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Negative Pressure Wound Therapy in Pyoderma Gangrenosum Treatment

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Patient: Male, 83-year-old
Final Diagnosis: Pyoderma gangrenosum
Symptoms: Infection
Medication: —
Clinical Procedure: Negative pressure wound therapy
Specialty: Dermatology • Geriatrics • Palliative Medicine • Surgery

Objective: Rare disease

Background: Pyoderma gangrenosum (PG) is a rare, non-infectious, fulminant dermatosis of the skin. The lack of objective diagnostic criteria requires differential diagnosis and exclusion of extensive ulcerative skin diseases. Currently, treatment includes a combination of systemic steroids, immunosuppressants, and topical agents, but after decades of research, no clear scientific evidence exists for a criterion standard treatment. The use of NPWT (negative pressure wound therapy) effectively reduces the wound area, eliminates exudate, and reduces bacterial titer, thereby stimulating neoangiogenesis.

Case Report: We present the case of an 83-year-old man with confirmed pyoderma gangrenosum. In the examination, a pink-red wound was observed, measuring 5×15 cm, II/III° according to National Pressure Ulcer Advisory Panel (NPUAP), covered with a non-physiological, crusty (scar-like) epidermis, from under which a foul purulent discharge emerged when pressed. NPWT therapy was started in August. During this period, wound healing was observed, without signs of undermining. After 52 days of treatment, NPWT was completely discontinued. Further local actions were then carried out using specialized dressings and periodic tacrolimus.

Conclusions: We observed the positive effect of NPWT on the wound, which, together with doxycycline treatment, led to the elimination of purulent exudate from the wound and inhibition of wound enlargement. The use of NPWT as a supportive method in the treatment of PG wounds is safe and effective, and it can be successfully used in nursing.

MeSH Keywords: Negative-Pressure Wound Therapy • Palliative Care • Pyoderma Gangrenosum

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Background

The growing number of elderly, sick, and disabled people with diverse and complex needs and higher expectations for health care has led to changes in interdisciplinary team activities. Many chronically ill patients want to remain in the home environment, among their immediate family, from whom they expect to receive support and non-professional care. Professional care can be provided at a high level in the patient's home as part of long-term or palliative care [1].

The occurrence of wounds of various etiologies in the elderly is common. Given the coexisting chronic diseases and limitations in self-care, chronic wound treatment is not always standard and radical [2]. Pyoderma gangrenosum (PG) is a rare, non-infectious, fulminant dermatosis of the skin. It is classified as an "orphan disease" because of its rarity. Newly diagnosed cases account for 3–10 cases per million annually, of which 50–70% are patients with autoimmune diseases (usually inflammatory bowel disease and rheumatoid arthritis) or hematological disorders (e.g., leukemia and lymphoma) [3,4]. The lack of objective diagnostic criteria requires differential diagnosis and the exclusion of extensive ulcerative skin diseases. PG is still a clinically difficult to treat and often misdiagnosed disorder [5]. Initial symptoms can include papules, vesicles, or pustules, which then transform into ulcerations with features of undermining and rapid destruction of the skin, as much as 1 to 2 cm daily [6]. Currently, treatment includes a combination of systemic steroids, immunosuppressants, and topical agents, but after decades of research, no clear scientific evidence exists for a criterion standard treatment. Systemic corticosteroids, immunosuppressants, and biological agents are the most commonly used and effective [7]. Systemic treatment is often combined with local treatment (e.g., steroid preparations, immunosuppression [tacrolimus] and mesotherapy), minimizing wound infection [8]. Negative pressure wound therapy is a physical method of wound treatment. It is a recognized and accepted method of treatment for open wounds of various etiologies that can be used both in the hospital and at home. NPWT requires creating a vacuum (70–150 mmHg on average) in the wound area, thus eliminating excess exudate together with microorganisms and increasing blood flow in the wound region. The latter accelerates the migration of fibroblasts and speeds regenerative processes within the wound [9–11]. The aim of this study was to assess local treatment of PG using NPWT in an elderly patient.

