

Case Report

Multimodal Management of Pyoderma Gangrenosum Using a Thermoplastic Elastomer NPWT Interface, Morphine-Infused Antibiotic Cement, and Patient-Directed Antimicrobial Irrigation

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Abstract

Pyoderma gangrenosum is a rare neutrophilic dermatosis characterized by painful, rapidly progressive ulceration and a marked propensity for pathergy, making lower-extremity wound management particularly challenging. Severe pain, exaggerated inflammatory response, and susceptibility to mechanical trauma often limit tolerance of standard wound care interventions and delay initiation of disease-directed therapy. This case report describes a multimodal stabilization strategy used during a defined six-week treatment period in a patient with biopsy-proven pyoderma gangrenosum of the medial ankle that had progressed despite prolonged outpatient care. Management focused on interruption of pain-driven deterioration, suppression of local infection, and minimization of mechanical trauma rather than immediate wound closure. The approach combined morphine-infused antibiotic-loaded resorbable calcium sulfate cement for sustained local analgesia and local antimicrobial therapy, low-pressure extended-interval negative pressure wound therapy delivered through a thermoplastic elastomer interface, and a patient-directed antimicrobial irrigation technique that preserved dressing integrity. During this period, pain control improved substantially, tolerance of advanced wound therapy was achieved, and fluoroquinolone-resistant *Pseudomonas aeruginosa* infection resolved without evidence of pathergic worsening. The wound transitioned to a clinically stable, infection-free state, allowing subsequent initiation of topical and systemic immunosuppressive therapy. To the authors' knowledge, this represents the first reported use of morphine-infused resorbable calcium sulfate cement as a local analgesic adjunct in lower-extremity wound care. This case highlights the importance of reframing success in complex inflammatory wounds around stabilization and tolerance of therapy and suggests a potential framework for managing pain-limited, pathergy-prone ulcers.

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Keywords: pyoderma gangrenosum (PG); thermoplastic elastomer negative pressure wound therapy (NPWT) interface; low-pressure extended-interval NPWT; morphine-infused calcium sulfate cement; local analgesic delivery; patient-directed wound irrigation; antimicrobial irrigation; pathergy-minimizing wound care

1. Introduction

Pyoderma gangrenosum (PG) is a rare, noninfectious neutrophilic dermatosis characterized by rapidly progressive, severely painful cutaneous ulcerations with undermined violaceous borders and a marked tendency toward pathergy. The estimated prevalence is approximately 5 to 6 cases per 100,000 adults, with the lower extremities involved in the majority of patients, making PG highly relevant to podiatric practice and lower-extremity

wound care [1,2]. Once considered a diagnosis of exclusion, PG is now recognized as an immune-mediated inflammatory disease driven by neutrophil dysfunction, dysregulated innate immunity, and aberrant cytokine signaling involving interleukin 1, interleukin 8, and tumor necrosis factor alpha [3,4]. These mechanisms account for both the aggressive ulcerative behavior of PG and its exaggerated inflammatory response to even minimal mechanical trauma.

Pathergy, defined as rapid ulcer expansion following minor injury, is a defining and clinically consequential feature of PG. Approximately 30 percent of patients demonstrate pathergic responses, which may be triggered by biopsy, debridement, dressing changes, or surgical intervention [5,6]. In the context of wound care, this phenomenon creates a therapeutic paradox: essential interventions aimed at wound bed preparation, infection control, and exudate management may themselves worsen inflammation, tissue injury, and pain. As a result, clinicians frequently limit sharp debridement and avoid advanced wound modalities, often leading to persistent inflammation, uncontrolled bioburden, and prolonged failure to heal.

Pain is a central and disproportionate feature of PG and is often severe relative to the size or depth of the ulcer. PG-associated pain is multifactorial, arising from intense local inflammation, ischemia at ulcer margins, and heightened nociceptor sensitization [2,7]. Procedural pain during dressing changes and wound manipulation represents an additional and frequently under-recognized burden. Studies in patients with chronic wounds consistently demonstrate that dressing changes and debridement provoke moderate to severe procedural pain in most patients, adversely affecting adherence, psychological well-being, and willingness to undergo necessary care [8,9]. In PG specifically, uncontrolled pain functions not only as a symptom but as a major barrier to effective wound management, often precluding adequate debridement and limiting the use of otherwise beneficial adjunctive therapies.

Negative pressure wound therapy (NPWT) is widely used in the management of complex acute and chronic wounds due to its ability to control exudate, decrease edema, promote granulation tissue formation, and stabilize the wound environment [10]. Its use in PG, however, remains controversial. Traditional NPWT protocols commonly employ suction pressures near 125 mmHg with frequent dressing changes, parameters that may exacerbate pain, tissue compression, and ischemic risk in inflamed or fragile wounds. Concerns regarding pathergy, ischemia, and pain have therefore historically limited NPWT adoption in neutrophilic dermatoses [11,12]. A systematic review of NPWT in PG suggests that although improvement is reported in many cases, the available evidence is limited to low-level studies and emphasizes the importance of careful technique, concurrent immunosuppression, and minimization of mechanical trauma [12].

