Mycophenolate Mofetil Is an Effective Treatment for Peristomal Pyoderma Gangrenosum

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

An 18-year-old woman with Crohn disease was referred by her gastrointestinal surgeon for treatment of possible peristomal pyoderma gangrenosum (PPG). She had undergone a total proctocolectomy with ileoanal anastomosis when she was 10 years old. Her inflammatory bowel disease (IBD) had been quiescent for a few years; however, she had an acute onset of anal fistulas and pouchitis, which led to a revision of the S pouch and an ileostomy formation. Two weeks after surgery, tenderness occurred around the stoma site, and intravenous infliximab therapy was initiated. During the initial infusion, shortness of breath developed, and the infliximab therapy was discontinued.

Physical examination findings revealed an erythematous, indurated area without ulceration inferomedial to the ostomy site. Superficial erosion of the incision wound and central dehiscence were also evident. The perineal and buttocks regions were erythematous, and there was pus exuding from the Seton drains. The results of laboratory investigations included hemoglobin and hematocrit levels of 11.1 g/dL and 33.5%, respectively. The Westergren erythrocyte sedimentation rate was 39 mm/h (reference value, <20 mm/h). The rest of the laboratory findings were within normal limits. Ileoscopy and visualization of the stoma revealed no active Crohn disease.

Over the course of several weeks, 3 ulcers with violaceous undermined borders and granulation tissue in the bases developed. The largest ulcer, which was located medially at the inferior margin of the stoma, measured 4.5×3.5 cm in diameter; the lateral ulcer measured 2.5 cm in diameter; and the midline ulcer along the healing incision wound measured 1 cm in diameter, with skip areas attached by strips of intact skin (Figure 1). Several immunomodulatory drugs, such as intravenous infliximab (5 mg/kg), oral prednisone (40 mg), azathioprine (100 mg/d), and dapsone (50 mg/d), were administered. During the infliximab infusion, the patient developed shortness of air and angioedema, which were treated with discontinuation of the infusion and with diphenhydramine hydrochloride. Prednisone therapy was unsuccessful, and the patient was beginning to develop cushingoid features. Azathioprine and dapsone therapy resulted in intolerable nausea. Topical 0.1% tacrolimus ointment was prescribed for application to the peristomal and midline ulceration on the days that the patient’s dressings or appliance was changed, but there was little response to the treatment.

THERAPEUTIC CHALLENGE

Peristomal pyoderma gangrenosum often responds to treatment with systemic corticosteroids and/or other immunosuppressive drugs. However, either our patient’s condition failed to improve or a toxic reaction to intravenous infliximab, oral prednisone, azathioprine, and dapsone therapy developed. Therefore, a safe and effective alternative treatment was needed.

SOLUTION

After treatment with several other immunomodulatory medications was tried, mycophenolate mofetil therapy (1 g twice daily) was begun. Application of 0.1% tacrolimus ointment to the ulcers was continued on the days that the patient’s dressings or appliance was changed. After 1 month of treatment with mycophenolate mofetil, the midline ulcer was completely healed. Five months after initiation of therapy, all areas were healed except for the small ulcer (<2 cm in diameter) that was located...
Peristomal pyoderma gangrenosum is a disease that is seen primarily in patients with IBD. The relationship between IBD and PPG is not understood. Pathergy, the development of pyoderma gangrenosum at the site of cutaneous trauma, is a phenomenon whereby debridement, biopsies, stoma formation, or relocation can cause PPG. Studies suggest that there is variability in the time from the formation of an ileostomy or a colostomy and the appearance of PPG. Therefore, it is likely that in susceptible individuals trauma to the skin precipitates PPG. The diagnosis of PPG is often difficult, and many nondermatologists consider the condition an irritation or infection and treat it with relocation of the stoma site or debridement and antibiotics before the correct diagnosis is made. The diagnosis is one of exclusion and in this case was made after cultures failed to reveal a pathogen. No biopsy was performed, but when the patient’s ulcerations developed, her IBD was quiescent, and it seems less likely that the ulcerations represent cutaneous Crohn disease.

