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clinical practice

Skin ulcers complicating sickle cell disease: an interlinked reparative model

A. MORGANTE, A. LI DESTRI

SUMMARY: **Skin ulcers complicating sickle cell disease: an interlinked reparative model.**

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Skin ulcers represent a common complication of sickle cell disease, especially in homozygous forms, with multifactorial pathogenetic mechanisms and frequent location at lower extremities; more specifically perimalleolar areas are favourite location because of a chronic microvascular disturbance and capillary stasis in a district with low fatty tissue. Chronicization and recurrence of unhealable lesions significantly have a high impact on quality of life of these patients in terms of pain management and psycho-physical dysfunction. When we deal with a chronic ulcer, as it often happens in patients affected by hemoglobinopathies, the key-point is to make the skin lesion healable and vital by reactivating blocked repair process. Although it's controversial topic, patterns of patients with higher HbF concentrations might be more protective in accordance with reduced HbS polymerization; indeed, clinical features of ulcer represent the best predictors suggesting the correct strategy to achieve a good final outcome. Hereafter we report the case of a young woman with skin complications secondary to drepanocytosis, in which an interlinked reparative model consisting of surgery and advanced medications in addition to an adequate transfusional support, especially in earlier phases, has allowed to achieve clinical success after several years of care failure.

KEY WORDS: Skin ulcer - Transdermal continuous oxygen therapy - Sickle cell disease.

Introduction

Skin ulcers represent a common complication of sickle cell disease, especially in homozygous forms, with multifactorial pathogenetic mechanisms and frequent location at lower extremities. Chronicization and recurrence of unhealable lesions significantly have a high impact on quality of life of these patients in terms of pain management and psycho-physical dysfunction; pain severity often leads to abuse of antalgic drugs and unsatisfactory patient compliance towards dressings changes and local wound care.

Hereafter we report the case of a young woman with skin complications secondary to drepanocytosis in which an interlinked reparative model consisting of surgery and advanced medications associated to an adequate transfusional support, especially in earlier phases, has allowed to achieve clinical success after several years of care failure.

Clinical summary

A 28-year old female coming from North Africa was admitted at our hospital with diagnosis of pelvic swelling related to left ovarian cysts, simultaneously complaining of a painful skin ulcer (pain NRS 8 and unknown etiology) above medial malleolus of right leg (diameter 8x4 cm), from which she had suffered for about six years, associated to another new satellite microlesion.

Lower limbs doppler ultrasonography showed patency and continence of saphenous veins together to triphasic flows on tibial arteries; physical examination pointed out a widespread dyschromia of periulcerative skin area and a mild-moderate exudate pro-

Division of Vascular Surgery, Guzzardi Hospital, Vittoria (RG), Italy

Corresponding author: Alessandro Morgante,
e-mail: a.morgante4@virgilio.it

duction from wound that was extremely painful and almost untouchable at dressings changes.

Bacterial or mycotic infection of skin lesion was kept out by two repeated negative microbiological cultures, while laboratory tests revealed a chronic anemic status by nature even after transfusional therapy, a reactive thrombocytosis and a hyperbilirubinemia mainly unconjugated (total bilirubin 2 mg/dL with indirect amount 1.6 mg/dL); suspected hemolytic anemia was confirmed by a following hemoglobin electrophoresis that detected abnormal levels of HbS (94.9%), thus leading to the diagnosis of a homozygous sickle cell disease (SCD).

After ovarian cysts removal from gynaecologists, later we performed under anesthesia a sharp surgical debridement of leg ulcer cleaning wound bed and edges, taking out fibrin, devitalized tissue and some fibroblasts hyperproliferation areas.

Once obtained active bleeding and a regular wound surface, the patient underwent immediately local oxygen wound therapy and a transfusional support in order to maintain hemoglobin values over 10 mg/dL. Therefore, the patient was discharged few days after surgical debridement.

Dressings change was more frequent in the first two weeks in relation to increased amount of exudate, later being deferred up to 5/7 days. We also used intermittently an elastic bandage avoiding, by small gauzes, decubitus of thin diffusor tube that connected sterile wound interface to the oxygen generator.

Transdermal continuous oxygen turned out to be very easy and comfortable for the patient through a portable device that delivered to the lesion 98% pure humidified oxygen generated by water electrolysis; simultaneously, bromelain at high concentrations and serratio-peptidase were administered to modulate chronic phlogosis related to the increase of proteases.