Biomechanical and perfusion studies suggest that increasing negative pressure may increase tissue compression and adversely affect microvascular perfusion in susceptible wounds [13,14]. Lower-pressure NPWT has demonstrated effective fluid evacuation while potentially reducing these effects [15,16]. Wound-interface characteristics may further influence pressure transmission and treatment tolerance. Compared with conventional reticulated open-cell foam, a thermoplastic elastomer NPWT interface (PREVENT; Clear Choice Therapeutics, Inc., Raleigh, NC, USA) is designed to facilitate exudate evacuation at lower negative pressures while limiting tissue ingrowth and dressing-related trauma [14,17]. Early clinical experience has supported its use at lower negative pressures with extended wear intervals [17].

Local infection control represents an additional challenge in PG wounds, in which repeated topical manipulation may increase the risk of pathergy. Wound irrigation provides an adjunctive strategy for reducing surface bioburden while minimizing mechanical manip-

ulation [18]. Chlorhexidine gluconate demonstrates broad-spectrum antimicrobial activity at low concentrations [19,20], and 0.05% chlorhexidine has demonstrated bacterial-load reduction and in vitro biofilm activity [21,22]. Irrisept® Antimicrobial Wound Lavage (Irrimax Corporation, Atlanta, GA, USA), a commercially available 0.05% chlorhexidine gluconate irrigation solution, has undergone safety evaluation for wound cleansing [23,24], with additional evidence supporting the antimicrobial activity of low-concentration chlorhexidine irrigation [21,25].

Negative pressure wound therapy with instillation and dwell time (NPWTi-d) combines NPWT with periodic delivery of topical solutions to facilitate wound cleansing and microbial-burden management [26,27]. However, conventional NPWTi-d systems rely on automated cycling and specialized components. In patients with PG, minimizing dressing disruption and mechanical trauma is particularly important because of the risk of pathergy [12]. In contrast, the non-porous design and low-resistance flow characteristics of the thermoplastic elastomer NPWT interface allow for adjunctive irrigation through a stable dressing construct, reducing the need for repeated dressing removal.

In pathergy-prone inflammatory ulcers such as PG, effective wound management requires strategies that minimize mechanical trauma, preserve perfusion, control infection, and address pain as a primary limiting factor. Resorbable calcium sulfate has an established role as a local antibiotic delivery platform; however, its use as a carrier for opioid analgesics in lower-extremity wound care has not previously been described. To our knowledge, this represents the first reported application of morphine-infused resorbable calcium sulfate cement, STIMULAN® Rapid Cure, Biocomposites Ltd., Keele, UK; Wilmington, NC, USA), to a lower-extremity wound to provide sustained local analgesia while simultaneously delivering targeted antimicrobial therapy.

Against this background, this case report describes the management of a biopsy-proven PG ulcer using a multimodal strategy emphasizing low-pressure extended-interval NPWT at 50 mmHg delivered through a thermoplastic elastomer NPWT interface (PREVENT), morphine-infused antibiotic-loaded resorbable calcium sulfate cement for sustained local analgesia and local antimicrobial therapy, and a novel PREVENT-based configuration enabling multiple daily patient-directed Irrisept irrigations while maintaining NPWT dressing integrity. This approach directly addresses the intersecting challenges of pain, pathergy, perfusion, and infection that define wound care in pyoderma gangrenosum.

2. Case Report

A 53-year-old male was referred for evaluation of a chronic, severely painful ulceration involving the medial aspect of the left ankle. The wound had been present for over one year and had progressively enlarged despite comprehensive outpatient wound care, including compression therapy, topical antimicrobial dressings, application of amniotic and dermal allografts, and multiple courses of empiric and culture-directed systemic antibiotics. The patient described constant baseline pain with pronounced exacerbation during dressing changes and any wound manipulation, resulting in poor tolerance of routine wound care.

The patient's medical history was significant for chronic venous insufficiency and long-standing hypertension. He denied a personal or family history of inflammatory bowel disease, inflammatory arthritis, hematologic malignancy, or other known systemic inflammatory disorders. Previous wound interventions included serial sharp debridement and intermittent short-term negative pressure wound therapy; however, these treatments were poorly tolerated due to severe procedural pain. Several dressing changes were followed by apparent rapid enlargement of the ulcer, raising clinical concern for a pathergic response.

On examination, the patient had a large, irregular ulcer over the medial ankle extending proximally onto the distal lower leg (Figure 1). The ulcer demonstrated violaceous,

undermined borders with surrounding erythema and hypergranulation tissue. The wound bed was moist with copious serous drainage and malodor. Significant pain was elicited with even minimal manipulation of the wound or periwound tissues. Peripheral pulses were palpable, capillary refill was brisk, and there was no clinical evidence of acute arterial insufficiency. No systemic signs of infection, such as fever or leukocytosis, were present at the time of evaluation.



Figure 1. Baseline clinical appearance of a chronic medial ankle ulcer prior to multimodal stabilization. The wound demonstrates irregular morphology with violaceous, undermined borders and surrounding inflammatory changes consistent with pyoderma gangrenosum, contributing to severe pain and increased risk of pathergy.

