CASE REPORT

A favourable response to surgical intervention and hyperbaric oxygen therapy in pyoderma gangrenosum

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Key words
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Abstract
Pyoderma gangrenosum (PG) is a neutrophilic dermatosis characterised with ulcerations. Inflammatory bowel diseases (ulcerative colitis and Crohn’s disease) and haematologic diseases (leukaemia, preleukaemia and monoclonal gammopathy) have been reported in about 40–50% of PG patients in whom the treatment of the underlying disease is important for the improvement of the lesions. We herein report a colorectal adenocarcinoma patient with PG, who responded partially to topical treatments and systemic immunosuppressants and healed completely with the aid of surgical wound repair and hyperbaric oxygen therapy.

Case
A 45-year-old man was referred to our clinic with expanding ulcers on his left leg despite treatment with various topical and systemic antibiotics with a 9-month history. He was injured accidentally by a chain saw and was administered first aid by surgeons at the emergency service. Seventeen days after the removal of sutures, small ulcers began to develop on the suture area and enlarge gradually. Ulcerations were very painful and the patient was highly distressed. Various local and systemic antibiotics were given, despite which no microorganism could be found in cultures and no improvement was observed.

He had also been diagnosed with colorectal adenocarcinoma a year ago and received chemotherapy with a combination of bevacizumab–irinotecan, folinic acid and 5-fluorouracil. However, he was medication-free for last 3 months, because oncologists following up him considered that immunosuppression would deteriorate wound healing.

The results of routine liver and kidney function tests were within normal limits. The consecutive tests of serum glucose levels, erythrocyte sedimentation rates and acute phase reactants were all normal. Repeated periphere artery examinations and arteriovenous doppler ultrasonography required by the surgeons showed no pathological findings. The culture specimens taken from the ulcerous area and the hepatitis markers yielded negative results. Electromyelographic examination of the neuronal transmission on the lower extremities was normal. General physical examination was normal.

Key Messages
- pyoderma gangrenosum (PG) is a rare, inflammatory, neutrophilic skin disease of unknown origin which can be accompanied with malignant gastrointestinal tumors
- trauma is a trigger factor for PG which may lead to immunological abnormality characterized by exaggerated responses such as “pathergy phenomenon”
- thus, surgical intervention for PG is generally avoided due to the pathergy phenomenon
- conventional therapy with immunosuppressants and anti-inflammatory agents are fundamental for the treatment
- hyperbaric oxygen therapy has been recently shown to be effective for PG patients with recalcitrant ulcers
- our case showed that the combination of surgical intervention and hyperbaric oxygen therapy can be successfully used as an adjunctive therapy for refractory PG lesions

Dermatological examination showed four well-demarcated, linearly arranged various-sized ulcers ranging from 6 to 10 cm in size, with necrotic base, and raised erythematos border on the posterior surface of his leg.

A punch biopsy was taken from one of the ulcers, with a preliminary diagnosis of pyoderma gangrenosum (PG). Histopathological examination of tissue specimen showed superficial fibrin and debris, capillary vessel proliferation in the dermis, pink amorphous material in vessel lumen and
mixed-type inflammatory cell infiltration with predominance of neutrophils around the vessels. All special stains performed for infectious organisms showed negative results. The findings were assessed to be indicative of PG.

Clinical and histopathological evaluations led to the final diagnosis of PG and prednisolone (100 mg/day) was initiated after consulting with the patient’s oncologist. In addition, an ointment including collagenase that provides enzymatic wound debridement was applied topically. Of the four PG ulcers, two smaller ones completely healed at the end of one month and slight improvement was observed in the other ulcers. While the prednisolone was tapered, however, the two remaining ulcers coalesced and became one larger ulcer in a month (Figure 1). Considering the long-term side effects, steroid therapy was stopped and 200 mg daily cyclosporine was initiated. Cyclosporine dose was reduced to 150 mg/day on the 20th day of the therapy because of the increase in serum creatinin levels (Figure 2). Improvement was no longer observed and the cyclosporine was stopped. The patient was referred to plastic surgeons, and primary wound repair was decided upon to accelerate healing process. After the surgery, hyperbaric oxygen (HBO) therapy protocol consisting of 15 sessions for a total of 30 hours at 2.5 ATA (atmosphere absolute) was started. He did not receive any other local or systemic treatment during HBO therapy. The patient tolerated the therapy well and no side effects were seen. The ulceration completely healed in 2 months (Figure 3). One year since and the patient is still under surveillance and no recurrence has been observed.

