CASE REPORT. POSITIVE EFFECT OF HYBRID STABLE COOPERATIVE COMPLEXES OF HIGH AND LOW MOLECULAR WEIGHT HYALURONIC ACID IN LOCALIZED PSORIASIS PLAQUES.

Dr. Gabriel Siquier-Dameto[1], MD, MsC – Aesthetic Physician
Dr. Laura Solalinde[2], MD, PhD – Dermatologist

1. Dameto Clinics International, the Netherlands & Spain
1. Research Group of Clinical Anatomy, Embryology and Neuroscience (NEOMA), Department of Medical Sciences, Universitat de Girona (UdG), Girona, Spain
2. Dermoestética del Centro Médico La Costa, Asunción, Paraguay

BACKGROUND

Psoriasis, a common, chronic, relapsing, inflammatory skin disease characterized by multiple erythematous papules and plaques with silvery scales, affects 0.5% - 3% of the world's population.

Topical treatment remains important since most patients have mild disease affecting less than 2% of the body surface area. However, its treatment is challenged by the limited amount of drug reaching the inflamed skin.

Unfortunately, topical treatments are not often very successful because of limited penetration of the active ingredient through the stratum corneum, a very effective skin barrier, which results in poor patient compliance and consequently low therapeutic efficacy.

OBJECTIVE

Based on this background, three cases are presented in which was evaluated the effect of an injectable treatment based on hybrid stable cooperative complexes of high and low molecular weight hyaluronic acid (HCC) in adult patients affected by psoriasis.

INTRODUCTION

Psoriasis is an immune-mediated hereditary disease that is prone to recurrence and causes systemic damage [1]. As an inflammatory skin disease, psoriasis is characterized by excessive proliferation and abnormal differentiation and apoptosis of keratinocytes [2]. Hyperproliferation of keratinocytes is associated with the induction of a variety of cytokines, such as TNF-α, IL-22, and IL-17, while causing keratinocytes to produce chemokines, cytokines, and antimicrobial peptides, thereby aggravating the inflammatory response [3].

Topical administration is one of the important approaches to treat psoriasis, since most of the time it affects only the skin. The drug is applied directly to the affected skin and can directly work on the inflammatory region to improve the symptoms of psoriasis. However, the stratum corneum limits the amount of drug being percutaneously absorbed, resulting in drug wastage and poor clinical efficacy after topical administration [4].

Recent studies have found that in the epidermis of psoriatic inflamed skin, the expression of CD44 protein is higher than that in the normal skin, and hyaluronic acid (HA) distribution is markedly reduced, suggesting that overexpressed CD44 protein can serve as a potential target to regulate expression of inflammatory molecules [5].

HCC, which binds to specific receptors, such as CD44, stimulates fibroblasts and keratinocyte proliferation, providing nourishment and deep hydration [6].

HCC can provide both anti-inflammatory and biostimulating effect, and can also activate other signaling pathways through the interaction with cell membrane receptors such as CD44, TLR-4, and RHAMM. Besides, hyaluronans proved wound healing capacity [7] and the ability to prevent ROS damage. In this case, we apply HCC by deep-dermal injection to localized plaques of psoriasis in patients previously treated with poor results.

MATERIALS AND METHODS

Two females aged 37 and 55 years old, and a male aged 45, with frequent recurrence of psoriasis plaques not adequately controlled with topical treatment underwent the HCC procedure. At least 2 treatment sessions in the first six months were suggested to the patients. The first session was offered as a test. After at least 4 weeks the patient was asked to decide whether to proceed with further sessions or not (the shortest interval between two sessions therefore being 4 weeks). Treatments started in March 2019.

The injectable method used was intra and perilesional deep-dermal bolus for 2 cm2 of treated area with 0,2 mL per bolus.

We used this technique to improve spreadability of the products and to reduce possible side effects. Contraindications are considered to be conditions such as active infection of the skin, pregnancy and age of under 18 years.

No serious side effects were observed, with the exception of a single bruising in one session, which healed without scarring or complications within 48 hours.

