

**LETTER TO THE EDITOR**

## Ulcerative necrobiosis lipoidica diabetorum successfully treated with topical sevoflurane and punch grafting

Dear Editors,

Necrobiosis lipoidica diabetorum (NLD) is a rare granulomatous condition usually associated with diabetes mellitus. It can lead to ulcerations in up to 30% of patients. These ulcers can represent a therapeutic challenge for clinicians, and associated pain may impair patients' quality of life. Although several drugs have been used, no standardised protocol of treatment exists, and usually, these atypical wounds are refractory to several lines of treatment. Here, we describe a patient with ulcerative NLD successfully treated with topical sevoflurane and punch grafting, achieving complete epithelisation in 3 weeks.

A 28-year-old woman, with well-controlled type 1 diabetes mellitus, presented with several weeks' history of an extremely painful ulcer located on the distal anterolateral aspect of the left leg. She suffered from incoercible pain (10/10 points on the pain visual analogic scale [VAS]) and pain-related sleep loss in the last 2 weeks notwithstanding treatment with non-steroidal anti-inflammatory drugs in combination with opioids. Physical examination showed a 6x5cm superficial ulcer, with irregular edges and a purpuric peripheral halo. The wound bed was mainly covered with red granulation tissue, with some localised slough (Figure 1). On the right leg, there was a well-demarcated yellow-brown plaque with violaceous borders, central waxy atrophic appearance, and telangiectasias. Lesions were compatible with necrobiosis lipoidica, and the more recent one was complicated with ulceration.

We used topical sevoflurane (1 mL/cm<sup>2</sup>) to irrigate the bed of the painful ulcer before cleansing, after obtaining informed consent because of the off-label use of this anaesthetic. After sevoflurane irrigation, we performed punch grafting to cover the wound bed. Punch grafts were obtained from the anterolateral side of the thigh. The patient benefited from pain reduction in less than 24 hours and progressive reduction in dosage of analgesics until she stopped it completely within the third day after the procedure. She also reported significant improvement in quality of life because of uninterrupted sleep after punch grafting.

The patient showed complete pain suppression within the first week after the procedure (0 points in VAS). In the fifth wound dressing change at the third week after punch

grafting, complete epithelisation of the ulcer could be observed (Figure 2).

Ulcerative necrobiosis lipoidica is a rare and extremely painful condition mostly seen in diabetic patients.<sup>1</sup> It is a difficult-to-treat dermatosis, impairing patients' quality of life. Ulcers normally run a refractory course, and even though several drugs have been tried, none of them has shown consistent effectiveness.<sup>2</sup>

There is currently no standardised and effective treatment for ulcerative NLD in clinical practice.<sup>3</sup> First-line therapies include control of cardiovascular risk factors and topical or intra-lesional corticosteroid injections.<sup>1,3</sup> Other therapies that have been tried include systemic corticosteroids; topical calcineurin inhibitors; aspirin and dipyridamole; wound-healing enhancers (platelet-derived growth factor, collagen gel); surgery; and immunomodulators such as cyclosporine, dimethyl-fumarate, or thalidomide. Some authors have reported significant improvement with psolaren-UV-a, photodynamic therapy, and pulsed dye lasers.<sup>4</sup> Biological drugs, such as anti-TNF (infliximab or etanercept),<sup>3</sup> ustekinumab,<sup>5</sup> and janus kinase-inhibitors,<sup>6</sup> have also been tried with varying degrees of success. To our knowledge, this is the first report of a case of ulcerative necrobiosis lipoidica treated with topical sevoflurane and punch grafting.

Punch grafting is a traditional and minimal invasive technique to enhance wound healing, which has been associated with significant and quick pain reduction in ulcers with different underlying causes.<sup>2,7</sup> These split-thickness skin grafts, which contain epidermis and papillary dermis, are obtained under local anaesthesia with a punch, curette, or surgical blade and are placed directly on the wound bed. The donor site is normally the thigh, which heals by secondary intention. The procedure can be performed on an outpatient basis. Punch grafting has been typically used for other kind of ulcers, such as venous, arterial, post-surgical, post-traumatic, and Martorell ulcers. This is the first report so far of an ulcerative necrobiosis lipoidica case successfully treated with punch grafting.

Sevoflurane is a highly fluorinated, ether-derived molecule widely used as an inhaled anaesthetic in the induction and maintenance of general anaesthesia. Some evidence



**FIGURE 1** Superficial ulcer with irregular edges and a purpuric peripheral halo on the left leg, compatible with ulcerative necrobiosis lipoidica



**FIGURE 2** Ulcer showed complete epithelisation after 3 weeks

suggests that direct instillation of sevoflurane into chronic wounds has a rapid, intense, and long-standing anaesthetic effect.<sup>8</sup> Its exact mechanism of action it is still unknown, and it also includes an anti-inflammatory effect because of vasodilatation. Pain reduction allows a more intensive debridement of ulcers in every wound dressing, so this would also help to achieve a faster epithelisation.<sup>9</sup> Several studies have been published about the off-label use of topical sevoflurane in chronic ulcers, most of them in venous leg ulcers.<sup>10,11</sup> It is safe and well tolerated, and there has not been any reported case of systemic toxicity because of the topical use of sevoflurane.<sup>10</sup>

Combined therapy based on topical sevoflurane and punch grafting may have a synergic effect. Topical sevoflurane also improves wound bed conditions, resulting in a higher percentage of graft taking. Final results of this combination are long-standing analgesic effect and pain suppression in many cases, faster wound healing in comparison


with traditional treatments, and improvement in the quality of life of patients.