Aerobic wound cultures repeatedly demonstrated growth of *Pseudomonas aeruginosa* resistant to the fluoroquinolones ciprofloxacin and levofloxacin, while retaining susceptibility to gentamicin, imipenem, meropenem, and piperacillin/tazobactam. Prior to hospitalization, the patient had received alternating courses of oral doxycycline and ciprofloxacin; notably, the subsequently isolated *P. aeruginosa* demonstrated in vitro resistance to ciprofloxacin. Following infectious disease consultation, the patient received intravenous piperacillin/tazobactam during hospitalization and was discharged on a 7-day course of intravenous cefepime (2 g every 8 h) with oral metronidazole (500 mg twice daily). Despite systemic antimicrobial treatment, serial cultures continued to demonstrate *P. aeruginosa*, supporting the use of adjunctive local antimicrobial therapy as part of the multimodal wound-stabilization strategy. Given the characteristic clinical appearance, severe pain out of proportion to wound size, evidence of pathergy, and refractory clinical course, pyoderma gangrenosum was strongly suspected. To confirm the diagnosis and exclude alternative etiologies, three full-thickness punch biopsies were obtained from both the ulcer edge and the wound bed. Histopathologic examination demonstrated a dense neutrophilic infiltrate with microabscess formation and ulceration, without evidence of vasculitis or malignancy. These findings were consistent with pyoderma gangrenosum (Figure 2).

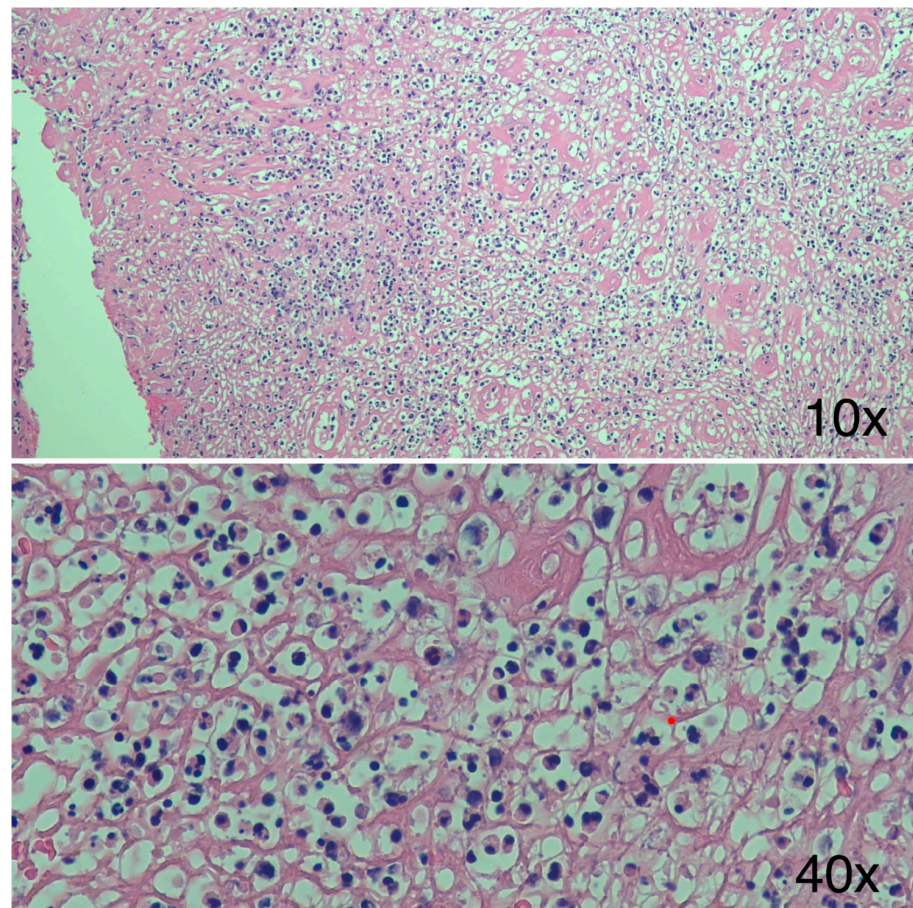


Figure 2. Histopathologic findings from biopsy of the left medial ankle ulceration. Representative hematoxylin and eosin–stained sections demonstrate a dense neutrophilic inflammatory infiltrate with microabscess formation and ulceration, without evidence of vasculitis or malignancy, findings consistent with pyoderma gangrenosum.

Following biopsy, further sharp debridement was discontinued to reduce the risk of exacerbating pathergy. A multidisciplinary discussion emphasized the need for a wound management strategy that prioritized pain control, minimized mechanical trauma, preserved periwound perfusion, and permitted ongoing management of microbial burden without repeated dressing disruption.

In light of the patient's inability to tolerate conventional wound care and previous intolerance of standard negative pressure wound therapy, a multimodal, low-trauma approach was selected. The treatment plan was designed to address pain as a primary limiting factor, thereby enabling tolerance of advanced wound therapy. This strategy incorporated three coordinated interventions: sustained local analgesia and local antimicrobial therapy using morphine-infused antibiotic-loaded resorbable calcium sulfate cement, low-pressure extended-interval negative pressure wound therapy delivered through a thermoplastic elastomer wound interface, and a patient-directed irrigation technique that preserved dressing integrity.

At the time of biopsy, 5 cc of resorbable calcium sulfate cement was prepared and mixed with imipenem–cilastatin (500 mg) and morphine sulfate (9 mg). After curing, the cement was applied directly to the wound bed and secured with nonadherent contact layers (Figure 3). This intervention was selected to provide sustained local analgesia and targeted antimicrobial activity while minimizing repeated topical manipulation. The use of morphine-infused calcium sulfate for wound analgesia represented an off-label application but was chosen due to the patient's otherwise prohibitive pain levels.