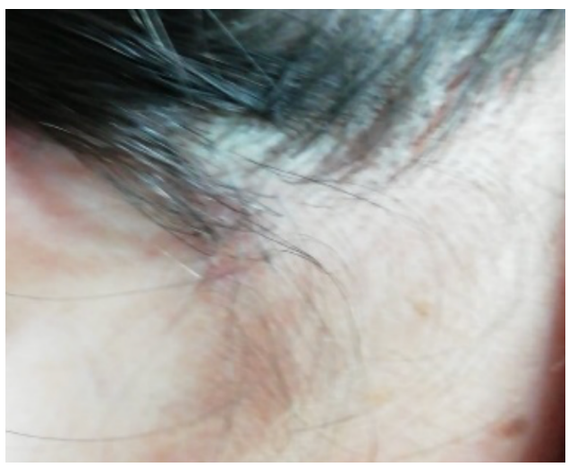
RESULTS

The injection of HCC produced a continuous, gradual therapeutic effect with significant improvements consistently decreased in a dose-time-dependent manner, with reduction in redness, desquamation, scaling and reduction in pruritus. Also, there is a macroscopic improvement on skin texture.
[as shown on images 1, 2 & 3]

IMAGE 1 Female, 37 yo, presents erythematous plaques, sharply demarcated, with silvery scales, in extensor surface of both elbows and forearms, measuring 14 x 8 cm.

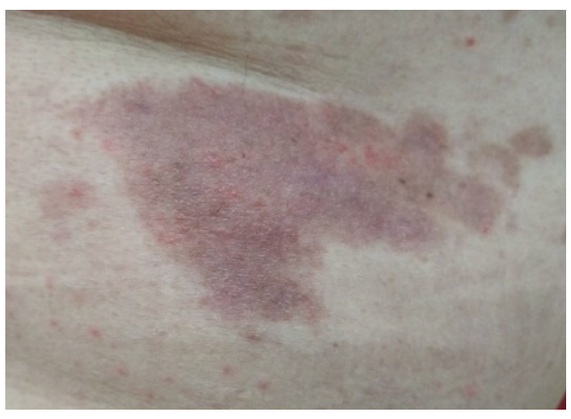
One month after perilesional injection of Profhilo 1 ml per side, the plaques remain erythematous but less flaky, with significant reduction of the scales.

IMAGE 2 Female, 55 yo, presents 3,5 x 2,5 cm sharply bordered plaques, with silvery scales, in scalp.



One month after perilesional inyection of 0,4 ml Profhilo, scales are not observed.

IMAGE 3 Male, 45 yo, presents erythematous desquamative plaque, with well-defined and irregular borders, 10 x 5 cm in lower lumbar area.



One month after injection of intralesional 2ml Profhilo persist a salmon red macula, important reduction of erythematous, with no scales or desquamation.

DISCUSSION

Faced with the multifactorial aspects of psoriasis, clinical management of these patients becomes a challenge due to possible complications. As includes the resurgence of the disease, requiring hospitalization and rigorous management.

Deep dermal injection of HCC appears to improve the features of psoriasis, their immunomodulatory ability can alleviate an inflammatory response.

CONCLUSION

This report sought to demonstrate that HCC treatment was effective in attenuating inflammation and maintaining the skin barrier in psoriasis.

These results imply that HCC may alleviate the symptom of psoriasis through the wound healing activity, modulation of keratinocytes, the maintenance of lipid barrier in epidermis, the regulation of mast cells activation and downregulation of inflammation.

In conclusion, HCC could be used as an alternative therapeutic approach in the management of psoriasis. Further studies about detailed mechanism of these protective immune responses are needed.

REFERENCES

1. Jashin J. Wu, MD. Contemporary Management of Moderate to Severe Plaque Psoriasis. Am J Manag Care. 2017;23:S403-S416

2. Boehncke WH, Schön MP. Psoriasis. Lancet. 2015 Sep5;386(9997):983-94

3. Zhang Y, Xia Q, Li Y, He Z, Li Z, Guo T, Wu Z, Feng N. CD44 Assists the Topical Anti-Psoriatic Efficacy of Curcumin-Loaded Hyaluronan-Modified Ethosomes: A New Strategy for Clustering Drug in Inflammatory Skin. Theranostics. 2019 Jan 1;9(1):48-64.

4. Lee JH et al. A hyaluronic acid-based microneedle patch to treat psoriatic plaques: a pilot open trial. Br J Dermatol. (2018).

5. Lindqvist U, Phil-Lundin I, Engström-Laurent A. Dermal distribution of hyaluronan in psoriatic arthritis; coexistence of CD44, MMP3 and MMP9. Acta Derm Venereol. 2012 Jul;92(4):372-7

6. Stellavato A, Corsuto L, D'Agostino A, La Gatta A, Diana P, Bernini P, et al. (2016) Hyaluronan Hybrid Cooperative Complexes as a Novel Frontier for Cellular Bioprocesses Re-Activation. PLoS ONE 11(10): e0163510.

7. D'Agostino et al. 2015 in vitro.