Epithelioma Cuniculatum Arising from Striate Keratoderma

Wook Lew, M.D., Kwan Chul Tark*, M.D., Soo Il Chun, M.D.

Departments of Dermatology and Plastic Surgery Yonsei University College of Medicine Seoul, Korea*

Epithelioma cuniculatum developed from linear keratoderma on the right sole in a 32-year-old woman. After surgical removal of the verrucous carcinoma, most of the linear keratoderma resolved spontaneously but recurred several months later. The keratoderma was improved by Tigason (etretinate) therapy but recurred upon discontinuation of the drug.

(Ann Dermatol 4:(2) 83-86, 1992)

Key Words: Epithelioma Cuniculatum, Keratoderma

Verrucous carcinoma is a low-grade squamous cell carcinoma which shows various clinical manifestations, such as giant condyloma of Buschke-Lowenstein, oral florid papillomatosis, and epithelioma cuniculatum. Epithelioma cuniculatum, which occurs on foot, is also known as plantar verrucous carcinoma and is an exophytic tumor having multiple sinuses. Epithelioma cuniculatum has characteristics of slow progression and ultimate deep invasion with a marked tendency for recurrence if incompletely removed(1). Histopathologically, this tumor shows high-grade hyperkeratosis without cellular atypia, characteristics of well-differentiated squamous cell carcinoma(2). In 1985, Barnett and Estes(3) reported the first case of multiple epithelioma cuniculata occurring in a multilating keratoderma. We report an unusual case of epithelioma cuniculatum arising from linear keratoderma of the foot in a 32-year-old woman.

REPORT OF A CASE

A 32-year-old woman visited our department because of a foul smelling mass on the right heel of 5 years duration. Family history and past history were non-contributory. She first noted a thickening of the pressure-bearing sites on both feet at five years of age. By age eight, the lesions were slightly enlarged, itchy and tender when standing, but limited to both feet. At the age of thirteen, the lesions extended to the toes and palms, with accompanying flexion contractures of the toes and the fingers. She was otherwise healthy, in good general condition. Examination revealed yellow-colored, linearly arranged, markedly hyperkeratotic plaques on the palms and palmar aspects of the fingers and flexion contractures of all fingers except the left ring finger (Fig. 1). Similar hyperkeratotic plaques were noted on the soles with flexion contractures on both sides of 4th and 5th toes and an egg-sized, foul-smelling, markedly hyperkeratotic verrucous nodule on the right heel (Fig. 2). No internal malignancies were identified. Laboratory tests including routine blood examination, urinalysis, serologic tests for syphilis were negative or within normal limits. Chest radiography revealed a fibrous nodular calcification on the right hilar area suggesting an old inflammatory lesion. Roentgenogram of the foot showed contractures on both sides of the 4th and 5th toes and a subcutaneous mass on the right heel. A skin biopsy from the linear verrucous lesion from the sole showed marked hyperkeratosis, parakeratosis, hypergranulosis with focal agranulosis, marked

Received September 28, 1991
Accepted for publication December 5, 1991
Reprint request to: Soo Il Chun, M.D., Department of Dermatology, Yonsei University College of Medicine, C.P.O. Box 8044 Seoul, Korea.

Annals of Dermatology
Vol. 4, No. 2, July 1992

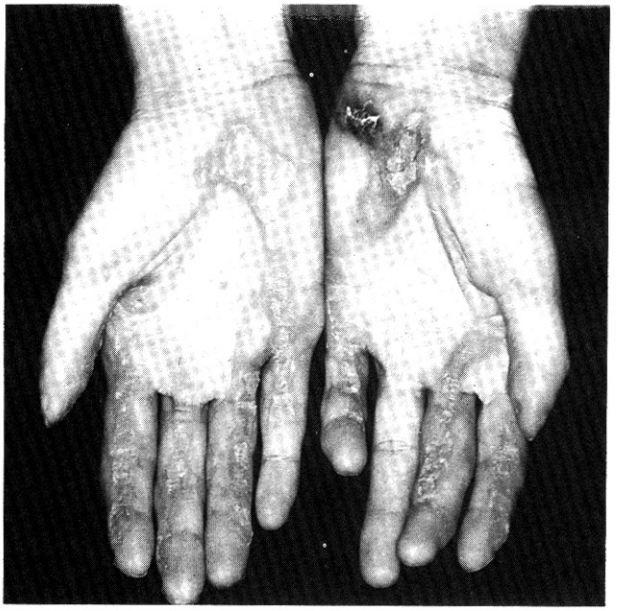

Fig. 1. Yellow-colored, markedly hyperkeratotic plaques with linear arrangement on the palms and palmar aspects of the fingers and flexion contractures of all fingers except the left ring finger.