There are several options in the treatment of PPG; however, there is no single therapy that is universally effective. Proper diagnosis and treatment of underlying systemic diseases such as IBD may lead to improvement of skin disease. Topical care of PPG ulcers is important in decreasing local inflammation and in reducing the risk of infection. Exudate absorbent dressings provide a barrier to leaking stool and improve reepithelialization. Superpotent topical corticosteroids such as 0.05% clobetasol propionate twice daily and intralesional injections of triamcinolone acetonide have been effective in the management of some reported cases of PPG. One retrospective analysis of 7 cases of PPG reported the effectiveness of topical clobetasol propionate therapy in conjunction with intralesional injections of triamcinolone acetonide in 3 cases, whereas topical cromomolyn sodium solution was effective in 1 case. The remaining 3 cases required systemic therapy. Another review that included 17 cases of PPG concluded that successful treatment of PPG depended on compulsive wound care and high-dose systemic steroid therapy (prednisone, 1-2 mg/kg per day).

Systemic treatment of PPG is usually classified as antibacterial, anti-inflammatory, or immunosuppressive. One study involved 20 patients with PPG complicated by IBD who were treated with systemic medications after local enterostomal care failed. The investigators found that patients with Crohn disease were more difficult to treat than those with ulcerative colitis. In the patients with Crohn disease, treatment with prednisolone alone did not result in resolution of any of the PPG ulcers. Five patients’ ulcers were healed with metronidazole therapy. Two patients whose conditions were refractory to treatment with corticosteroids and antibiotics responded to intravenous cyclosporin therapy, and 2 patients received infliximab infusions, which resulted in the healing of PPG in one of them. Another patient underwent a proctectomy, which temporarily led to healing; however, the ulcer recurred and subsequently responded to 4 months of sulfasalazine therapy.

Systemic medications, such as high-dose corticosteroids, dapsone, minocycline, clofazamine, and cyclosporin, were used alone or in combination in 2 studies that included 30 patients with PPG and Crohn disease. Infliximab, an anti–tumor necrosis factor monoclonal antibody, was successfully used to treat a 13-year-old girl with refractory PPG that was associated with Crohn disease.

The therapeutic options mentioned above are effective in most cases of PPG; however, refractory cases, such as the one reported herein, require alternative therapies. Our patient had adverse reactions to treatment with infliximab, dapsone, and azathioprine and was at risk for toxic effects from long-term corticosteroid therapy, so we opted for a trial of mycophenolate mofetil.

**COMMENT**

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**Figure 2.** Follow-up after 5 months of mycophenolate mofetil therapy. The midline ulceration and the one above the panty line have completely healed. The superior peristomal ulcer has reepithelialized, and the medial peristomal ulcer is approximately half its original size.

**Figure 3.** Follow-up after 12 months. All ulcerations have completely healed despite continued activity of perianal and bowel disease.
Mycophenolate mofetil has been used to treat rheumatoid arthritis, psoriasis, Wegener granulomatosis, and bullous pemphigoid and to prevent renal allograft rejection. Mycophenolate mofetil is a prodrug of mycophenolic acid, which is hydrolyzed and transformed into its active form by the liver. The active form is an inhibitor of inosine monophosphate dehydrogenase, which is the rate-limiting enzyme in the de novo synthesis of guanosine nucleotides. Inhibition of this pathway has a cytostatic effect on T and B lymphocytes. Therefore, mycophenolate mofetil therapy inhibits T- and B-cell proliferation and antibody production. Several case reports have documented the effectiveness of the use of mycophenolate mofetil in combination with corticosteroids and/or cyclosporin for pyoderma gangrenosum but not for PPG. We believe that mycophenolate mofetil therapy should be considered as an alternative to traditional therapies for PPG and that further study of the use of this agent is warranted.

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REFERENCES