Clinical Remission of Loricrin Keratoderma with Tamoxifen: A Case Report

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Loricrin keratoderma (LK), also defined as Camisa disease, is a rare variant of Vohwinkel's syndrome characterized by ichthyosis, palmo-plantar keratoderma and digital constriction (pseudoainhum) with preserved hearing function.

We report a case of an adult patient affected by LK that showed a complete remission of all the cutaneous signs accidentally occurred during a treatment with an anti oestrogen receptor for a concomitant breast cancer.

This case supports the importance that oestrogens plays in the epidermal keratinocytes differentiation process and suggests the potential role of oestrogen receptors in loricrin differentiation.

CASE REPORT

We report here a case of a 50-year-old woman who attended our Dermatology Unit for evaluation of extremely widespread xerosis of the skin, present since childhood, associated with progressive thickening of the palmoplantar skin. She also referred progressive annular narrowing of the skin of some fingers during adulthood (**Fig. 1**A). Moreover, the involved fingers showed progressive functional impairment. Physical examination revealed mild ichthyosis, severe palmo-plantar keratoderma (PPK) and initial pseudoainhum of the fifth finger of both hands (Fig. 1A). The patient was treated for PPK with topical retinoids applied twice daily on palms and soles and emollients for the ichthyosis applied over all the skin surface 2 or 3 times a day.

Loricrin is a protein of the cornified envelope, codified by the gene *LOR* on the epidermal differentiation complex on chromosome 1q21. Mutations in the loricrin gene lead to abnormalities in the integrity of the stratum corneum, with consequent increase in transepidermal water loss, PPK and mild ichthyosis (1, 2).

Loricrin keratoderma (Camisa syndrome), a variant of Vohwinkel syndrome was suspected. The diagnosis was confirmed genetically by detection of the mutation c[678_679dupG]; [=](p.[(Scr229ValfsTcr107)]; [(=)]: the genomic variant c.678_679dupG in heterozygosity in the *LOR* gene and the corresponding protein variant p.Ser229ValfsTer107. This variant has not been reported previously; however, its role in *LOR* gene function suggests a possible correlation with loricrin keratoderma. The same mutation was also detected in the patient's 7-year-old daughter, who presented with ichthyosis, but not PPK.

