

The Cutting Edge

Epidermal Grafting Using a Novel Suction Blister-Harvesting System for the Treatment of Pyoderma Gangrenosum

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Report of Cases

Patient 1

A woman in her 40s without other significant medical history presented in 2013 with an 8-month history of an exquisitely painful ulcer on the distal left lateral leg. She noted that the lesion began as "a small red bump" that she believed to be an insect bite. A physician at another institution performed an incision and drainage to treat a suspected abscess and prescribed oral antibiotics, but the lesion deteriorated. A biopsy performed in 2012 had nonspecific results and Gram, acid-fast, and Fite stains were negative for organisms. Venous and arterial insufficiency were excluded by lower limb duplex ultrasound. She received a diagnosis of pyoderma gangrenosum (PG) and was prescribed prednisone 60 mg daily and topical clobetasol propionate ointment, 0.05%, to the wound edges. On referral, physical examination revealed a sharply demarcated ulcer with purple undermined borders, consistent with the PG diagnosis. The prednisone dosage was tapered because of adverse effects, and cyclosporine 400 mg daily and weekly leg compression were initiated. Although the inflamed undermined borders improved, the wound failed to reduce in size after 2 months of therapy (Figure 1).

Patients 2 Through 5

Four additional patients with chronic, recalcitrant lower extremity ulcers diagnosed as PG were included in this series. Demographic and wound assessment data for each patient are given in the eTable in the Supplement.

Therapeutic Challenge

Pyoderma gangrenosum is a neutrophilic dermatosis characterized by chronic, recurrent ulcerations of the skin. Currently, most first-line and second-line treatments are anecdotal and no gold standard treatment for PG exists. Although patients may respond to systemic medications aimed at reducing underlying inflammation associated with PG, in many cases, large wounds remain. Skin grafting is problematic because of the potential for pathergy, a phenomenon in which new or worsening ulcerations may develop following trauma or surgery. In addition, application of tissue-engineered skin often is not reimbursed; thus, limited clinical options exist to provide wound coverage.

Solution

Epidermal grafts harvested by suction blisters provide autologous keratinocytes with minimal donor site trauma. Use of a novel device (CelluTome, Kinetic Concepts, Inc) designed to harvest autologous epidermal micrografts through the formation of suction blisters without

Figure 1. Pyoderma Gangrenosum Ulcer on the Left Lateral Leg



A 2.1-cm² ulcer secondary to pyoderma gangrenosum prior to the micrografting procedure.

anesthesia, which has recently received Food and Drug Administration clearance, has potential for treatment of ulcers secondary to PG. Through the application of heat to 40°C and 200 mm Hg of negative pressure, the device creates and harvests either 42 epidermal microdomes to cover a 2.5 × 1.75-cm area or, with a larger harvester, 128 epidermal microdomes. The blisters, or microdomes, are cleaved through the lamina lucida of the dermal-epidermal junction.

All patients received a single harvest of epidermal blisters from the medial thigh with subsequent transfer of the micrografts to the wound via a fenestrated transparent film dressing. Overlying absorbent foam dressings were applied, and the patients' legs were wrapped in 4-layer compression bandages. Both leading up to and following the procedure, patients continued to receive their established medical care for PG.

In May 2013 at 1-week follow-up, the first patient's wound measured 1.3 × 0.6 cm (0.78 cm²), a 63% wound area reduction. The donor site had also completely healed by this time. She continued to receive daily cyclosporine treatment and weekly compression wraps until the wound fully reepithelialized at 7 weeks (Figure 2).

The remaining 4 patients improved with either complete healing or a substantial reduction in wound area following the treatment. Two patients healed following epidermal micrografting, 1 at 5 weeks and another at 12 weeks. The other 2 patients showed a reduction in ulcer size of 64% and 99% within 8 weeks. All patients reported minimal pain associated with the procedure, and all donor sites healed within 1 week. No complications occurred at donor or recipient sites.

Discussion

The classic form of PG presents as an erythematous nodule or pustule that rapidly progresses to a painful ulcer. Pyoderma gangrenosum most commonly affects the lower extremities and trunk. Peak

Figure 2. Healed Pyoderma Gangrenosum Ulcer Following Suction Blister Micrografting



Complete reepithelialization at 7 weeks following a single application of suction blister micrografts.

incidence occurs at 20 to 50 years of age, and it is more frequent among women.¹ Approximately 50% of patients with PG have an associated systemic condition including inflammatory bowel disease, arthritis (rheumatoid and seronegative), hematologic malignancy, systemic lupus erythematosus, and hepatitis.²

The diagnosis of PG is supported by the presence of its typical clinical features and through the exclusion of similar ulcerating conditions. Biopsy and laboratory test results are generally nonspecific but may assist in ruling out other etiologies. Once diagnosis has been established, screening for associated systemic diseases is recommended because control of these underlying conditions often results in improvement or resolution of ulcers. Treatment of idiopathic PG generally consists of reducing underlying inflammation. Oral corticosteroids are often used in the initial management; however, many patients find that their disease fails to adequately respond. In a review of systemic therapies for idiopathic PG, Miller et al³ ranked prednisone, cyclosporine, and methotrexate (in descending order) as the top 3 treatments on the basis of safety, efficacy, cost, and experience.

Whereas split-thickness skin grafting (STSG) may be performed, it is typically avoided out of concern for pathergy at the do-

nor site. Although STSG with concurrent medical control of the inflammatory process has been advocated, this option has yielded inconsistent results.^{4,5} In addition, STSG may be associated with large operating room expenses and donor site morbidity.^{6,7} Tissue-engineered skin represents another option in the treatment of PG. Whereas large randomized clinical trials support the use of selected tissue-engineered skin products for the treatment of venous leg ulcers and diabetic foot ulcers, the level of evidence supporting their use in PG is less robust. Product and procedure costs are incurred, compared with only reimbursed procedure costs for epidermal grafting.

In our experience, the epidermal micrografts represent a safe and efficacious method for treating PG ulcers. Unlike traditional STSGs, the device cleaves the skin at the lamina lucida following suction blister formation. This minimally invasive depth may be less likely to provoke an inflammatory response and may account for the absence of pathergy and rapid healing of the donor site experienced by our patients. In addition, a substantial reduction in wound size was demonstrated by all 5 patients, with complete wound closure occurring in 3 patients.

Of note, in our patients the epidermal micrografts did not appear to “take” to the underlying granulation tissue. Instead, reepithelialization occurred from the wound edges. Whereas the exact mechanism of the micrografts is not known, it is conceivable that the grafts served as a biological dressing and may have stimulated healing through the release of growth factors. The use of autologous suction blister grafts has been shown to be successful in the treatment of chronic lower extremity wounds.⁸ Similar to our findings, Costanzo et al⁸ reported a lack of graft survival in the majority of patients, postulating that suction blister grafts may perform like bioengineered skin.

In this case series, patients with ulcers secondary to PG improved following a single application of autologous epidermal micrografts. Epidermal grafting was also a low-risk procedure that caused little to no pain during the harvesting of skin and no pathergy. Further evaluation of the treatment efficacy of this novel epidermal harvesting system in randomized clinical trials is warranted.

ARTICLE INFORMATION

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