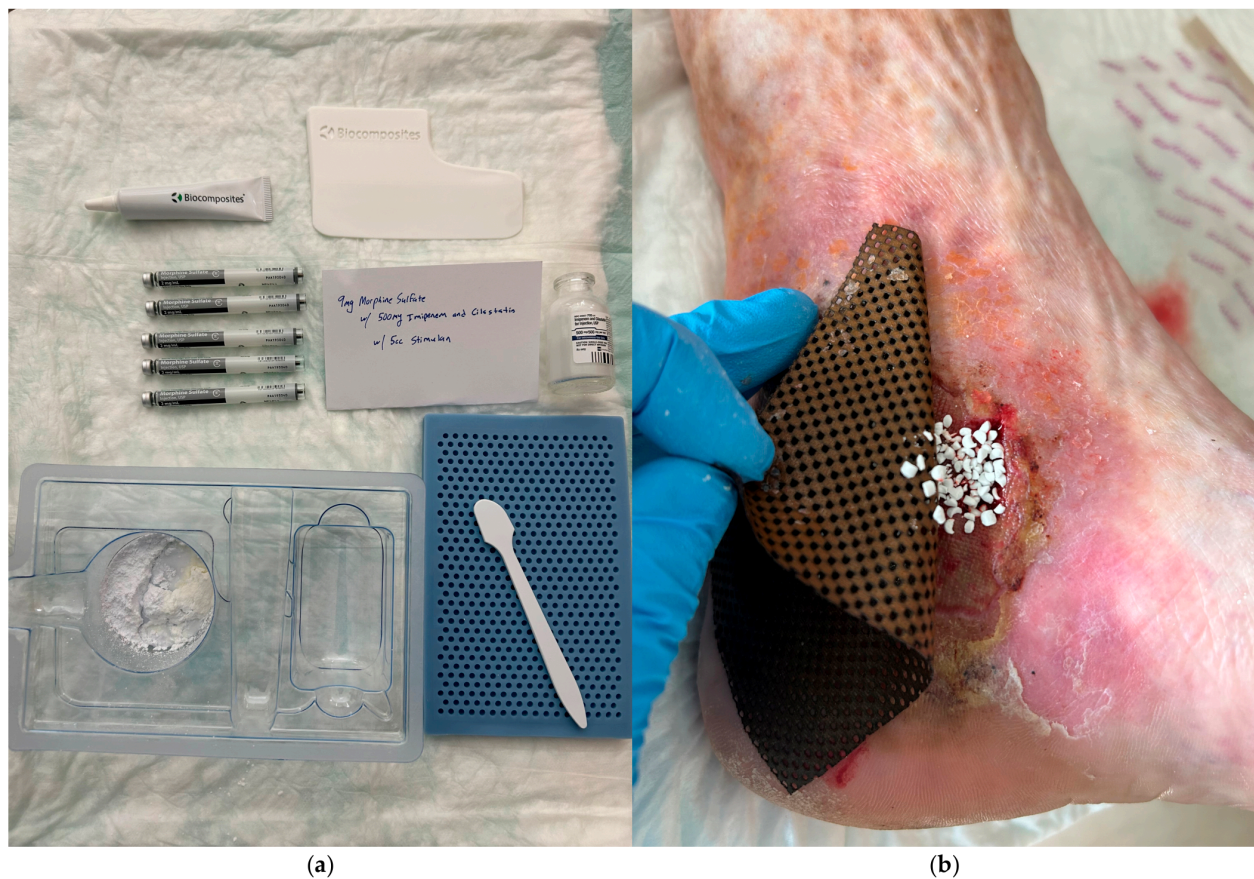


Figure 3. Preparation and application of morphine-infused, antibiotic-loaded resorbable calcium sulfate cement used during the wound stabilization phase. **(a)** Mixing of resorbable calcium sulfate cement with imipenem–cilastatin and morphine sulfate prior to application, creating an antibiotic-loaded matrix intended to provide sustained local antimicrobial activity and analgesia. **(b)** Application of morphine-infused antibiotic calcium sulfate cement beads to the wound bed, secured with a nonadherent contact layer to maintain position while minimizing mechanical trauma during subsequent wound therapy.

The PREVENT TPE dressing was applied directly over the wound bed and was permitted to contact the exposed antibiotic- and morphine-loaded calcium-sulfate cement. At each dressing change, residual calcium-sulfate cement was removed from the wound bed, the wound was irrigated, and the remaining cement was reapplied before replacement of the TPE dressing. This process was repeated at subsequent dressing changes until the calcium-sulfate cement had fully dissolved, which occurred over approximately 3–4 weeks. No clinically apparent adverse interaction between the TPE interface and the calcium-sulfate material was observed during therapy.

Following stabilization of pain, negative pressure wound therapy was initiated at 50 mmHg continuous suction using a thermoplastic elastomer negative pressure wound interface (Figure 4). Dressing changes were intentionally extended to approximately 7-day intervals to minimize mechanical trauma and pathergic risk. No evidence of ischemia, worsening inflammation, or ulcer expansion was observed during therapy.

