiated at 2 mg per kg per day (40 mg total dose) to diminish the hyperkeratosis and to prevent further digital constriction or autoamputation. The patient tolerated the retinoid well and after a 12-week course had only the side effects of dry skin and cheilitis. There was minimal to moderate improvement of hyperkeratosis, especially on the dorsa of the digits. In addition, the fissures of the right fifth finger had resolved and there was no evidence of ainhum-like constriction elsewhere.

DISCUSSION

Systemic retinoids are a new modality for the treatment of certain disorders of keratinization. Both isotretinoin (5, 6) and etretinate (4, 7–9) have been used effectively in the various palmoplantar keratodermas, but the latter agent appears to effect a more dramatic response within a shorter time. The mechanism by which retinoids exert their therapeutic action is unknown, but numerous effects have been described. Retinoids have been shown to inhibit rapidly growing epithelia and excessive keratinization.

Our patient was able to tolerate isotretinoin without difficulty. Mild improvement was noted in the digital hyperkeratosis, with resolution of the fissuring. Further improvement of the palmoplantar keratoderma did not occur. Recent reports in the literature of premature closure of the epiphyseal plates (10) and skeletal hyperostosis (11) suggests that long-term use of retinoids must be approached with caution. We felt the risks outweighed the benefits in this case, and isotretinoin was discontinued after 12 weeks of treatment. Follow-up one year later showed that the patient's condition had remained stable with administration of topical keratolytics, without further constriction or autoamputation.

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