Case Report

The patient was an 83-year-old man with concomitant chronic lymphocytic leukemia, persistent atrial fibrillation, iron deficiency anemia (4.0 µmol/l [8.8–32.4 µmol/l], red blood cells (RBC) 2.72 mln/µl [4.00–5.5 mln/µl], hemoglobin (HGB) 9.1 g/dl [12.0–18.0 g/dl], white blood cell (WBC) 4300/µl [4000–10 000/µl] and hematocrit (HCT) 26.5% [36.0–55.0%]), CRP (C reactive protein – 58 mg/l [0–5 mg/l]), and 25 points on the Barthel scale, which indicates "severe" dependency. In August 2016, he had a pacemaker fitted, and shortly after its implantation a fulminant wound developed in the left subclavian area. The pacemaker was removed, and an unsuccessful attempt to heal the wound was made. Histopathological assessment of the wound and its margins confirmed non-specific tissue necrosis and inflammatory infiltration, mainly composed of lymphocytes and neutrophils. The patient was consulted dermatologically and surgically, and local wound dressings, antiseptics, and tacrolimus (Protopic 0.1%) were used. No decision was made regarding cyclosporin treatment because of the risk of renal failure and the patient's age (creatinine 119 µmol/l [53–115 µmol/l]). In the examination, a pink-red wound was observed, measuring 5×15 cm, II/III° according to National Pressure Ulcer Advisory Panel (NPUAP), covered with a non-physiological, crusty (scar-like) epidermis, from under which a foul purulent discharge emerged when pressed (Figure 1).

Figure 1. Wound before starting NPWT therapy (1 August 2017).

The margins of the wound were undermined and irregular with increased soreness of the wound and skin around it (NRS 4–6 points). In July 2017, the patient was qualified for ongoing research on the use of innovative and alternative methods of wound care in long-term/palliative care implemented at the University of Rzeszów (Poland). The patient's condition was assessed, biochemical control was recommended, and a swab was taken. On the culture report from 20 July 2017,

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Figure 2. Pyoderma gangrenosum. Patient before application of negative pressure wound therapy (NPWT) (**A**), after 5 weeks of NPWT (**B**), after removing NPWT from the skin graft (5 days after skin grafting) (**C**), and at follow-up 6 weeks after skin grafting (**D**).

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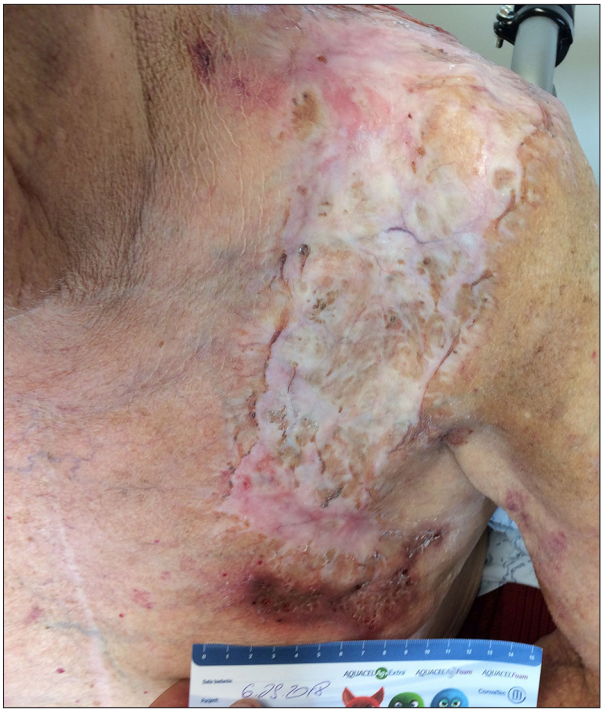

Figure 3. Skin condition on September 9 2018. Non-physiological folded epidermis reminiscent of a scar after a burn is noticeable. The duration of care was 9 months.