To facilitate ongoing irrigation and bioburden control without repeated dressing removal, a dual-port configuration was created using the thermoplastic elastomer interface (Figure 5). This setup allowed the patient to perform irrigation with 10 cc of Irrisept antimicrobial wound lavage. During each irrigation, negative-pressure suction was temporarily paused, the irrigation solution was introduced through the secondary access port and allowed to remain in contact with the wound for approximately 90 s, after which

negative-pressure therapy was resumed. The patient was instructed to perform this protocol 2–3 times daily. The 90-s contact period was selected pragmatically by the treating physician to balance antimicrobial contact time with the feasibility of repeated patient-directed irrigation and anticipated patient adherence. This interval was not selected on the basis of a validated time-to-kill or biofilm-eradication threshold and should not be interpreted as an established optimal exposure time. The patient reported consistent adherence to the prescribed irrigation schedule; however, adherence was not prospectively quantified.



Figure 4. Thermoplastic elastomer negative pressure wound therapy interface (PREVENT) trimmed to the areal dimensions of the wound prior to application. The barrier was cut to fit within the wound margins to facilitate low-pressure exudate evacuation while minimizing contact with intact periwound skin and reducing mechanical trauma.

Serial wound cultures were obtained at approximately weekly to biweekly intervals during the treatment course. Early cultures repeatedly demonstrated moderate-to-heavy growth of fluoroquinolone-resistant *Pseudomonas aeruginosa*. Persistent heavy growth was identified on subsequent cultures obtained approximately 1–2 weeks apart. As treatment progressed, the recoverable bacterial burden decreased to light growth, followed approximately one week later by an aerobic culture demonstrating no growth, with no organisms identified on Gram stain. This microbiologic improvement occurred during the multimodal treatment period and paralleled the clinical reduction in drainage, malodor, and local inflammatory findings.

Within days of cement placement, the patient reported marked reduction in pain, with numeric pain scores decreasing from 7–8 out of 10 at baseline to 1–2 out of 10. At each weekly dressing change, residual antibiotic- and morphine-loaded calcium sulfate cement was removed, the wound was irrigated, and the remaining cement was reapplied. This process continued until the calcium sulfate material had fully dissolved over approximately 3–4 weeks. The improvement in pain enabled tolerance of negative pressure wound therapy and wound irrigation that had previously been poorly tolerated.

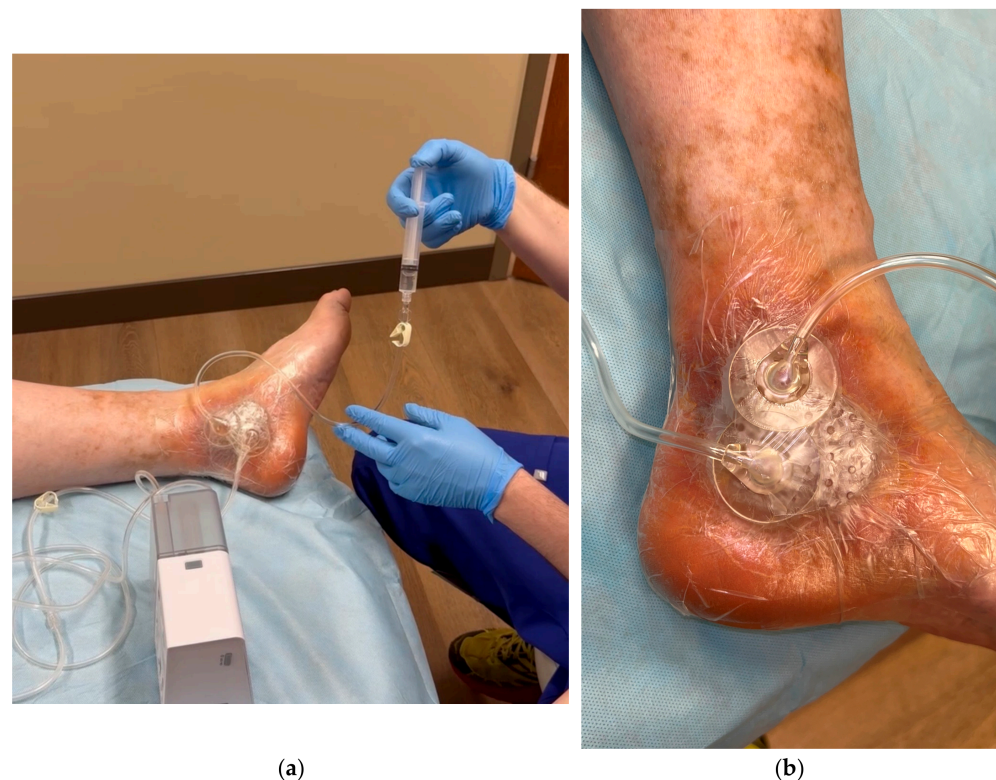


Figure 5. Dual-port configuration of the thermoplastic elastomer negative pressure wound therapy interface (PREVENT) used to facilitate patient-directed antimicrobial irrigation. (a) Overview of the irrigation setup showing a 10-cc syringe containing Irrisept antimicrobial wound lavage connected to the dressing while maintaining the negative pressure wound therapy system in place. (b) Close-up view of the dual-port interface demonstrating separation of the negative pressure out-flow port and secondary access port, allowing controlled low-volume irrigation without disruption of dressing integrity.

At dressing changes, the wound bed demonstrated progressive, robust granulation tissue formation without clinically appreciable tissue ingrowth into or adherence to the TPE dressing. A transient patterned imprint corresponding to the TPE wound interface was observed on the granulation tissue following dressing removal. This pattern diminished after removal of negative pressure and did not appear to represent tissue injury (Figure 6).