We would like to stress not only the success in epithelisation but the astonishing and quick pain reduction reported by the patient because of sevoflurane and growth factors delivered from punch grafts. This treatment strategy allowed the stopping of opioids consumption and uninterrupted sleep at night, improving the patient's quality of life. The low cost of these procedures is another advantage of these treatment options.

These findings suggest that punch grafting and topical sevoflurane not only reduce pain control but may achieve it faster than other treatments that have been tried. They also have shown to cause fast epithelisation. As they are simple and well-accepted techniques, which can be performed on an in- and outpatient basis, we should consider them an option in the treatment of ulcerative necrobiosis lipoidica.

Atypical wounds, such as ulcerative necrobiosis lipoidica, are not only a diagnostic but also a therapeutic challenge for clinicians. Pain control is a key aspect in the treatment of these patients.

Punch grafting and topical sevoflurane should be considered in the treatment of ulcerative NLD. They are simple and inexpensive options that can be performed on an outpatient basis and may show a quick and maintained pain suppression. Further investigation should be undertaken to confirm these results.

Lucía Quintana-Castanedo<sup>1</sup>   
 Lorena Recarte-Marín<sup>2</sup>  
 Laura Pérez-Jerónimo<sup>2</sup>  
 Elena Conde-Montero<sup>3</sup>  
 Pablo de la Cueva-Dobao<sup>3</sup>

<sup>1</sup>*Department of Dermatology, La Paz University Hospital, Madrid, Spain*

<sup>2</sup>*Department of Dermatology, Centro de Especialidades Vicente Soldevilla, Madrid, Spain*

<sup>3</sup>*Department of Dermatology, Hospital Universitario Infanta Leonor y Virgen de la Torre, Madrid, Spain*

#### Correspondence

Lucía Quintana-Castanedo, Department of Dermatology, La Paz University Hospital, Paseo de la Castellana 261, Z.C 28046 Madrid, Spain.

Email: luciaquintana.e@gmail.com

#### ORCID

Lucía Quintana-Castanedo  <https://orcid.org/0000-0001-5136-841X>

## REFERENCES

1. Franklin C, Stoffels-Weindorf M, Hillen U, Dissemond J. Ulcerated necrobiosis lipoidica as a rare cause for chronic leg ulcers: case report series of ten patients. *Int Wound J*. 2015;12(5):548-554.
2. Isoherranen K, O'Brien JJ, Barker J, et al. Atypical wounds. Best clinical practice and challenges. *J Wound Care*. 2019;28(suppl 6):S1-S92.
3. Hu SW, Bevona C, Winterfield L, Qureshi AA, Li VW. Treatment of refractory ulcerative necrobiosis lipoidica diabetorum with infliximab: report of a case. *Arch Dermatol*. 2009;145(4):437-439.
4. Borgia F, Vaccaro M, Cantavenera LG, Aragona E, Cannavò SP. Ulcerative necrobiosis lipoidica successfully treated with photodynamic therapy: case report and literature review. *Photodiagnosis Photodyn Ther*. 2014;11(4):516-518.
5. Hassoun LA, Sivamani RK, Sharon VR, Silverstein MA, Burrall BA, Tartar DM. Ustekinumab to target granulomatous dermatitis in recalcitrant ulcerative necrobiosis lipoidica: case report and proposed mechanism. *Dermatol Online J*. 2017;23(7):1.
6. Lee JJ, English JC. Improvement in ulcerative necrobiosis lipoidica after Janus kinase-inhibitor therapy for polycythemia vera. *JAMA Dermatol*. 2018;154(6):733-734.
7. Atkin L, Bučko Z, Conde Montero E, et al. Implementing TIMERS: the race against hard-to-heal wounds. *J Wound Care*. 2019;23(suppl 3a):S1-S50.
8. Dámaso Fernández-Ginés F, Cortiñas-Sáenz M, Mateo-Carrasco H, et al. Efficacy and safety of topical sevoflurane in the treatment of chronic skin ulcers. *Am J Health-Syst Pharm*. 2017;74(9):e176-e182.
9. Imbernón-Moya A, Frutos JO, Sanjuan-Alvarez M, Portero-Sanchez I. Application of topical sevoflurane before cleaning painful skin ulcers. *Actas Dermosifiliogr*. 2018;109(5):447-448.
10. Imbernon-Moya A, Ortiz-de Frutos FJ, Sanjuan-Alvarez M, Portero-Sanchez I, Merinero-Palomares R, Alcazar V. Treatment of chronic venous ulcers with topical sevoflurane: a retrospective clinical study. *Br J Anaesth*. 2017;119(4):846-847.
11. Imbernon-Moya A, Ortiz-de Frutos FJ, Sanjuan-Alvarez M, Portero-Sanchez I, Merinero-Palomares R, Alcazar V. Healing of chronic venous ulcer with topical sevoflurane. *Int Wound J*. 2017;14(6):1323-1326.