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Letter

Diclofenac sodium 3% gel for darier's disease treatment

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Abstract

Background: Darier's disease (DD) is an autosomal dominant skin disorder which causative gene, ATP2A2, is located at chromosome 12q23–24. The lesions of DD are skin-coloured to brown, hyperkeratotic, greasy papules that coalesce into warty plaques commonly involving the seborrhoeic areas of the trunk and face, especially the scalp margins, temples, ears, and scalp. The most common complaint associated with the disease is itching, with exacerbations attributed to heat, sweating, sunlight, lithium, steroid therapy, stress, and menstruation

Objectives: We report a patient with DD treated with topical diclofenac sodium 3%.

Methods: We report a 33-year-old patient with Darier's Disease. He was followed in our department since 2009, and we had tried to control several flares of lesions during follow-up, but oral isotretinoin was not tolerated because of adverse effects; and oral doxycycline showed lack of efficacy.

At April 2014, patient presented with new lesions, involving anterior chest wall, abdomen, back and shoulders areas. We started with diclofenac sodium 3% in hyaluronic acid 2.5% once daily, only applied at abdomen and anterior chest wall.

Results: After six-month therapy, hyperkeratotic papules were flattened and less harshness of them was noticed, even some of them disappeared.

Conclusions: We consider topical diclofenac therapy as a useful alternative treatment for DD patients, in which previous therapies have not shown efficacy. We did not observed topical adverse effects, neither systemic absorption symptoms, but we recognized further and larger studies are needed to asses the efficacy and safety of this treatment in DD.

Case synopsis

A 33-year-old patient with clinically and histologically confirmed Darier disease (DD), experienced an extensive flare of his skin lesions and treatment was started with 0.5 mg/kg/d of oral isotretinoin (30 mg/day). After one-month of therapy, partial improvement was seen, but the patient did not tolerate the adverse effects such as cheilitis, epistaxis, and xerosis. Despite a decrease in dose to 10mg per day, the adverse effects were still present. After three months of treatment, no further improvement was seen. After a new flare occurred, 100mg/day of oral doxycycline therapy was prescribed and taken for 4 months, again without improvement.

Another severe flare exhibited extensive involvement of the anterior chest wall, abdomen, back, and shoulders areas (Figure 1). Recently Millán-Parrilla et al. had reported two patients with resolution of DD lesions after therapy with diclofenac sodium 3% gel twice daily [1].