Low-pressure negative pressure wound therapy was well tolerated, with no evidence of pathergic worsening or ischemic compromise. Dressing changes at extended intervals were completed without significant pain escalation. Serial wound cultures demonstrated progressive suppression and complete resolution of *Pseudomonas aeruginosa* infection within approximately 6 weeks of the initial application of the morphine-infused antibiotic calcium sulfate cement and initiation of patient-directed irrigation therapy. With the wound stabilized, free of active infection, and no longer demonstrating rapid inflammatory progression, immunosuppressive therapy was subsequently initiated, consisting of topical tacrolimus applied to the wound margins and oral cyclosporine therapy, to address the underlying inflammatory disease process. At approximately six weeks, the wound demonstrated healthy granulation tissue with controlled inflammation and no evidence of recurrent infection or pathergic progression.

Following stabilization of the wound and completion of the multimodal wound-care regimen, topical tacrolimus and systemic cyclosporine were continued for management of the underlying pyoderma gangrenosum. Over the subsequent 7 weeks, the wound demonstrated progressive epithelialization and ultimately achieved complete closure. A

final clinical photograph demonstrating complete epithelialization without the previously observed TPE-associated surface imprinting is provided in Figure 7.



Figure 6. Clinical appearance of the medial ankle wound at approximately six weeks following initiation of multimodal stabilization therapy, demonstrating healthy granulation tissue and controlled inflammation without clinical evidence of active infection or pathergic deterioration. This image reflects wound stabilization achieved during the defined treatment interval prior to initiation of immunosuppressive therapy.



Figure 7. Complete wound healing following multimodal treatment of pyoderma gangrenosum. Clinical photograph obtained approximately 7 weeks after completion of the negative pressure wound therapy phase, demonstrating complete epithelialization of the previously ulcerated area following continued treatment with topical tacrolimus and oral cyclosporine. The previously observed TPE-associated surface imprinting is no longer present.

3. Discussion

Pyoderma gangrenosum presents a unique therapeutic challenge in lower-extremity wound care due to the convergence of severe pain, exaggerated inflammatory response, and susceptibility to pathergy. These factors frequently render standard wound care interventions poorly tolerated or actively harmful, resulting in prolonged tissue instability despite appropriate systemic therapy. This case highlights a targeted, multimodal approach designed not to achieve immediate wound closure, but rather to stabilize an actively deteriorating inflammatory ulcer during a critical six-week interval in which conventional therapies had repeatedly failed.

The central focus of this report is the discrete treatment phase characterized by the combined use of morphine-infused antibiotic-loaded resorbable calcium sulfate cement, low-pressure extended-interval negative pressure wound therapy delivered through a thermoplastic elastomer interface (PREVENT), and patient-directed antimicrobial irrigation. During this period, the therapeutic goals were deliberately limited to pain control, suppression of local infection, prevention of pathergic progression, and creation of a biologically permissive wound environment. Importantly, the intent was not definitive wound healing, but rather stabilization of a hostile wound state to permit subsequent disease-directed therapy.

Morphine was selected as the local analgesic based on the established biologic rationale for peripheral opioid-mediated analgesia in inflamed tissues and prior clinical experience with topical opioid administration for painful wounds [28–30]. In contrast to shorter-acting local anesthetic strategies, incorporation of morphine into the resorbable calcium sulfate carrier was intended to provide prolonged local exposure while avoiding repeated application to the highly pain-sensitive wound surface. The feasibility of incorporating morphine into calcium sulfate has previously been described in an operative setting [31]. However, to the authors' knowledge, the use of morphine-loaded resorbable calcium sulfate cement as a topical analgesic directly within a chronic wound has not previously been described. Therefore, the pharmacokinetics, elution characteristics, optimal dose, systemic absorption, duration of analgesic effect, and potential tissue toxicity of this specific delivery method remain unknown. No clinically apparent local toxicity attributable to the morphine-containing cement was observed in this case; however, this single observation cannot establish tissue safety or superiority over alternative analgesic approaches.

Pain control proved to be a critical enabling factor. In pyoderma gangrenosum, uncontrolled pain is often both a symptom and a barrier to necessary wound care. Following placement of the morphine-infused calcium sulfate cement, the patient experienced a marked reduction in pain that permitted previously poorly tolerated wound-care interventions to proceed. The calcium sulfate material fully dissolved over approximately 3–4 weeks; however, the pharmacokinetics, morphine-elution profile, and duration of local opioid exposure from this delivery method were not measured. Accordingly, the observed clinical analgesic response should not be interpreted as establishing sustained morphine delivery throughout the entire period of cement resorption. To the authors' knowledge, this represents the first reported use of morphine-infused resorbable calcium sulfate cement in lower-extremity wound care as a local analgesic adjunct.

The analgesic effect observed during the stabilization phase in this case is supported by a growing body of evidence demonstrating that opioid receptors are expressed on peripheral sensory neurons, keratinocytes, endothelial cells, and immune cells within inflamed and injured skin. Under conditions of tissue injury and inflammation, these peripheral opioid receptors become functionally active, allowing locally delivered opioids to exert analgesic effects without reliance on central nervous system signaling [28–30]. Clinical studies evaluating topical morphine applied to painful cutaneous wounds have

demonstrated clinically meaningful reductions in pain scores with minimal detectable systemic absorption, supporting a predominantly local mechanism of action [30]. Preclinical investigations further suggest that peripheral opioid signaling may modulate neurogenic inflammation and endothelial activity, providing analgesia while permitting progression of granulation and tissue stabilization when appropriately timed and dosed [30].