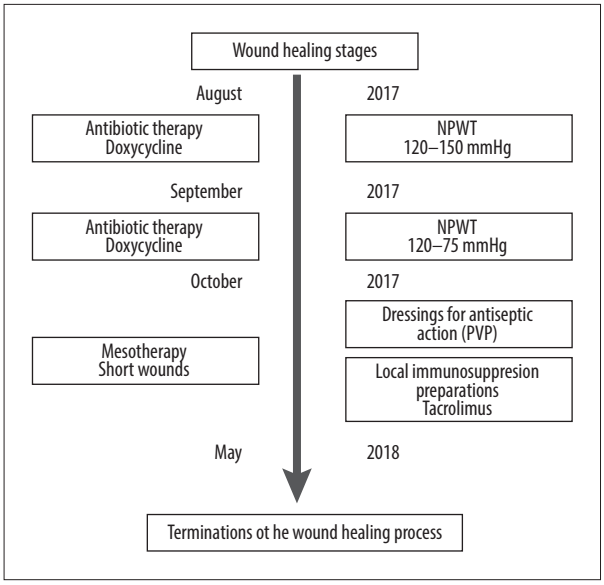

Figure 4. Stages of wound treatment.

methicillin-resistant *Staphylococcus aureus* (MRSA) (++++) sensitive to doxycycline, gentamicin, and amikacin was grown. It was proposed to use NPWT on the wound to eliminate the purulent exudate. On 1 August 2017, NPWT therapy was started. The ActiVac system (KCI, San Antonio, USA) was set up, with the vacuum set at 125 mmHg in continuous mode; Inadine® (Aspirionix, Poland) was used as the dressing. Painkiller treatment with paracetamol/tramadol (37.5 mg/325 mg) at a dose of 2 tablets daily and on an ad hoc basis prior to dressing changes was maintained. NPWT dressings were changed every 3–5 days. The amount of exudate varied in the first week of therapy, with 100–150 ml of bloody purulent discharge per day. On 15 August 2017, the vacuum was increased to 150 mmHg due to the retention of secretions in the lower pole of the wound (Figure 2), and a biochemical analysis was performed. Due to low morphotic values (HGB 8.4 g/dl [12.0–18.0 g/dl]), the patient was referred to the hospital, where he stayed for 8 days, during which NPWT was continued. On 27 August 2017, a red wound, II/III° in NPUAP, with 250 ml of bloody purulent discharge was drained, and it was recommended to change the dressing to Protopic 0.1%, with the vacuum set at 75 mmHg due to increased local soreness. From 31 August 2017 to 19 September 2017, the patient took doxycycline 2×100 mg for 7 days, then 1×100 mg for 14 days. During this period, wound healing was observed without signs of undermining. After 52 days of treatment (06/09/2017), NPWT was completely discontinued (the wound condition is presented in Figure 2). Further local actions were then carried out using specialized dressings and periodic tacrolimus (Protopic® 0.1%), with close monitoring for potential infection and the features of wound undermining suggestive of lymphocytic infiltration. Wound treatment was terminated in May 2018. However, observations and minor therapeutic and nursing activities were carried out until September 2018 (Figure 3). The whole process of wound management and treatment is shown in Figure 4.

Discussion

Accurate clinical examination and macro- and microscopic assessments are a key element of diagnostics. Quick diagnosis provides the basis for effective and targeted treatment. The basic form of empirical treatment of PG is long-term use of systemic immunosuppression and corticosteroids. Whereas corticosteroids and cyclosporine were previously considered first-line treatments, the emergence of TNFα inhibitors is transforming the therapeutic ladder, with infliximab being the only systemic agent with level I evidence supporting its use for the treatment of PG [12]. Surgical treatment is risky and controversial due to the phenomenon of patergism, resulting in the formation of new lesions or rapid expansion of an existing ulcerative wound in response to any type of injury, as well as due to surgical activity [13]. According to Goshtasby et al., surgical treatment is possible only in a small group of patients [14], stressing that 30–60% of patients are at risk of recurrence. Therefore, surgical interventions may fail, especially without the implementation of immunosuppressive therapy aimed at reducing the risk of patergism and treatment failure. PG ulcers without skin grafts require long healing and conservative management, during which the risk of wound infection