Start of re-epithelialization was already appreciable after only two weeks with a smaller wound size in a one-month treatment in association to a quick pain reduction (Figures 1, 2); we stopped oxygen wound therapy after 6 weeks by adopting subsequent medications consisting in silver spray with hyaluronates and sulphadyazina up to the total lesion healing.

Discussion

Pathogenesis of skin ulcers in drepanocytic patients relies mainly on hyperviscosity and slowing of deformed red cells after oxygen tissutal delivery; the rigidity of erythrocytes morphing a sickle shape causes

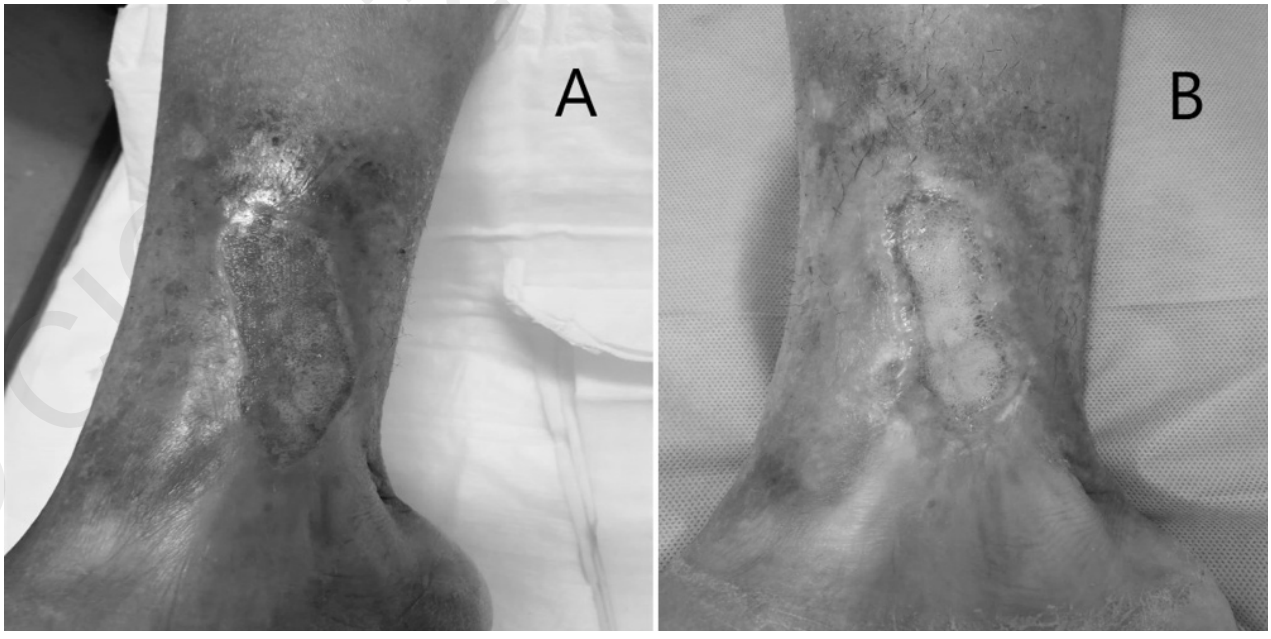

Figure 1 A, B - View of skin lesion after surgical debridement (A), whereas start of re-epithelialization is already appreciable after 15 days of transdermal continuous oxygen therapy (B).