Calcium sulfate represents a favorable delivery matrix for this application due to its predictable resorption, customizable surface area, and long-standing clinical use as a local antibiotic carrier in musculoskeletal and soft-tissue settings. The feasibility of combining morphine with antibiotic-loaded calcium sulfate cement has been demonstrated in spine surgery, where intraoperative placement of analgesic calcium sulfate beads containing morphine resulted in improved postoperative functional outcomes and reduced hospital length of stay compared with controls [31]. Although that work focused on postoperative spinal pain rather than wound care, it provides proof of concept for the feasibility of incorporating morphine into calcium sulfate as a local analgesic delivery strategy. To the authors' knowledge, the present case represents the first reported application of this strategy in lower-extremity inflammatory wound care, where pain itself frequently constitutes the primary barrier to effective therapy.

Local anesthetics represent another potential strategy for peripheral pain control; however, their use in chronic wounds is accompanied by important limitations. Multiple in-vitro and in-vivo studies have demonstrated that commonly used agents such as lidocaine, bupivacaine, and ropivacaine can exert dose- and duration-dependent cytotoxic effects on keratinocytes, fibroblasts, endothelial cells, muscle, and cartilage. These effects include mitochondrial dysfunction, induction of apoptosis, and impaired cellular proliferation, raising concern that prolonged or repeated exposure within an open wound environment may impede tissue repair and granulation [32–34]. While short-duration or low-dose exposure to local anesthetics is generally well tolerated in surgical settings, their pharmacologic profile is less favorable for sustained analgesia in chronically inflamed wounds.

In contrast, peripherally acting opioids may provide prolonged analgesia without direct membrane toxicity when delivered locally at controlled concentrations. In this case, the intent of local opioid delivery was not to accelerate wound closure, but rather to interrupt pain-driven escalation, limit pathergic progression, and permit tolerance of low-trauma wound care. Viewed in this context, morphine-infused calcium sulfate cement functioned as an enabling intervention that allowed stabilization of a hostile inflammatory wound long enough to safely transition to definitive immunosuppressive therapy.

In this case, direct contact between the PREVENT TPE interface and the antibiotic- and morphine-loaded calcium-sulfate cement was well tolerated, without an observed adverse interaction between the materials. Importantly, the cement was not left undisturbed beneath the dressing for the duration of therapy. At each dressing change, residual cement was removed, the wound was irrigated, and the remaining cement was reapplied; this process continued until the calcium-sulfate material had fully dissolved. Although no clinically apparent incompatibility was observed, this represents an observation from a single case and should not be interpreted as establishing material compatibility.

Extended-interval, low-pressure NPWT delivered through a thermoplastic elastomer interface further minimized mechanical trauma during this vulnerable period. Traditional reticulated open-cell foams necessitate higher negative pressure settings and are associated with tissue ingrowth, increased pain at dressing changes, and frequent dressing disruption. In contrast, the non-porous design and low resistance flow characteristics of the thermoplastic elastomer interface enabled effective exudate evacuation at 50 mmHg, reduced compressive forces at the wound surface, and allowed dressing intervals to be safely

extended. This biomechanical shift was particularly advantageous in a pathergy-prone wound where repeated manipulation had previously resulted in ulcer expansion.

Pain associated with NPWT may arise through multiple mechanisms, including tissue ingrowth and adherence at the wound–dressing interface, as well as mechanical deformation and tissue strain generated during application of negative pressure. In this case, the TPE wound interface was selected in part to minimize adherence to the wound bed and associated dressing-change trauma. Additionally, the use of lower negative pressure (−50 mmHg) was intended to reduce pressure-dependent discomfort, mechanical stress, and excessive centripetal edge contraction while maintaining wound fluid evacuation. Lower suction may also theoretically reduce focal tissue compression and associated microvascular perfusion compromise at the wound margins, particularly over bony prominences or areas with limited soft-tissue coverage. Although the patient demonstrated improved tolerance with this approach, perfusion was not directly measured, and the relative contributions of the TPE interface and reduced negative pressure cannot be independently determined from a single case.

The patterned appearance of the wound bed immediately following dressing removal may represent visible surface deformation produced by transmission of negative pressure through the TPE interface. Although this observation is consistent with the concept of microdeformation associated with NPWT, microdeformation was not directly measured or histologically evaluated in this case. Importantly, clinically significant tissue ingrowth into the TPE dressing was not observed, and the patterned appearance was transient following removal of negative pressure.

Equally important was the ability to maintain ongoing antimicrobial exposure through a patient-directed irrigation technique without dismantling the NPWT construct. Conventional NPWT instillation systems often require automated cycling, specialized components, and frequent dressing access, which may be impractical or poorly tolerated in inflammatory ulcers. The configuration described in this case allowed controlled, low-volume irrigation of chlorhexidine-based solution through a stable dressing seal, facilitating suppression and eventual clearance of multidrug-resistant *Pseudomonas aeruginosa* within six weeks. This outcome underscores the value of preserving dressing integrity while maintaining antimicrobial control in wounds where repeated access carries inherent risk.

