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NEWS, VIEWS, & REVIEWS

What's Old Is New: An Emerging Focus on Dermatoporosis

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INTRODUCTION

Defined by Kaya and Saurat in 2007, dermatoporosis is a chronic syndrome of excessive skin insufficiency/fragility.[1] This loss of the skin's mechanical strength is due to modifications of the extracellular matrix (ECM) and decreased viscoelasticity of the skin, primarily through the degradation of dermal collagen and elastic fibers and reduction of the glycosaminoglycan hyaluronate (HA) that stabilizes these fibers.[1] The most commonly diagnosed form is primary dermatoporosis, a result of chronological aging and chronic UV radiation exposure; secondary dermatoporosis is due to chronic topical or oral corticosteroid use. A limited number of studies from Europe have assessed the prevalence of dermatoporosis, with an estimated prevalence of 30.7–37.5% in patients 60 years and older, yet the prevalence is likely to increase as the aging population grows globally.[2,3]

Clinical Features of Dermatoporosis

Morphological features of dermatoporosis are skin atrophy, solar purpura, stellate pseudoscars, and superficial excoriations, particularly on sun-exposed sites (Figure 1).[4] The clinical staging of dermatoporosis considers clinical signs of skin fragility and skin thickness measured by ultrasonography (Table 1). Complications of dermatoporosis range from skin lacerations and delayed wound healing to deep dissecting hematomas that require surgical evacuation. Not simply a cosmetic concern, dermatoporosis truly impacts the morbidity and mortality of patients.[1]

Figure 1. (A) Dermatoporosis with pronounced skin atrophy and solar purpura, and a small laceration covered with a bandage. **(B)** Dermatoporosis following 11 months of topical treatment with daily application of calcipotriene 0.05% ointment and nightly application of tazarotene 0.045% lotion. Note improvement of skin atrophy and solar purpura, particularly on the forearms.

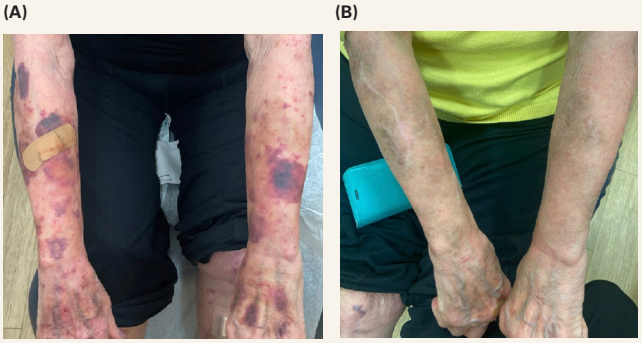

Table 1. Dermatoporosis Scoring System[4]

Clinical features	Absent	Present
Skin atrophy	0	1
Solar purpura	0	1
Stellate pseudoscars	0	1
Superficial excoriations	0	1
Small lacerations	0	2
Large lacerations	0	3
Superficial hematomas	0	4
Deep dissecting hematomas	0	5
Skin necrosis	0	6
Skin thickness (ultrasonography)	**Score**	
≤0.5 mm	3	
0.51–0.75 mm	2	
0.76–0.99 mm	1	
≥1 mm	0	
Score of dermatoporosis*	**Significance**	
0	No dermatoporosis	
1–7	Early stage	
8–9	Early intermediate stage	
10–12	Later intermediate	
13–16	Early advanced stage	
>16	Advanced stage	

*The global score of dermatoporosis is obtained by calculating the sum of all individual scores.

Pathophysiologic Mechanisms

HA and its cell surface receptor, CD44, are intricately linked to the pathogenesis of dermatoporosis, shown by the interaction of HA and CD44 to stimulate keratinocytes and the association of low levels of CD44 in dermatoporotic skin compared to young controls.[5,6] Moreover, levels of HA and expression of CD44 are known to decrease with age and following UVA and UVB exposure.[1,7] Histologically, dermatoporosis shows significant epidermal atrophy and a significantly increased number of cells in the epidermis positive for $p16^{Ink4a}$, a known biomarker of senescence.[8] Additional epidermal cellular markers of dermatoporosis include the preservation of Lrig1+ progenitor cells which inhibit the epidermal growth factor receptor, the decrease of Wnt signaling through loss of CD44 regulation, and the decreased expression of the calcium channel Orai-1 involved in keratinocyte proliferation.[8,9]

Treatment

Various topical and systemic therapies have been studied to treat dermatoporosis, including targeting the mechanistic pathways

discussed above, as well as supplementing with oral vitamin C and a bioflavonoid complex.[10,11] A mainstay of treatment is the application of topical retinoids as they upregulate HA and CD44 synthesis in mouse skin and reduce the signs of photoaging in clinical studies.[5,12,13] Moreover, the application of topical retinaldehyde plus intermediate-size hyaluronate fragments shows synergistic effects, with clinical improvement of purpura and skin thickness in addition to a significant reduction in $p16^{Ink4a}$-positive cells in the epidermis and dermis.[14–16]

Moreover, while vitamin D (VD) is a critical regulator of systemic calcium absorption and storage, it has essential functions in the skin. Notable effects of VD relevant to dermatoporosis include stimulating collagen synthesis, modulating the expression of genes contributing to epidermal development and maintenance, mitigating chronic inflammation associated with aging through anti-inflammatory effects, and providing cytoprotection in the setting of UV irradiation.[17] Given this relationship between VD and normal skin homeostasis, the use of VD analogs to treat dermatoporosis may be promising. The use of calcipotriene, a synthetic derivative of vitamin D3 (calcitriol), is well-established for the treatment of psoriasis through its inhibition of keratinocyte proliferation and induction of keratinocyte terminal differentiation.[18] Calcipotriene also improves wound healing through its promotion of keratinocyte migration and upregulation of human cathelicidin antimicrobial protein (hCAP18), a regulator of the innate immune response in the setting of tissue injury that promotes re-epithelialization and tissue repair.[19,20] Considering these results, focal supplementation of VD in the skin using an active analog such as calcipotriene may serve to reverse the dermatoporotic state, particularly in combination with a topical retinoid (Figure 2).

CONCLUSION

Dermatoporosis is a detrimental condition to the aging population and warrants continued study of its mechanisms and novel treatment options. While topical retinoids are well-known to effectively treat dermatoporosis, a vitamin D3 analog such as calcipotriene may be an additional, useful tool for treating and preventing this prevalent and deleterious skin disease.

Disclosure

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