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## Short-Contact Therapy With Topical Tazarotene in Darier Disease<sup>☆</sup>

### Terapia de contacto corto con tazaroteno tópico en Darier segmentaria

*To the Editor:*

We read with interest the clinical science letter by de la Hera and coworkers<sup>1</sup> and wish to share our positive experience with topical tazarotene in the treatment of linear Darier disease. Our good results contrast with the weak efficacy and poor tolerance described by those authors.

Mild Darier disease is treated with topical retinoids, although the use of such therapy is limited by local irritation.<sup>2</sup>

Tazarotene is a retinoid indicated for the treatment of psoriasis.<sup>3</sup> Isolated cases have been reported in which tazarotene was used to treat acne, lichen planus, keratosis pilaris, ichthyosis, confluent and reticulated papillomatosis, keratoderma blennorrhagica, discoid lupus erythematosus, and Darier disease.<sup>2,4,5</sup>

We present the case of a 48 year-old woman with a 20-year history of linear Darier disease, who was being treated with topical corticosteroids. She reported poor control of lesions for a period of over 1 year, prompting her referral to our service. At the time of the consultation the patient presented brownish keratotic lesions on the left side of her forehead, the back and left side of her neck, and her lower back. These clinical signs were indicative of Darier disease and the diagnosis was subsequently confirmed by biopsy and histological analysis (Fig. 1).

As the lesions were localized to the areas described, therapy with 0.1% tazarotene was prescribed. The treatment was applied nightly and washed off with water 15 minutes after application.

The lesions disappeared after 1 month of treatment (Fig. 2).

The neck lesions did not recur during 1 year of follow-up, even during the summer. Lesions in the lumbar and frontal regions persist, although to a lesser degree, and are

controlled by the patient with topical tazarotene. The patient reported no irritation at any stage of the treatment.

Tazarotene is a third generation retinoid. This prodrug is rapidly converted by skin esterases to its active metabolite, tazarotenic acid. Systemic exposure to the drug is low due to its rapid metabolism. Its greatest affinity is for the retinoic acid receptors RAR- $\beta$  and RAR- $\gamma$ , through which it exerts its biological effect. These receptors interact with genes and influence their expression.<sup>6</sup> Although the mechanism of action of tazarotene in Darier disease is unknown, it may be similar to that underlying its therapeutic effect in the treatment of psoriasis, another differentiation and keratinization disorder. Studies in psoriasis have shown that tazarotene exerts a potent antiproliferative effect by normalizing the differentiation and proliferation of keratinocytes. It also decreases markers of inflammation and regulates cytokine and gene expression by interacting specifically with RAR- $\beta$  and RAR- $\gamma$  receptors. Analyses of other retinoids in the treatment of Darier disease have also demonstrated altered expression of cytokeratin, which is associated with clinical and histopathological improvements and a reduction in acanthosis and hyperkeratosis.<sup>7</sup>



**Figure 1** Multiple keratotic lesions on the back and side of the neck.

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**Figure 2** Complete disappearance of lesions after 1 month of topical treatment with 0.1% tazarotene.

The irritation described following retinoid use for the treatment of Darier disease may contribute to the appearance of new lesions and discontinuation of treatment due to poor tolerance. This can be avoided by co-application of topical corticosteroids, by reducing the concentration of tazarotene, or by progressively increasing the frequency of tazarotene application.<sup>4,5</sup>

In the present case, after reviewing the literature, we decided upon short-contact therapy with tazarotene, which involved application of the product followed by its removal 15 minutes later. In line with the results reported by some other authors in cases of acne, psoriasis, and Darier disease treated with tazarotene, we observed no irritation and a rapid disappearance of lesions with no side effects.<sup>8,9</sup>

The Koebner phenomenon or isomorphic response is characterized by the appearance of specific skin lesions on areas of healthy skin previously exposed to different kinds of trauma or triggers, including ultraviolet radiation, irritation, and friction.<sup>10</sup> Accordingly, the irritation sometimes caused by tazarotene may provoke an isomorphic phenomenon and may give rise to the appearance of new

lesions in Darier disease. Interestingly, the lack of irritation observed with short-contact tazarotene therapy has been previously described,<sup>5</sup> and may partially explain the continued improvement of our patient.

In conclusion, we highlight the effectiveness of short-contact therapy with topical tazarotene in the present case and in other cases reported in the literature. We propose it as a simple topical alternative for the treatment of linear or localized Darier disease that is effective, well tolerated, and lacks the potential side effects of oral retinoid treatment. Further studies are needed to obtain a better understanding of the mechanism of action of tazarotene in the treatment of Darier disease.

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