This irrigation technique should be distinguished from conventional NPWT with automated instillation and dwell time (NPWTi-d). In the configuration used in this case, the patient manually introduced a controlled volume of irrigation solution through a secondary access port while leaving the NPWT dressing construct intact. Negative-pressure suction was temporarily paused during the approximately 90-s contact period and then resumed. This approach permitted repeated patient-directed wound irrigation without requiring dressing removal or a dedicated automated NPWTi-d system. However, the optimal irrigation volume, contact time, frequency, and comparative efficacy of this technique have not been established and warrant further investigation.

Whether a similar approach could be successfully implemented using conventional collapsible foam or gauze NPWT interfaces was not evaluated in this case. The TPE interface was selected specifically because minimizing tissue ingrowth, wound-bed adherence, and mechanical trauma during dressing removal was considered particularly important in this patient with severe pain and a propensity for pathergy. Although conventional NPWT interfaces may permit similar delivery of negative pressure, they should not be assumed to provide the same wound-interface characteristics or treatment tolerance observed with the TPE dressing. Comparative evaluation would be necessary to determine whether the clinical benefits observed in this case are attributable specifically to the TPE interface or could be reproduced using other NPWT wound-contact materials.

A defining feature of this case is the intentional transition point at which immunosuppressive therapy was initiated. Once the wound demonstrated clinical stability, pain control, and resolution of active infection, topical tacrolimus and systemic cyclosporine therapy were introduced to address the underlying inflammatory disease process. In this case, immunosuppressive therapy was introduced after mechanical and infectious destabilizers were controlled, once the wound demonstrated clinical stability and improved tolerance of local wound care. The six-week stabilization window created by the described approach allowed this transition to occur without precipitating further tissue loss.

It is important to emphasize that this report does not seek to claim definitive wound healing as its primary outcome. Instead, the clinical success of this case lies in the conversion of an actively deteriorating, pain-limited, infected ulcer into a stable, infection-free wound capable of tolerating disease-modifying therapy. In this context, wound closure becomes a downstream objective rather than the immediate measure of success. By reframing treatment goals around stabilization rather than closure, clinicians may expand the range of feasible interventions in patients with pathergy-prone inflammatory wounds.

Although this multimodal approach was employed in the setting of pyoderma gangrenosum, several components may have applicability to other complex wounds. The nonadherent TPE interface and lower-pressure NPWT may be particularly useful when conventional NPWT is limited by pain, tissue adherence, or concern for mechanical stress and perfusion compromise at the wound margins. Likewise, the dual-tubing irrigation technique may offer an alternative approach for wounds requiring irrigation while preserving the NPWT dressing construct between treatments. Resorbable calcium-sulfate cement may provide an additional platform for localized therapeutic delivery in appropriately selected wounds. These principles may potentially translate to other complex wound etiologies, including diabetic, postoperative, traumatic, and other difficult-to-heal wounds. However, the modalities described in this report were used concurrently in a single patient with pyoderma gangrenosum; therefore, their individual contributions and applicability to other wound populations cannot be established from this case alone and warrant further clinical investigation.

As a single-case report, this experience has inherent limitations, including the inability to isolate the relative contribution of each intervention. Nonetheless, the clear temporal association between the combined intervention and wound stabilization suggests a potential framework for managing similar cases. Further investigation is warranted to evaluate the broader applicability of local analgesic delivery platforms, thermoplastic elastomer NPWT interfaces, and patient-directed irrigation strategies in inflammatory wound care.

4. Conclusions

This case demonstrates that a focused, time-limited wound stabilization strategy may play an important role in the management of pathergy-prone pyoderma gangrenosum affecting the lower extremity. By emphasizing sustained local analgesia, minimization of mechanical trauma, preservation of perfusion, and continued antimicrobial control, a painful and actively worsening ulcer was transitioned into a clinically stable, infection-free state that could tolerate initiation of disease-directed immunosuppressive therapy. In this context, clinical success was defined not by immediate wound closure, but by interruption of pain-driven deterioration and pathergic progression that had previously limited effective care.

To the authors' knowledge, this represents the first reported use of morphine-infused resorbable calcium sulfate cement as a local analgesic adjunct in lower-extremity wound care. When combined with low-pressure extended-interval negative pressure wound therapy delivered through a thermoplastic elastomer interface and patient-directed antimi-

crobial irrigation, local analgesic delivery appeared to function as an enabling component of wound stabilization rather than as a stand-alone intervention. While further study is needed to evaluate broader applicability, this case suggests that prioritizing stabilization and tolerance of therapy may be a reasonable interim goal in the management of complex inflammatory wounds where pain and pathergy are the primary barriers to care.

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Institutional Review Board Statement: Formal institutional review board approval was not required for this single-patient case report. The report describes the clinical course and treatment of an individual patient and was not conducted as a systematic investigation designed to develop or contribute to generalizable knowledge as defined under 45 CFR 46.102 (L). No prospective research protocol, randomization, or research-directed alteration of patient management was undertaken.

Informed Consent Statement: Written informed consent was obtained from the patient for the off-label therapeutic interventions described in this case report. Written informed consent was also obtained from the patient for publication of the clinical course and accompanying clinical and histopathologic images.

Data Availability Statement: No datasets were generated or analyzed during the preparation of this case report. Data supporting the reported findings are contained within the article. Additional information is available from the corresponding author upon reasonable request, subject to privacy and ethical restrictions.

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