Nevoid Hyperkeratosis of the Nipple and Areola mammae: Ineffectiveness of Etretinate Therapy

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A woman with nevoid hyperkeratosis of the nipple and areola appearing during puberty is described. It remained unchanged during two pregnancies and caused no problem when breast feeding her two children. Etretinate (1 mg/kg/day) was ineffective in the treatment of this dermatosis. (Received September 19, 1985.)

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Hyperkeratosis of the nipple and areola mammae have been seen in patients with ichthyosis. A nevoid form characterized by verrucous thickening and brownish discoloration appearing at puberty or during pregnancy has been described (1, 2). This very rare condition can occur on the nipple, the areola or both. Here we report our findings in such a patient.

CASE REPORT

The patient is a 38-year-old otherwise healthy woman. At the age of 17, she noticed a thickening of the nipple and areola mammae. Since then, the lesions have not changed and they remained unaltered during two pregnancies (Fig. 1). She had no problem when breast feeding her two children. No family history of similar changes were obtained. The ptient began a regimen of 1 mg/kg/day of the synthetic retinoid etretinater. Six weeks later, the lesions remained unchanged and the treatment was discontinued after two months.

Histology

A biopsy showed areas with a thin epidermis with a linear dermo-epidermal junction in contrast to scattered areas where the epidermis was acanthotic and papillomatous. In the center of the latter there were several deep crater-formed depressions filled with keratin (Fig. 2). Between the deepest part of the craters, fine epithelial anastomosis were seen.

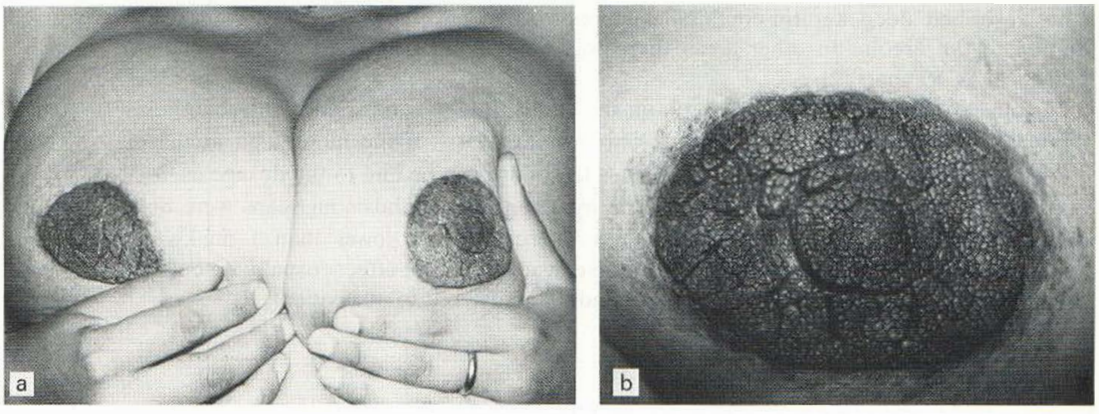

Fig. 1 a–b. Hyperkeratosis of the nipple and areola.

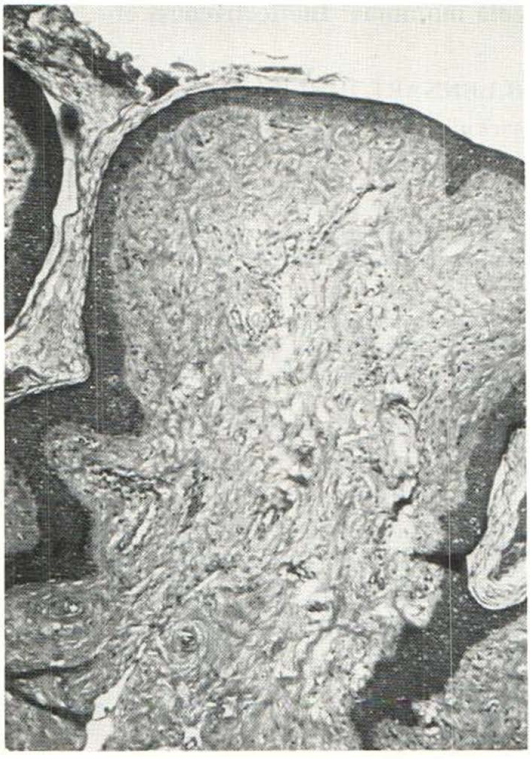

Fig. 2. Biopsy showing papillomatosis and depressions filled with keratin.

