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The TLC-NOSF (Technoly Lipido-Colloid Plus Nano-Oligo Saccharide Factor) protease inhibitor for treatment of ulceration in rheumatic disease. A case report

Cutaneous Lupus Erithematosus is one of the most common manifestation of Systemic Lupus Erithematosus and can be featured by the onset of cutaneous vasculitis which can bring to skin ulcers, expecially on the extremities. The "common" aetiopathogenesis can be summarized as following: 1) an antiself response to the endothelial cells which brings to frequent ischemic or thrombotic episodes, 2) the drugs therapy; recently authors have been demostrated a correlation between Metalloproteinase Matrix (MMP) and Cutaneous LES. Here we present the case of a 33 y.o. woman affected by a rheumatic disorder, which has developed a chronic ulcer on her left leg. After several and different unsuccessful approaches, as homologous and autologous skin graft, and considering both the refusal of other surgery even if enhanced by Negative Pressure Therapy and the compromised vascularization which contraindicated the use of flaps, we decided to use a dressing based on the TLC-NOSF (Technology Lipido-Colloid plus Nano-Oligo Saccharide Factor) protease inhibitor, a metalloproteinase regulator. The dressing was changed 2 times/week for the first 2 months and 1 time/week for other 2 months. The ulcer became smaller at every session and we obtained a full coverage at 4th month.

KEY WORDS: Nano-oligo saccharide factor, Wound

Introduction

Cutaneous Lupus Erithematosus is one of the most common manifestation of Systemic Lupus Erithematosus and can be featured by the onset of cutaneous vasculitis which can bring to skin ulcers, expecially on the extremities. The "common" aetiopathogenesis can be summarized as following: 1) an antiself response to the endothelial cells which brings to frequent ischemic or thrombotic episodes, 2) the drugs therapy; recently authors have been demostrated a correlation between Metalloproteinase Matrix (MMP) and Cutaneous LES.

The Metalloproteinase Matrix family are zinc dependent extracellular protease which are involved in inflammatory responses. In 2018 Ertugrul et al. [1] demonstrated that an upregulation of MMP-2 and MMP-9 are directly correlated with the Cutaneous LES severity. Indeed the MMP-2 and 9 are overexpressed in inflammatory cells and in particular in patients treated with the association of steroids plus hydroxycloroquine.

MMP-2 and MMP-9 are also involved in chronic wounds; even if they are fundamental for a correct wound healing both in the re-epithelization and remodelling phase, their upregulated production can lead to

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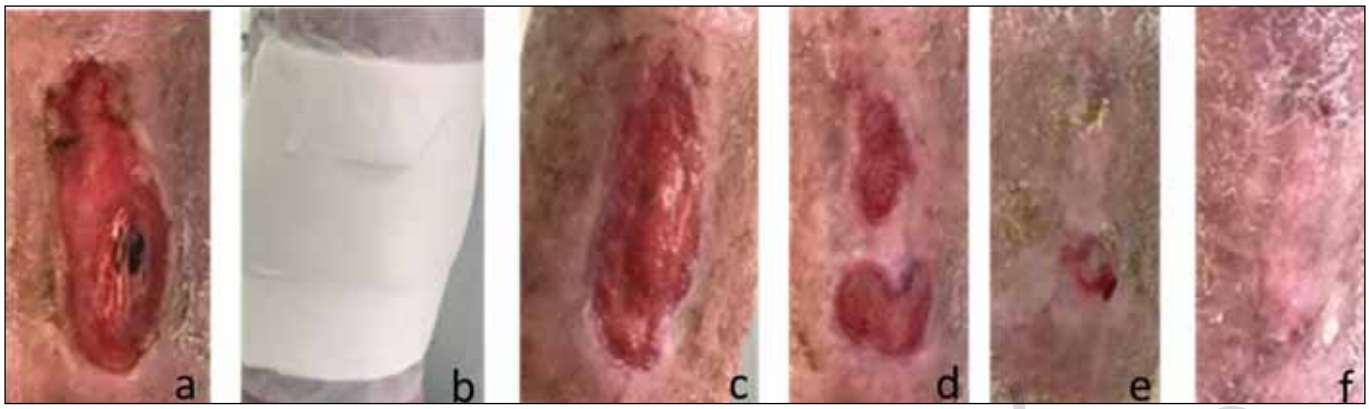

Fig. 1: A) Rheumatic ulcer with tendon exposition; B) the dressing applicated; C) after 1 month the tendon is almost completely covered; D) after 2 months: the tendon is completely covered and there's been rehepitelization from the borders to the center; E) after 3 months: the wound is almost closed; F) after 4 months: the wound is definitely closed and stable.

an increased collagen and matrix-degradation and consequently to an impaired wound healing. Currently these processes can be inhibited by advanced dressings which can regulated protease activity, hence considering that MMP's overexpression is also correlated to a LES Cutaneous manifestation, we supposed to use the protease inhibitors for these manifestations too.
In this paper we report the case of a 33 y.o. woman affected by a chronic rheumatic ulcer on her left leg which has been treated with the TLC-NOSF (Technology Lipido-Colloid plus Nano-Oligo Saccharide Factor) protease inhibitor, a metalloproteinase regulator, with a consequent complete resolution.