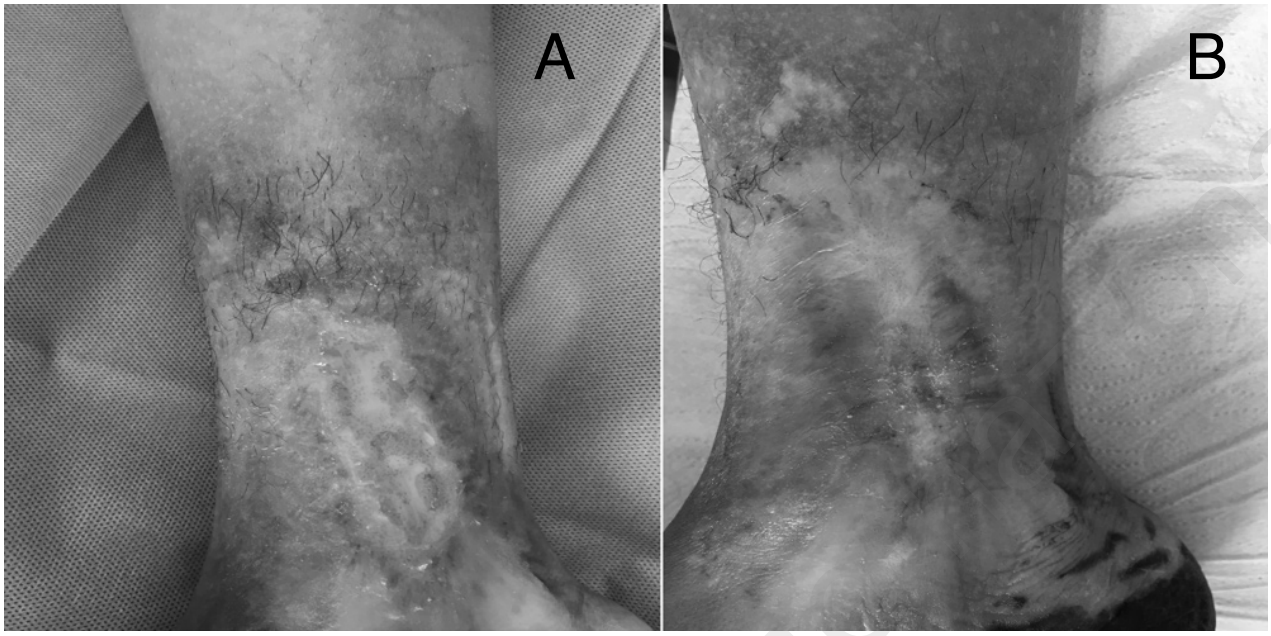

Figure 2 A, B - Drepanocytic ulcer with a clear smaller size after 1 month of therapy (A); '*restitutio ad integrum*' of skin lesion with complete healing after about 2 months.

their entrapment into microvascular district with consequent microvasal occlusions associated to ischemia-reperfusion damages phenomena and increased oxidative stress (1, 2). Reduced bioavailability of nitric oxide promotes the activation of endothelial cells producing surface adhesive molecules that lead to endothelium phlogistic damage and a local abnormal response with increased rates of pro-inflammatory cytokines and impaired balance of growth factors.

Once created the ulcerative lesion, low oxygen carrying capacity, typical for drepanocytic patients affected by chronic anemia, not only contributes to the onset of injury but implies its chronicization in relation to reduced tissue oxygenation.

In approaching the ulcers of patients affected by hemoglobinopathies, the key point is to make the skin lesion healable and vital by reactivating blocked repair process; a starting 'lesion analysis' is imperative assessing mainly the extent and macroscopic view according to TIME criteria of EWMA, in addition to a quantitative and qualitative evaluation of secretion that gives us useful information about health status of lesion. Indeed, clinical features of ulcer represent the best predictors suggesting the correct strategy to achieve a good final outcome (3).

A meticulous debridement must be the first step aiming to remove physical barriers to healing, like necrotic tissues and fibrin as well as bacterial biofilms or sloughs, in association to a microbiological study to rule out a colonization or infection of the lesion. Once achieved a good macroscopic view of wound and microbiological absence of infection, a transdermal continuous oxygen therapy (TCOT) is able to modify natural trend of a chronic unhealable lesion and can be considered the 'gold standard' among advanced medications for drepanocytic skin ulcers because it acts on their physiopathological basis (4, 5): impaired oxygen delivery and severe baseline anemia determine a local hypoxia within wound surface, which becomes consequently unable to heal completely. TCOT may be very useful under a compressive bandaging in cases of patients affected by a concomitant chronic venous disease; moreover, topic oxygen therapy allows us to avoid risks to create further skin lesions as it may occur in donor sites of patients undergoing an autologous skin grafting for the treatment of SCD-ulcers. Pain reduction is the first finding achievable earlier after TCOT application; pain management in SCD patients is a challenging issue since an altered nociceptive stimulation also prevents dressing changes that may be deferred step-by-step in accordance with exudate production. Otherwise wound size, even if initially may increase paradoxically because of perilesional hyperhidrosis, generally is smaller already after about 3-4 weeks of treatment with a colour

improvement of wound bed and granulation tissue occurrence up to evident skin re-epithelialization.

Eventually we point out the functional role of transfusional therapy in order to enhance blood supply to support wound healing; an ideal value of hemoglobin > 10 g/dl should be advisable especially in the first weeks of TCOT placement when skin lesion must become 'acute', later aiming to a more realistic value about 9 g/dL in order to improve oxygen carrying capacity (1).

Conflict of interest

The Authors declare no conflict of interest relevant to this publication.

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