Successful low-dose corticosteroid treatment of aggressive pyoderma gangrenosum with irritable bowel syndrome: a case report

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Abstract
Pyoderma gangrenosum (PG) is a rare and chronic neutrophilic dermatosis with a global prevalence estimated at two to 10 cases per million population annually (1). Although the disease can occur in both sexes, it is slightly more common in women, especially in the 4th and 5th decades (2). The exact etiopathogenesis of PG is yet to be established (3, 4). The disease is characterized by the appearance of sterile pustules containing neutrophilic granulocytes that rapidly enlarge and evolve into large, painful ulcers with violaceous borders. Approximately 50 to 70% of all PG cases are accompanied by systemic diseases such as inflammatory bowel disease (IBD), rheumatoid arthritis, ankylosing spondylitis, psoriasis, monoclonal gammopathy, leukemia, myelodysplasia, lymphoma, Behçet’s disease, Sweet’s syndrome, hepatitis, human immunodeficiency virus infection, systemic lupus erythematosus, Takayasu arteritis, thyroid diseases, or diabetes (1, 4, 5).

The diagnosis of PG is often made clinically after repeated failure of antibiotic therapy and surgical debridement, whereby lesions will usually worsen (6). The management of aggressive PG is through a combination of adequate wound care and systemic therapy using high-dose corticosteroids, with an equivalent to prednisone 40 to 120 mg/day being preferred (5–7). However, this can lead to side effects such as gastrointestinal bleeding, especially in patients with autoimmune diseases such as inflammatory bowel disease (IBD). We report the case of a 54-year-old female patient with PG that was initially misdiagnosed as cellulitis and furunculosis along with IBD. She was treated using a low-dose regimen of methylprednisolone, which resulted in significant clinical improvement and complete resolution after 2 months of therapy.

Keywords: pyoderma gangrenosum, inflammatory bowel disease, low dose, corticosteroids, dermatology

Introduction
Pyoderma gangrenosum (PG) is a rare and chronic neutrophilic dermatosis with a global prevalence estimated at two to 10 cases per million population annually (1). Although the disease can occur in both sexes, it is slightly more common in women, especially in the 4th and 5th decades (2). The exact etiopathogenesis of PG is yet to be established (3, 4). The disease is characterized by the appearance of sterile pustules containing neutrophilic granulocytes that rapidly enlarge and evolve into large, painful ulcers with violaceous borders. Approximately 50 to 70% of all PG cases are accompanied by systemic diseases such as inflammatory bowel disease (IBD), rheumatoid arthritis, ankylosing spondylitis, psoriasis, monoclonal gammopathy, leukemia, myelodysplasia, lymphoma, Behçet’s disease, Sweet’s syndrome, hepatitis, human immunodeficiency virus infection, systemic lupus erythematosus, Takayasu arteritis, thyroid diseases, or diabetes (1, 4, 5).

The diagnosis of PG is often made clinically after repeated failure of antibiotic therapy and surgical debridement, whereby lesions will usually worsen (6). The management of aggressive PG is through a combination of adequate wound care and systemic therapy using high-dose corticosteroids, with an equivalent to prednisone 40 to 120 mg/day being preferred (5–7). However, this can result in a myriad of potential side effects, such as gastrointestinal bleeding, behavioral changes, sleep disturbances, hyperglycemia, hypokalemia, or infections (8). In addition, surgical intervention should only be performed when lesions are stable, given the pathergy nature of this disease, which can lead to the formation of new lesions (9). To minimize these potential side effects, a treatment regimen of a low-dose corticosteroid can be considered. We report the case of a 54-year-old female patient with PG and IBD that was successfully treated with low-dose methylprednisolone with significant clinical improvement and subsequent resolution after 25 days of treatment.

Case report
A 54-year-old female, who was being treated in the internal medicine ward for IBD, was referred to the dermatology department with a painful wound on her posterior trunk that had developed 7 days prior (Fig. 1A–D). The lesion initially appeared as a small pimple that enlarged and ruptured, forming an ulcer. The patient also complained about a painful lump filled with clear yellow pus along with crust on her knee (Fig. 2A–D). In addition, tense bullae were observed on the left leg; these ruptured, forming a large ulcer along with pus and crusting 3 days prior to referral (Fig. 3A–C). The patient experienced no fever or pruritus. Her medication and allergy history were unremarkable. The diagnosis of IBD was confirmed through endoscopy examination and histopathology.