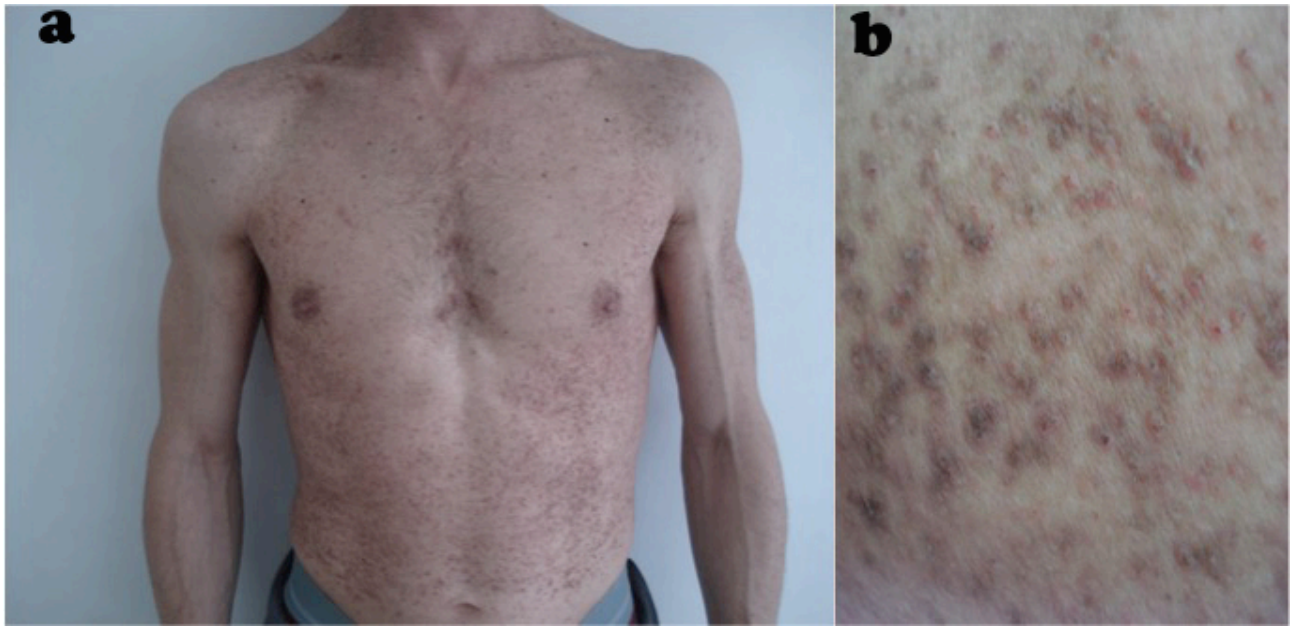

Figure 1. Pretreatment. Brown, hyperkeratotic, papules that coalesce distributed at anterior chest wall and abdomen (a). Details of lesions at left abdomen (b).

Our patient began applying diclofenac sodium 3% in hyaluronic acid 2.5% (Solaraze®) once daily, at first just to the abdomen and anterior chest wall. After three months of therapy, the hyperkeratotic papules were flattened (Figure 2). The patient reported no itching, pain sensation, paresthesia, photosensitivity, or local reactions.

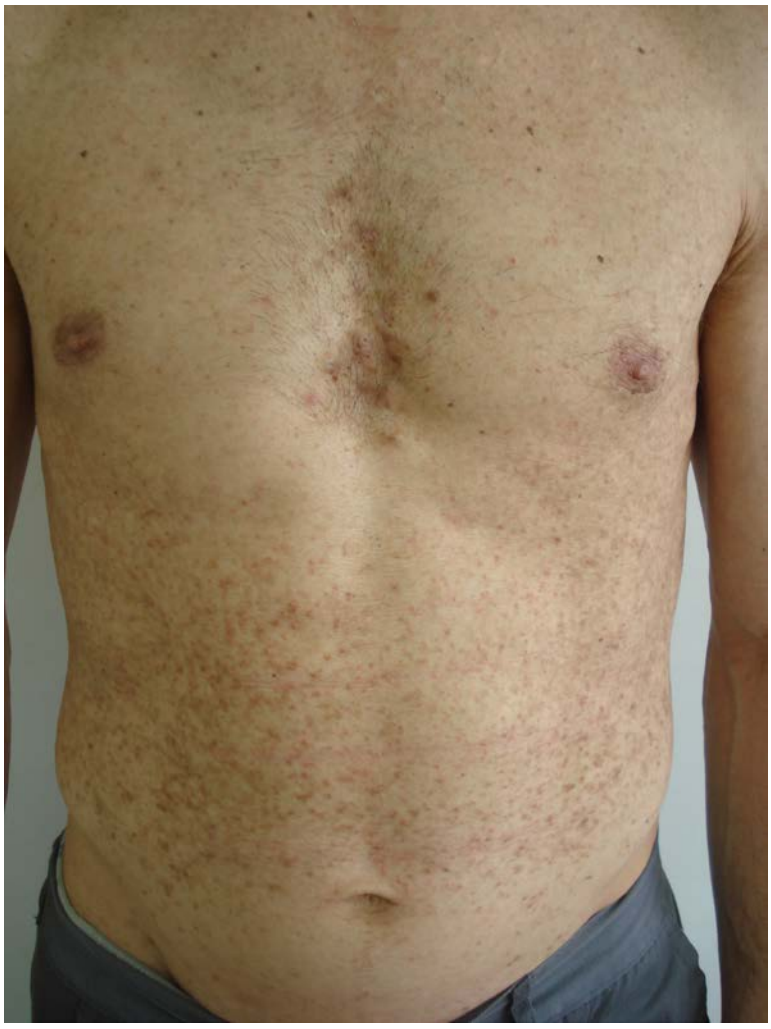

Figure 2. After application of diclofenac sodium 3% gel once daily for 3 months, improvement was seen.

The diclofenac therapy was continued for three months more and further improvement was seen. Papules were even more flattened and had a lighter tone; some of them disappeared (Figure 3). No improvement was seen on untreated areas. The patient denied any adverse effect.

