SHORT COMMUNICATION



# Ultra-high Potency Topical Corticosteroids as a Potential Trigger for Reactive Perforating Collagenosis

Matiar MADANCHI[1]*, Riccardo CURATOLO[1], Hazem A. JURATLI[1], Cristina MANGAS[2] and Carlo MAINETTI[3]
*[1]Department of Dermatology, University Hospital Basel, Burgfelderstrasse 101, CH-4055 Basel, [2]Dermatology and Oncology Department, Istituto Oncologico Svizzera Italiana (IOSI), Ente Ospedaliero Cantonale (EOC), Bellinzona, and [3]Private Practice dermatology, Bellinzona, Switzerland. *E-mail: matiar.madanchi@usb.ch*
Submitted Jun 5, 2024. Accepted after revision Aug 6, 2024
Published Aug 23, 2024. DOI: 10.2340/actadv.v104.40950. Acta Derm Venereol 2024; 104: adv40950.

Over the years, we have frequently observed that patients suffering from eczema or prurigo, usually on the back, and receiving long-term treatment with very strong topical corticosteroids like clobetasol propionate, often develop reactive perforating collagenosis during treatment. Based on this observation, we have developed 2 hypotheses regarding the association between high-potency topical corticosteroids and the aggravation of reactive perforating collagenosis.

Reactive perforating collagenosis is a subtype of perforating collagenosis (1, 2). Reactive perforating collagenosis is defined by the trans-epithelial elimination of altered collagen (1). It can be either familial or acquired. Usually, it manifests in patients of middle age, between 50 and 60 years old (1, 3). It typically presents as disseminated or linearly grouped erythematous, firm papules or plaques with central ulceration and a hard, firmly adherent keratotic plug (1, 2). Its pathophysiology is not yet well understood, leading to various theories and hypotheses in this respect. It has been observed that reactive perforating collagenosis can be caused by various factors (Table SI) including malignancy (4), infections, or medications such as sorafenib (2). It has been also observed that reactive perforating collagenosis is often associated with microvascular disorders, such as in patients with diabetes mellitus, chronic renal disease, or hypertension (5).

Topical steroids are used for many dermatological conditions and are available in various formulations (creams, ointments, lotions, foams) (6). The main goal of topical steroids is to reduce inflammation and irritation (6, 7). However, they are known to have side effects such as skin atrophy and decreased collagen synthesis (8). Topical steroids can be classified into potency classes based on their vasoconstrictive properties (Table SII) (6). Steroids with higher vasoconstrictive action are classified as very strong topical steroids, while those with less vasoconstrictive action are classified as mild topical steroids, which may be less effective but have fewer side effects (6).

## DISCUSSION

In our cases, we have frequently observed the development or an aggravation of reactive perforating collagenosis in patients undergoing steroid therapy with clobetasol propionate (very strong). We have observed a higher incidence in patients affected by atopic dermatitis or prurigo nodularis who undergo treatment with ointments compared with creams. This may be attributed to the occlusive nature of ointment treatments, leading to stronger steroid effects than with creams. However, we have also noticed that simply changing the class of the topical steroid from very strong to strong/mild, such as mometasone furoate, often led to resolution of the reactive perforating collagenosis.

Therefore, as a first hypothesis, we suspect that the high vasoconstrictive capacity of high-potency topical steroids may, like diabetes mellitus or hypertension (2), disrupt microcirculation, thereby favouring the formation of reactive perforating collagenosis.

A second hypothesis involves decreased collagen synthesis mediated by p38 in the skin. According to the study by Quoc-Vu Le et al. (9), it is reported that the use of clobetasol propionate negatively regulates the transcription factor of collagen synthesis via p38 mammalian MAP kinase (9, 10). Further studies are needed to confirm these hypotheses. However, this could be an important point to study in order to better understand the pathophysiology of reactive perforating collagenosis, to gain a deeper insight into the disease, and to find a targeted treatment for this condition in the future.

Topical steroids are among the therapeutic choices for reactive perforating collagenosis. In our cases, we observed that changing from very strong corticosteroids to strong/mild topical steroids was often sufficient to treat the condition in patients who developed reactive perforating collagenosis after strong corticosteroid application.

Therefore, we consider it extremely important to further investigate our hypothesis to better understand the pathophysiology of reactive perforating collagenosis and to use more appropriate treatment, thereby avoiding delays in initiating suitable therapy.

*The authors have no conflicts of interest to declare.*

## REFERENCES

1. García-Malinis AJ, Del Valle Sánchez E, Sánchez-Salas MP, Del Prado E, Coscojuela C, Gilaberte Y. Acquired perforating dermatosis: clinicopathological study of 31 cases, emphasizing pathogenesis and treatment. J Eur Acad Dermatol Venereol 2017; 31: 1757–1763. https://doi.org/10.1111/jdv.14220
2. Lederhandler M, Beasley JM, Brinster NK, Nagler AR. Unusual eruption in association with sorafenib: a case of acquired perforating dermatosis, reactive perforating collagenosis type.

Dermatol Online J 2018; 24: 13030/qt8b40k5kg. https://doi.org/10.5070/D32412042445
3. Bk P, Asati D, Panwar H, Joshi D. Unraveling the enigma of perforating itches: a comprehensive report of reactive perforating collagenosis in three patients. Cureus 2023; 15: e44531. https://doi.org/10.7759/cureus.44531
4. Rivera-Rodríguez A, Prieto-Torres L, Felipo-Berlanga F, Ara-Martín M. Acquired reactive perforating collagenosis associated with Hodgkin disease. Clin Exp Dermatol 2017; 42: 934–936. https://doi.org/10.1111/ced.13192
5. Nebel R, Fiedler E, Danz B, Marsch WC, Kreft B. Acquired reactive perforating collagenosis associated with diabetes mellitus and renal insufficiency requiring dialysis. Dtsch Med Wochenschr 2007; 132: 2624–2626. https://doi.org/10.1055/s-2007-993108
6. Wollenberg A, Kinberger M, Arents B, Aszodi N, Avila Valle G, Barbarot S, et al. European guideline (EuroGuiDerm) on atopic eczema – part II: non-systemic treatments and treatment recommendations for special AE patient populations. J Eur Acad Dermatol Venereol 2022; 36: 1904–1926. https://doi.org/10.1111/jdv.18429
7. Goa KL. Clinical pharmacology and pharmacokinetic properties of topically applied corticosteroids: a review. Drugs 1988; 36: 51–61. https://doi.org/10.2165/00003495-198800365-00011
8. Coondoo A, Phiske M, Verma S, Lahiri K. Side-effects of topical steroids: a long overdue revisit. Indian Dermatol Online J 2014; 5: 416–425. https://doi.org/10.4103/2229-5178.142483
9. Le QV, Wen SY, Chen CJ, Huang CY, Kuo WW. Reversion of glucocorticoid-induced senescence and collagen synthesis decrease by LY294002 is mediated through p38 in skin. Int J Biol Sci 2022; 18: 6102–6113. https://doi.org/10.7150/ijbs.73915
10. Ponec M, de Haas C, Kempenaar JA, Bachra BN. Effects of glucocorticosteroids on cultured human skin fibroblasts. V. Influence of anabolic steroids on the inhibitory effects of clobetasol-17-propionate on cell proliferation and collagen synthesis. Arch Dermatol Res 1979; 266: 75–82. https://doi.org/10.1007/BF00412864