Dermatological examination found nodules and ulcers along with pus on the posterior trunk, and hypopyon bullae were found on the medial malleolus of the left foot and on the right thumb. The patient was initially diagnosed with cellulitis and furunculosis, and she was treated with systemic and topical antibiotics. However, the patient showed no improvement after 2 days of treatment, and new lesions in the form of erythematous and painful nodules appeared on the patient’s left knee that ruptured 2 days later, forming new ulceration. Subsequently, pus, tissue, and blood cultures showed no bacterial growth. PG was then suspected, and the diagnosis was confirmed after a biopsy was performed, in which the histopathology found superficial dermal and epidermal necrosis along with numerous neutrophils accompanying perivascular and vascular fibrinoid degeneration as well as erythrocyte degeneration, which supports the diagnosis of PG (Fig. 4). Based on these results and the course of the disease, a diagnosis of aggressive pyoderma gangrenosum was established. The patient was then treated using intravenous methylprednisolone at a low dose of 20 mg twice daily. In addition, topical treatment of
sulfadiazine ointment and a wound dressing using 1:5,000 potassium permanganate solution and Oxoferin solution at night were also given to prevent secondary bacterial infection as well as to promote wound healing. Clinical improvements were observed, and after 2 months of therapy there was complete clinical resolution (Figs. 2E–F, 3D–F).

**Discussion**

The diagnosis of PG in this patient was made based on a history of typical clinical and histopathological features along with a history of IBD as a concomitant disease as well as exclusion from other diseases with similar clinical features (8, 10). Because no diagnostic tests are yet available, diagnostic criteria are divided into major and minor criteria, whereby PG is confirmed if two major criteria and at least two minor criteria are fulfilled. Our patient exhibited two major criteria of painful ulcers with sudden onset without any systemic symptoms and unremarkable drug intake history, as well as confirmation through histopathology to exclude infections, malignancies, and vasculitis. In addition, minor criteria found in this patient included a history of systemic disease of IBD, classic histopathological findings suggestive of PG, and response to corticosteroid treatment (8). IBD is one of the most common diseases associated with PG, most notably the pustular type (11).

In mild cases of PG with superficial ulcers, treatment with topical corticosteroids or intralesional corticosteroids is often sufficient (10, 12). However, in more severe cases, the first-line therapy and mainstay treatment recommended is systemic glucocorticoids used for their anti-inflammatory and immunosuppressive properties either as monotherapy or combined with other immunosuppressive drugs such as cyclosporine and mycophenolate mofetil. Other treatment modalities that can also act as steroid-sparing agents include anti-neutrophilic drugs such as colchicine and dapsone, as well as biologic agents. However, anti-neutrophilic drugs are mainly used as adjunct therapies and have shown limited effectiveness, and biologic treatments such as infliximab are reserved as second-line therapy in cases of failed corticosteroid or cyclosporine treatment (11, 13).

To date there are still no established treatment guidelines for PG, and to our knowledge there are also no publications available regarding the use of low-dose corticosteroids in treatment of aggressive PG. A review article proposed that, in severe cases of PG, corticosteroid treatment is recommended at a dosage of 1 mg/kg/day methylprednisolone followed by 40 to 60 mg prednisone tapered slowly until the patient achieves full clinical resolution (8, 11, 14). A response to systemic glucocorticoids can usually be seen within 1 to 2 weeks of therapy. Another article reported the treatment of PG accompanied by IBD disease using pulse dose methylprednisolone treatment of 500 mg daily for 3 days followed by oral methylprednisolone 80 mg/day, which showed full resolution after 20 days of therapy (15).

However, the risk of gastrointestinal bleeding and perforation can increase by 40% with such a high dosage of corticosteroids (16). In our case, the patient had a history of gastrointestinal bleeding and IBD, and therefore the administration of pulse dose therapy with a high-dose corticosteroid was not feasible. On the other hand, systemic corticosteroid is the only available treatment at our institution in the absence of other treatment modalities such as cyclosporine or mycophenolate mofetil. Therefore, we opted for a low-dose therapy of intravenous 20 mg methylprednisolone twice daily, which is equivalent to 0.9 mg/kg/day. This regimen is also in accordance with corticosteroid therapy for IBD at 1 mg/kg/day (17). After 25 days of treatment, the patient showed significant clinical improvement and complete resolution after 2 months of treatment, indicating the potential use of low-dose corticosteroid treatment as an option for treatment of aggressive PG with fewer side effects that can be utilized in a resource-scarce setting. However, further research is still needed in this regard.

**Conclusions**

Low-dose corticosteroids have shown good therapeutic results in the treatment of aggressive PG and can reduce the potential side effects related to high-dosage use of corticosteroid therapy as commonly used for treatment of PG such as gastrointestinal bleeding. This can be beneficial in patients with concomitant autoimmune diseases such as IBD.
Figure 2 | Evolution of an erythematous bump that rapidly evolved into ulcers along with pus and crusting (A–D) and clinical improvement after low-dose corticosteroid therapy (E–F).

Figure 3 | Tense bullae on the left leg that ruptured into a large ulcer along with pus and crusting (A–C); clinical improvements after low-dose corticosteroid therapy (D–F).
References


Figure 4 | Superficial dermal and epidermal necrosis along with numerous neutrophils accompanying perivascular and vascular fibrinoid degeneration as well as erythrocyte degeneration (A–D).