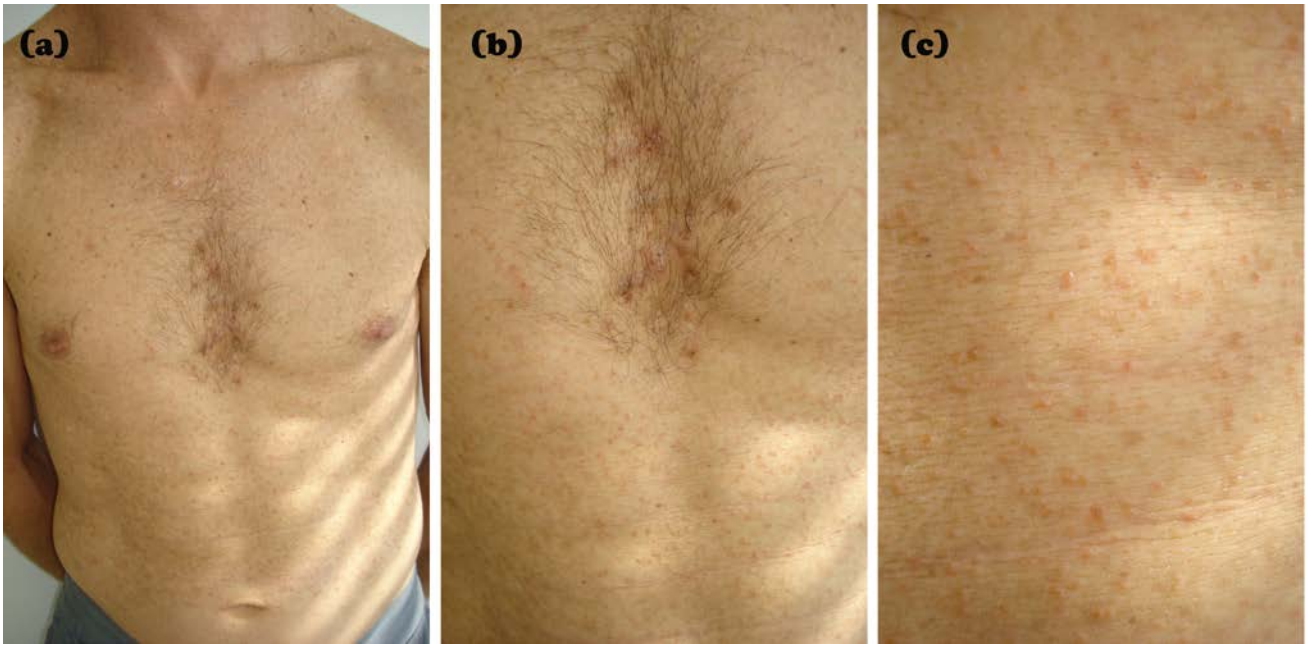

Figure 3. After application of diclofenac sodium 3% gel once daily for 6 months, papules were flattened, and had a lighter tone (a). Improvement observed at pectoral and sternal areas (b). Details of lesions at left abdomen (c), some of them have disappeared.

Discussion

Darier disease is an autosomal dominant skin disorder related to mutations in the gene *ATP2A2*, located at chromosome 12q23–24. This gene encodes for the sarco/endoplasmic reticulum Ca2+-ATPase-2 (SERCA-2) [2]. Insufficient function of SERCA-2b leads to abnormal intracellular Ca2+ signaling, notably of the endoplasmic reticulum. The result is a loss of suprabasilar cell adhesion (acantholysis) and an induction of apoptosis (dyskeratosis) [3].

The lesions of DD are skin-colored to brown, hyperkeratotic, greasy papules that coalesce into warty plaques commonly involving the seborrheic areas of the trunk and face, especially the scalp margins, temples, ears, and scalp [3]. Several treatments for DD have been described including topical corticosteroids, topical retinoids, calcipotriol, topical antibiotics and antifungal agents for colonization and infections, topical 5-fluorouracil, oral retinoids, oral cyclosporine, and some surgical approaches, such as, grafting, dermabrasion, laser removal, or photodynamic therapy.

Millán-Parrilla et al. suggested that the efficacy of diclofenac relates to the capacity of suppressing prostaglandin E2 (PG E2), by cyclooxygenase-2 inhibition, as it is known that PG E2 down-regulates ATP2A2 expression [1].

Diclofenac and retinoids may share a mechanism of action as Mestre et al. suggested that retinoids markedly suppressed production of COX-2 and the production of PG E2 [4]. Further investigation of the role of COX-2 inhibition in DD is needed, as this may be a key point in the pathogenesis of DD; some patients with DD may benefit from systemic COX-2 inhibitors.

Millán-Parrilla et al. used topic diclofenac twice daily [1]. We opted to treat our patient with this therapy once a day because a wider area was treated. We did not observe topical adverse effects or systemic absorption symptoms. Further and larger studies are needed to assess the role of this therapy in DD as well as the safety profile and dosage standardization.

Conclusion

We consider topical diclofenac as a useful alternative treatment for DD patients, in which previous therapies have not shown efficacy.

References

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