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is high and is a clinical problem for medical staff. In the case discussed here, the option of surgical intervention was abandoned due to the old age and generally poor clinical condition of the patient, which disqualified him from immunosuppressive treatment. Long-term systemic immunosuppressive therapy is associated with adverse reactions in approximately 65% of patients [15,16]; therefore, local immunosuppressive effects are preferred in high-risk patients. Tacrolimus, which has an immunosuppressive effect that inhibits lymphocyte proliferation, can be successful as local treatment [17,18]. Medical devices with antiseptic and exudative effects (alginates, hydrofibers, and foams) play a secondary role and should not be the basis for local treatment due to the pathogenesis of the disease. Reducing the bacterial count in the wound is crucial to prevent infection by skin-colonizing bacteria. The use of doxycycline in the treatment of PG is justified, but risky if kidney function is damaged. Monitoring the patient's condition and control of fluid balance, as well as periodic control of glucose-6-phosphate dehydrogenase and creatinine levels during systemic therapy, allows for safe treatment and is especially important with dapsone therapy [19]. The literature demonstrates that systemic corticosteroids (prednisone 0.5–1 mg/kg/day or methylprednisolone up to 0.8 mg/kg/day) are effective in many cases and are a common first-line systemic therapy. Infliximab, an anti-TNFα monoclonal antibody binding both soluble and membrane-bound TNFα, is the only biologic that has shown efficacy in classic PG in a randomized, double-blind, controlled trial (level I evidence) [20]. Other immunosuppressive therapies, including mycophenolate mofetil, methotrexate, and azathioprine, have been used with some success in PG, but are generally considered most effective as adjunctive treatments. Unfortunately, this form of treatment was not implemented in the present case [21]. In our patient, doxycycline was used at a dose of 2×100 mg for 7 days, followed by 1×100 mg for 14 days. Significant improvement associated with the lack of undermining and wound widening with decreases in the exudate and wound area were observed during this period. Garg and Leiphart made a similar observation [19,22]. After this period, therapy was discontinued after consultation with a nephrologist. Mesotherapy of the wound margins with a corticosteroid preparation was then begun (Diprophos®, sodium salt of betamethasone phosphate). It was first initiated every 2 weeks (1 amp, 6.43 mg betamethasone dipropionate) for 6 weeks, then once every 4 weeks (1 amp). Mesotherapy was carried out until the undermining of the wound margins was inhibited. The preparation used has strong anti-inflammatory, immunosuppressive, and anti-allergic effects. These properties are due to mechanisms associated with limiting the number of active immune cells within the inflammatory focus, reducing vasodilatation, stabilizing lysosomal membranes, and inhibiting phagocytosis, as well as inducing the expression of prostaglandins and related substances.

Surgical procedures in an elderly patient with multiple system failure are particularly prone to failure and can be life-threatening [21]. The local actions taken, recommended by consultants, were typical for palliative care. The inability to include immunosuppressants and corticosteroids by the systemic route disqualified this patient from a radical course of action and required palliative treatment. Considering the general condition of the patient, his age and pain felt due to the chest injury, and foul exudate, decisions were made to attempt topical treatment using NPWT.

The use of NPWT effectively reduces the wound area, eliminates exudate, and reduces bacterial titer, stimulating neoangiogenesis. The effect of hypotension in wounds of various etiologies has been described by many authors [22,23]. In a study by Neiderer et al. [13], NPWT was used as a supportive method in treating PG wounds, with good effects. Our own observations demonstrate the positive effect of NPWT on a wound, which, together with doxycycline treatment, led to the elimination of purulent exudate from the wound and the inhibition of wound enlargement. These actions contributed to wound healing, as well as improved quality of life by reducing pain and eliminating the foul smell. Neither skin irritation by the foil nor patergism were observed during NPWT. Banasiewicz, a pioneer of vacuum therapy in Poland, points out that this form of local treatment is safe and minimally invasive, but is still expensive and not covered by insurance [24]. In the present case, the cost of local NPWT was a secondary problem for the family and the patient, as the positive effects and reduction of troublesome symptoms were noticed, which allowed him to function better in the home environment.

Conclusions

The use of NPWT as a supportive method in the treatment of PG wounds is safe and effective, and it can be successfully used by specialized nursing staff.

Acknowledgments

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Institution where work was done

Center for Innovative Research in Medical and Natural Sciences, University of Rzeszów, Poland.

Conflict of interest

None.

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