Discussion

PG is a rare, inflammatory, neutrophilic skin disease of unknown origin. Several clinical variants of PG such as classic, pustular, and bullous have been described (1). The classic form, as in our patient, presents with rapidly expanding ulceration characterised by raised, violaceous border with a swollen necrotic base. Although typical morphology of ulcers in this form help to diagnose this entity, it occasionally poses a diagnostic challenge. Exclusion of other possible disorders which are considered in differential diagnosis provides benefit in these cases. Despite the non-specific histologic findings of PG, histopathologic examination can help to differentiate other causes of ulceration that may be bacterial or mycobacterial infections, malignancy, vasculitis and vascular insufficiency (1,2). All the aforementioned causes were excluded in our case by histopathological, microbiological and radiological examinations.

The aetiology of PG still remains unknown, but the common combination with systemic diseases suggests an underlying immunological abnormality. PG is known to be associated with an underlying disease in 40–50% of cases, especially with inflammatory bowel disease, arthritis and haematologic diseases (1). In our patient, PG was accompanied with colorectal adenocarcinoma. In the literature, a small number of PG cases have been reported in association with malignant gastrointestinal tumours (2–6). In our patient, PG occurred 3 months after the diagnosis of colorectal adenocarcinoma.
that seems to be relevant. Moreover, trauma may induce lesions and this is called pathergy phenomenon. Both of them existed in the patient. It is very probable that trauma has been a trigger factor for PG to occur with the underlying gastrointestinal malignancy, which might lead to immunological abnormality characterised by exaggerate responses to non specific stimuli (7).

As the pathogenesis is not well understood, there is not a specific treatment or guideline for PG (1). Treatment of underlying disease may result in improvement of PG lesions (8). Prednisolone is regarded as the main choice of the therapy considering its fast efficiency and cost-effectiveness. Cyclosporine, colchicine, dapsone, methotrexate, azathioprine, IVIG or plasmapheresis can also be used in PG (9). In our case, two of the ulcers healed with systemic corticosteroid therapy but two remaining were refractory. The dose of alternative treatment option cyclosporine had to be reduced because of its side effects, and neither improvement nor expansion was therefore observed.

As for surgical intervention for PG, it is generally avoided because of the pathergy phenomenon. The development of new lesions or aggravation of existing ulcerations with even minor traumas is a characteristic feature in pathergy phenomenon (10). Thus, conservative therapy with immunosuppressants and antiinflammatory agents, mainly systemic corticosteroids, are fundamental for the treatment. While surgical intervention or debridement worsens PG, in selected cases, non-aggressive surgical debridement may be helpful for cleaning ulcers and avoiding bacterial growth (11). Moreover, split skin grafts have been used successfully in some patients (12). According to current literature, surgical therapy should be given adjunct to systemic therapy in patients with stable disease (13). Saracino et al. reported that no pathergy or flare was observed in the ten patients who received 16 surgical procedures (14).

In several case studies in the literature, HBO therapy, that is increasingly used for a variety of medical conditions as primary or adjunctive therapy, has been shown to effectively treat PG ulcers and reduce pain associated with PG (15). In our case study, dramatic clinical response was obtained by the combination of surgery and then HBO therapy. Exacerbation or development of new lesions was not observed after the treatment.

Our case study showed a favourable response to the combination of surgical intervention and HBO therapy following immunosuppressant therapy. In conclusion, surgical primary wound repair and HBO therapy together may be thought of as an alternative treatment method in difficult PG cases. Yet, further clinical studies are needed to highlight the real benefits of adjuvant HBO therapy after surgery in patients with PG.

References