The Sucrose octasulfate potassium salt dressing

Created by Urgo Medical (Laboratoires Urgo Medical, Chenove, France), this dressing is a soft and non occlusive dressing composed by a lipidocolloid matrix, contained in a polyester mesh, and a nano oligosaccharide factor, which is called sucrose octasulfate potassium salt. This dressing is based on the ability of the potassium salt of sucrose octasulfate to inhibit the excess of Matrix Metalloproteinases in order to stop the degradation of growth factors and destruction of the extracellular matrix itself. This ability improves both growth factor function both rehepitelization. Furthermore, the presence of the hydrocolloid (carboxymetilcellulose) can absorbe the exudate, mantaining a correct moist enviroment and improving wound healing.
The dressing is indicated for exuding chronic ulcer (low to moderate exudate) such as leg ulcers or pressure sores; it is very confortable for the patients and very easy to apply and remove. The time of removal depends on the exudate absorption and it can range from 2 to 7 days.

Material and Method

Case Report

A 33 y.o. woman was affected by a Systemic Lupus Erithematosus which has been complicated by a vasculitis panarterite nodosa-like which brought to multiple digital thrombotic episodes with consequent amputation of the toes. The patient took corticosteroids and hydroxycloroquine and she came to our attention for the onset of multiple skin ulcers infected by microroganisms such as Pseudomonas Aeruginosa, Stenotrophomonas, Serratia Marescens. The microorganisms colonization has been treated with locally and systemic antibiotic therapy in accordance with the Tropical and Infectious Disease Unit.
After a first surgical debridement plus homologous skin graft and a following application of autologous skin graft, the patient presented a relapse of skin ulcer on the lateral part of the left leg; the ulcer was complicated by a tendon exposition. Her compromised vascularization contraindicated the use of flaps, and the patient refused another autologous skin graft even if enhanced by a negative pressure therapy and/or dermal substitutes.
The ulcer was present since 6 months without any significant improvement even with the use of advanced dressing such as hydrofiber plus silver or alginate; it presented a moderate exudate and a quite good granulation tissue around the tendon exposition, so we considered to treat it with a Sucrose octasulfate potassium salt dressing. The dressing was changed 2 times/week for the first 2 months and 1 time/week for other 2 months.

Results

The wound became smaller at every session and the patient reported pain relief both during the daily activities and during the dressing. The tendon exposition was completely covered at 1 month after the treatment. Given the improvements, we continued with the application 1 time/week, and the wound was definitely closed at 4th month. (Fig 1)
TLC-NOSF dressing has been a good alternative to stimulate wound healing being very acceptable for the patient.

Discussion

As reported, the sulfated oligosaccharides are famous for their biological activity such as the promotion of hepatocyte growth factor or the inhibition of tumor growth and metastasis, and it has been noted that the potassium salt of sucrose octasulfate is particularly suitable for inhibiting metalloproteases and consequently for leading wound healing interacting with growth factors. As recently reported by Edmonds M. et al [2], many studies demostrated that the sucrose octasulfate dressing is a safe and very acceptable treatment for chronic wounds such as venous leg ulcers, mixed ulcers and diabetic foot ulcers [3-10].

Conclusions

This case report is, to our knowledge, the first application of the TLC-NOSF dressing on a rheumatic ulcer. Considering the failure of the autologous skin graft, the failure of the other advanced therapies and the complexity of the patient which refused any other kind of treatment, the TLC-NOSF dressing has been a good alternative to stimulate wound healing being very acceptable for the patient.

Riassunto

Il Lupus Eritematoso Cutaneo è una delle manifestazioni più comuni del Lupus Eritematoso Sistemico, e può essere caratterizzato dalla comparsa di una vasculite cutanea, e conseguente insorgenza di ulcerazioni, in particolare alle estremità. L'etiopatogenesi può essere sintetizzata come segue: 1) una risposta antiself contro le cellule endoteliali, con conseguenti frequenti episodi ischemici o trombotici, 2) una qualche terapia farmacologica. Recentemente infatti alcuni Autori hanno dimostrato una stretta correlazione tra Metalloproteinase Matrix (MMP) e LES cutaneo. In questo lavoro presentiamo il caso di una donna di 33 anni affetta da un'ulcera cronica alla gamba sinistra, di origine reumatica. Dopo molteplici e differenti approcci senza successo, come gli innesti cutanei omologhi e autologhi, e considerando sia il rifiuto di altri interventi chirurgici, anche se potenziati dalla Terapia a Pressione Negativa, sia la vascolarizzazione compromessa che controindicava l'uso di lembi, abbiamo deciso di utilizzare una medicazione basata sul TLC- Inibitore della proteasi NOSF (Technology Lipido-Colloid plus Nano-Oligo Saccharide Factor), un regolatore della metalloproteinasi. La medicazione è stata cambiata 2 volte a settimana per i primi 2 mesi e 1 volta a settimana per altri 2 mesi. L'ulcera è diventata più piccola ad ogni sessione e abbiamo ottenuto una copertura completa al 4° mese.

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