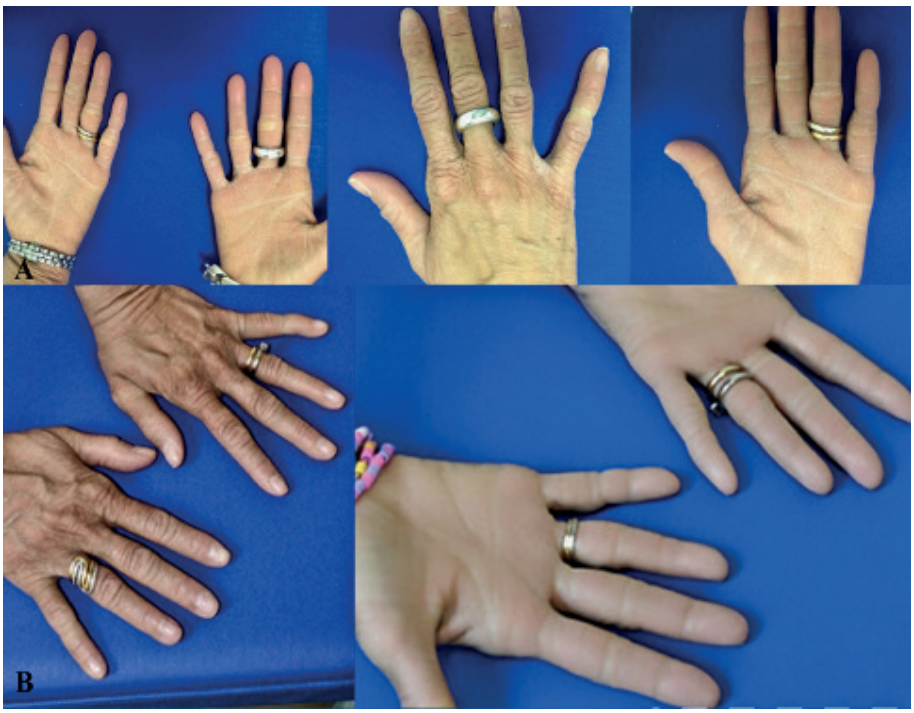

Fig. 1. Palmo-plantar keratoderma and initial pseudoainhum of the hands: (A) before and (B) after treatment with tamoxifen.

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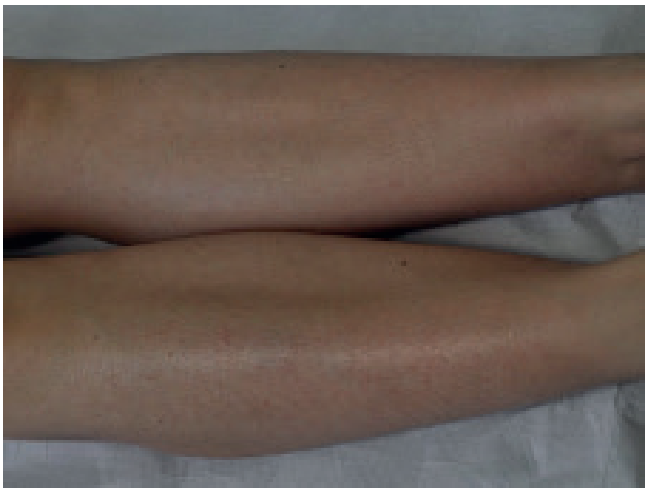

Fig. 2. Clinical improvement in ichthyosis after treatment with tamoxifen.

Subsequently, the patient was diagnosed with breast cancer and, to date, she has been treated with tamoxifen 10 mg, one tablet twice a day for a 5-year period. One year after the start of treatment, an almost complete remission of pseudoainhum and a complete remission of PPK and ichthyosis were observed (Fig. 1 and **Fig. 2**). At follow-up, 6 years later, the cutaneous remission persists and the patient applies only topical emollients.

DISCUSSION

Oestrogens play a crucial role in the human skin, because they are involved in skin ageing, homeostasis, pigmentation, sebum production, epidermal differentiation and in wound healing. They have well-known effects on skin physiology modulating the epidermal keratinocytes: in women an increase in the mitotic activity of the epidermal keratinocytes occurs in response to oestrogens (3). Oestradiol seems to play a crucial role in maintaining skin thickness, and some studies confirm that administration of oestradiol increases epidermal thickness in gonadectomized mice (4–6).

Keratinocytes express 2 oestrogen receptors: ERα and ERβ. A study by Thornton et al. showed that human scalp skin express ERβ *in situ* (7).

Tamoxifen is an oestrogen receptor (ER) antagonist used as first-line chemotherapy in breast cancer. It is a selective inhibitor of oestrogen receptors that competes with endogen oestradiol hormone and acts as a complete antagonist with the ERβ receptor.

Several studies have reported that topical tamoxifen reduces the proliferation of fibroblasts and has potential anti-psoriatic effects in mouse models (8, 9) and an anti-proliferative effect on human squamous cell carcinoma cultures (10). However no clinical studies have been published, and more prospective studies are needed to validate the inclusion of topical tamoxifen in clinical dermatological practice.

This case report highlights the importance of oestrogens in human skin, but, above all, supports the role of oestrogens in differentiation of epidermal keratinocytes and the possible involvement of the ERβ receptor in loricrin differentiation; the ERβ receptor could be considered as a target for developing treatment, such as topical tamoxifen in all the hyperkeratotic skin diseases (i.e. PPK, psoriasis) and, in the worst case, in automutilating pseudoainhum, as in the case reported here.

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The patient has given informed consent for the publication of the details of this case.

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