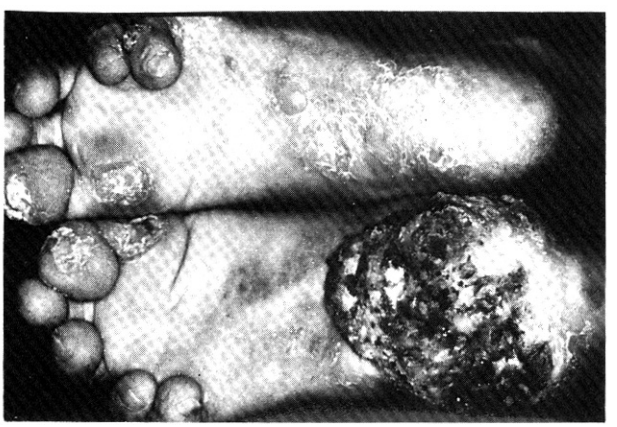

Fig. 2. Yellow-colored, markedly hyperkeratotic plaques with linear arrangement on the soles with flexion contractures on both sides of the 4th and 5th toes and an egg-sized, markedly hyperkeratotic verrucous foul smelling nodule on the right sole.

acanthosis, marked elongation of rete ridges and papillomatosis, with edema, telangiectasia and scarce cellular infiltrates in the papillary dermis suggestive of keratoderma (Fig. 3). Microscopic examination of the right heel tumor showed marked hyperkeratosis, parakeratosis and pseudocarcinomatous hyperplasia with cells composed of clear or eosinophilic cytoplasm (Fig. 4, Fig. 5). In addition, the tumor masses showed irregular

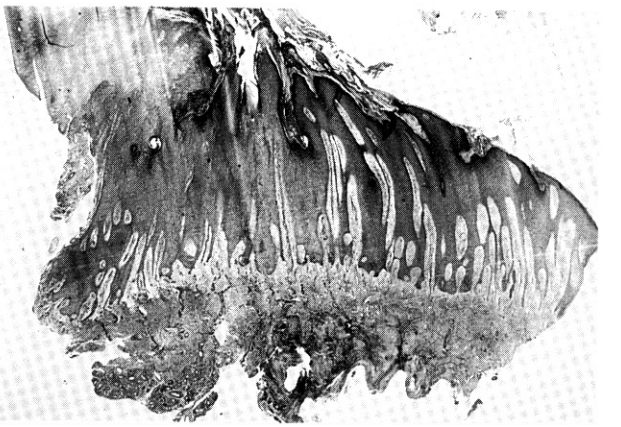

Fig. 3. Microscopic sections of the linear verrucous lesion from the sole show marked hyperkeratosis, parakeratosis, hypergranulosis with focal agranulosis, marked acanthosis, marked elongation of rete ridge and papillomatosis and edema, telangiectasia and scarce cellular infiltrates in the papillary dermis (H&E stain, ×10).

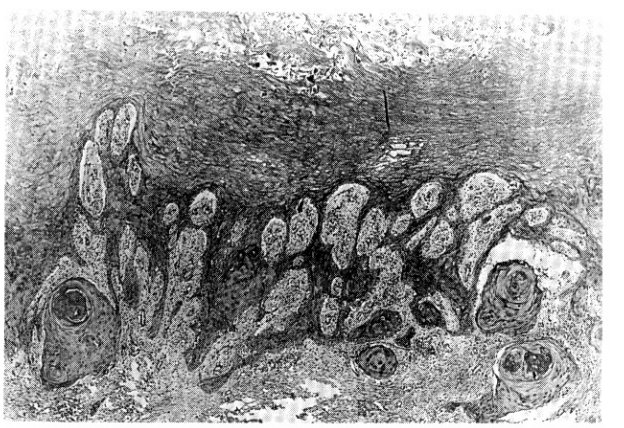

Fig. 4. Microscopic sections of the tumor on the right sole show marked hyperkeratosis, marked parakeratosis, and pseudocarcinomatous hyperplasia in which the cells are composed of clear or eosinophilic cytoplasm, squamous eddies, horn pearls, and irregular downward proliferation of epithelial strands (H&E stain, ×10).

downward proliferation of epithelial strands composed of well-differentiated keratinocytes with squamous eddies, horn pearls and loss of basal cell polarity, findings compatible with well-differentiated squamous carcinoma (Fig. 4, Fig. 5). Dermal fibrosis, capillary dilatation and mild dermal cellular infiltrates were noticed in the upper dermis. The large verrucous mass was excised surgically: complete excision and osteotomy was performed. A Latissimus dorsi myocutaneous free flap and split thickness skin graft were used to