COMMENTS

Schwartz (3) reported a 60-year-old man, in whom hyperkeratosis of the nipple and areola mammae developed after diethylstilbestrol treatment for cancer of the prostate. Otherwise the patients have been female and suggesting a hormonal influence when appearing. Once formed they remain fixed and in our patient they were unchanged during two pregnancies. Rodallec et al. (4), however, reported a case with unilateral hyperkeratosis which appeared only during pregnancies.

The histology of our patient resembles in some areas that reported by Dupré et al. (1), who described deep keratin-containing depressions in a case where the lesions were limited to the areola. In other areas there was a papillomatosis like that described by Mehregan & Rahbari (2).

Because of success with topical tretinoin and oral isotretinoin in patients with acanthosis nigricans (5), a disorder resembling nevoid hyperkeratosis of the nipple and areola, a clinical trial with etretinate appeared logical. Its failure can be due to the dosage used in our patient. Indeed, successful result in the treatment of acanthosis nigricans were only obtained in high doses (2 or 3 mg/kg/day) whereas dosage lower than 1 mg/kg/day apparently induced no benefit. Because of the considerable side effects usually associated with these dosages, a similar treatment was not administered to our patient.

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Benoxaprofen in Treatment of Systemic Sclerosis

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Halkier-Sørensen L, Ternowitz T, Bjerring P, Poulsen JH, Alsbirk KE, Herlin T, Ravnsbæk J, Zachariae E, Zachariae H. Benoxaprofen in treatment of systemic sclerosis. Acta Derm Venereol (Stockh) 1986; 66: 177–179.

Ten patients with systemic sclerosis were treated with benoxaprofen, a potent lipoxygenase inhibitor, for a period of 6 months. In an attempt to evaluate the efficacy a number of physical disease parameters were followed during the trial. None of these parameters revealed any significant differences. There was, however, a trend for a change towards normalisation of a defect monocyte chemotaxis. In view of the slow and progressive nature of systemic sclerosis the present study leaves undetermined whether benoxaprofen exerts a beneficial effect on systemic sclerosis. *Key word: Monocytes.* (Received June 18, 1985.)

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Systemic sclerosis is a chronic connective tissue disease, often associated with Raynaud's phenomenon. An early inflammatory stage, predominantly with mononuclear cells, is recognized (1).

Benoxaprofen is a non-steroidal anti-inflammatory agent (NSAID) with an action that differs from other NSAID's. It inhibits the arachidonate lipoxygenase system (2), a system that leads to formation of leukotrienes (3). On the other hand benoxaprofen has a far less pronounced inhibitory effect on the cyclo-oxygenase pathway (4), which produces prostaglandins and prostacyclin. Benoxaprofen has also been shown to reduce mononuclear cell migration into sites of inflammation (5). In rheumatoid arthritis, another connective tissue disease, benoxaprofen therapy has led to significant improvement (6). Furthermore treatment of Raynaud's phenomenon by intravenous infusion of prostacyclin (PGI_2) has been reported to be useful (7). Therefore theoretically benoxaprofen could be effective in systemic sclerosis by diminishing the inflammatory response without interfering with Raynaud's phenomenon. Our trial was performed before benoxaprofen finally was taken off the market, due to unacceptable side-effects (8, 9).

MATERIAL AND METHODS

Three males and 7 females, with mild to severe scleroderma, aged 22–65, were treated with 600 mg of oral benoxprofen (a gift from Eli Lilly & Co) daily for a period of 6 months. The average duration of their disease was 6 years. One month before admission to the study the patients were instructed to