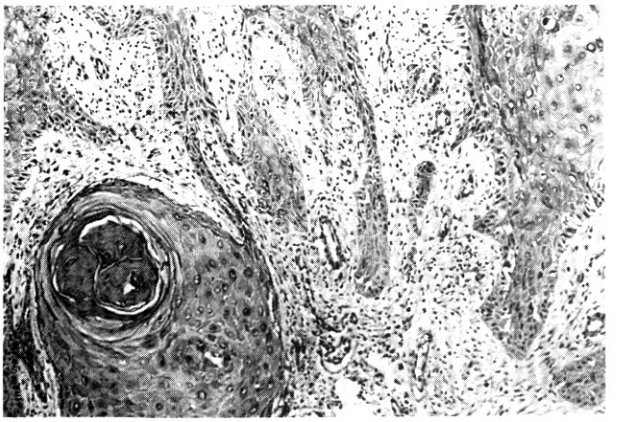

Fig. 5. High power view of Fig. 4 reveal well-differentiated keratinocytes, loss of basal cell polarity, squamous eddies, horn pearls and irregular downward proliferation of epithelial strands (H&E, stain, ×25).

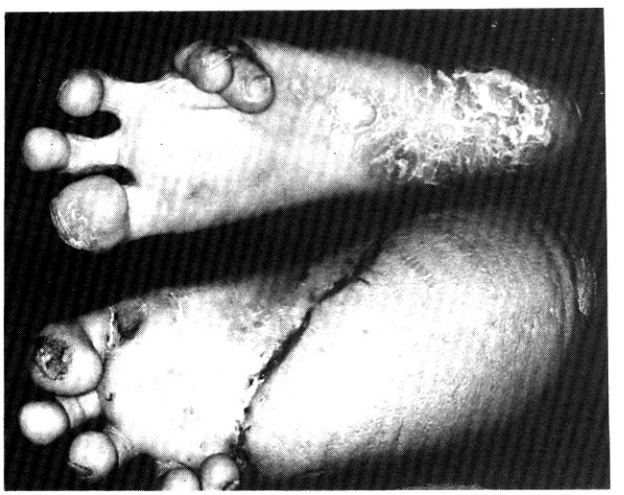

Fig. 6. Skin graft with flap on right posterior sole and yellowish, slightly hyperkeratotic plaques on both soles.

cover the excised lesion (Fig. 6). Several weeks after the operation, the pre-existing hyperkeratotic lesions on the palms and soles regressed considerably (Fig. 6), only to recur 3 months after the operation. These lesions showed further improvement with etretinate (30 mg/day) treatment for six weeks, but recurred upon discontinuation of the drug.

DISCUSSION

Epithelioma cuniculatum is a form of verrucous carcinoma that was initially thought to be limited to the foot. It is a low-grade squamous cell carcinoma that typically drains foul-smelling greasy, keratinous debris from multiple sinuses, and often persists for yeras prior to diagnosis[4]. Squamous cell carcinoma infrequently occurs as a primary lesion on the foot. It accounts for only 1.9% of all squamous cell carcinomas[5]. Squamous cell carcinoma may occur from preexisting hyperkeratotic patches such as actinic keratosis, Bowen's disease, leukoplakia, and epidermal nevus[1]. Arsenic ingestion is a well-established cause of keratosis with malignancy, but other carcinogens have also been suggested[6]. Chronic inflammatory conditions such as Hailey-Hailey disease, frequent friction and secondary infection should also be considered as possible etiologies[7]. Barnett and Estes[3] reported a case of a young man with congenital mutilating keratoderma in whom three epithelioma cuniculata occurred during a two-year period. Associated conditions included nonscarring alopecia, high-frequency hearing loss, retarded bone growth, and hypermobile joints. Recurrent infections, intermittent doses of immunosuppressive drugs, as well as the hyperkeratotic lesions may have all contributed to a fertile field for the development of verrucous carcinoma in this case[3]. In our case, epithelioma cuniculatum occurred in striate keratoderma without other associated abnormalities. Keratoderma, mechanical trauma and infection of the warty lesion may be the major factors for the development of malignancy from the benign keratodermatous lesion. Several weeks following surgical removal of the malignant tumor mass, the benign keratodermatous lesion regressed spontaneously. There are three possible mechanisms of the spontaneous regression of keratoderma. First, in epithelioma cuniculatum[8], sensitization of a common antigen during wide excision may be responsible for spontaneous regression. Second, simple avoidance of irritation by bed rest during admission. And third, possible production of hormones or growth factors by the tumor can also be considered[9]. The use of etretinate in treating recurrent keratoderma depends on its inhibiting effect on keratinization[10]. Six weeks following etretinate treatment, our patient continued to do well but required maintenance therapy. To date, two and half years following treatment, there have been no signs or symptoms suggesting bony

abnormality.

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