Clinical Features and Treatment of Peristomal Pyoderma Gangrenosum

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PYODERMA GANGRENUM IS AN idiosyncratic, inflammatory, ulcerative condition of the skin, initially described by Brunsting et al.1 The characteristic lesion is an ulceration with a well-defined, undermined, violaceous border.2 Pyoderma gangrenosum has been reported in association with inflammatory bowel disease (IBD), various arthritides, and hematologic diseases.3-6 Early lesions are often pustular, and fistulous tracts may also occur. Pyoderma gangrenosum is frequently painful, and healing typically results in a cribriform scar. The diagnosis is confirmed by exclusion of other processes, in particular infections and neoplasia. Cultures fail to reveal pathogenic organisms, and biopsy demonstrates a nonspecific inflammatory reaction usually characterized by dermal infiltration of neutrophils.

Peristomal pyoderma gangrenosum (PPG) is unusual and is frequently misdiagnosed as a stitch abscess, contact dermatitis, irritation from leaking feces or urine, extension of underlying Crohn disease, or a wound infection. It is primarily reported in patients with IBD.7-11 The onset of PPG from the creation of the stoma is extremely variable. There is no single effective therapy for PPG.

We performed a retrospective medical record analysis of 7 patients with PPG seen between 1988 and December 1999. Patients were included if they had peristomal ulceration(s) with a violaceous undermined border or a surface with multiple fistulous tracts of longer than 4 weeks’ duration. In each case infection was excluded by culture results; neoplasia, extension of underlying IBD, and vasculitis were excluded by biopsy findings. We reviewed the clinical features, associated disorders, histopathologic features, microbiologic findings, and the time from the creation of the stoma to the development of PPG, as well as the time to PPG recurrence when the stoma was moved.

RESULTS

Two patients had ulcerative colitis, 2 had Crohn disease, and 3 had abdominal malignancies (TABLE). The specific type of IBD was confirmed grossly and histopathologically. Of the patients with solid tumors, 2 had an enteric urostomy following cystectomy for bladder carcinoma and 1 had a colostomy following proctosigmoidectomy for rectal adenocarcinoma. Three of the 4 patients with IBD had multiple ulcerations at the time of initial presentation.

Histopathologic examination of specimens from all patients revealed a nonspecific inflammatory reaction consisting of a mixture of neutrophils, lymphocytes, and histiocytes. None of the biopsies revealed neoplasia, vasculitis, or granulomatous inflammation.

The time to onset of PPG after surgery ranged from 2 months to 25 years. Patients who had their original stoma relocated because of PPG developed an ulceration at the site of the new stoma shortly following the surgery (FIGURE).
Patient 4 had a total proctocolectomy for ulcerative colitis 25 years prior to ulceration at the previous site of the ileostomy. A, This new ulcer developed 1 month after the relocation of her stoma and failed to respond to systemic antibiotics for a presumed wound infection. Note the ulcer’s violaceous, overhanging, scalloped border. B, Healing of the lesion in the same patient following therapy with oral dapsone.

Table. Clinical Characteristics of Patients With Peristomal Pyoderma Gangrenosum (PPG)

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y and Underlying Disease</th>
<th>Time to PPG Onset After Surgery</th>
<th>Effective Therapies (Time to Healing)*</th>
<th>Ineffective Therapies*</th>
<th>Current Status of PPG</th>
<th>Other Medical History</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/72 Crohn disease</td>
<td>1 y</td>
<td>Topical clobetasol propionate (2 y); topical cromolyn sodium (1 y); infliximab (1 mo)</td>
<td>Sulfasalazine, metronidazole, triamcinolone acetonide</td>
<td>Mildly active</td>
<td>None</td>
</tr>
<tr>
<td>2/M/47 Crohn disease</td>
<td>13 y, and within 1 mo after stomal relocation</td>
<td>Dapsone, 200 mg/d (complete response for 2 episodes within 6 mo); cyclosporine, 4 mg/kg per day (4 mo)</td>
<td>Sulfasalazine, minocycline, prednisone (60 mg/d), topical clobetasone propionate, triamcinolone acetonide</td>
<td>Resolved</td>
<td>Deep vein thrombosis, prednisone-associated glaucoma, diabetes, cataracts</td>
</tr>
<tr>
<td>3/F/36 Ulcerative colitis</td>
<td>2 mo</td>
<td>Partial response to prednisone, 20 mg/d, and cyclosporine, 5 mg/kg per day</td>
<td>Sulfasalazine, mesalamine, metronidazole, triamcinolone acetonide</td>
<td>Resolved following proctectomy</td>
<td>Axillary scarring due to presumed hydradenitis suppurativa, cushingoid facies</td>
</tr>
<tr>
<td>4/F/56 Ulcerative colitis</td>
<td>25 y, within 1 mo after stomal relocation</td>
<td>Dapsone, 100-150 mg/d (3 mo for 3 separate occurrences)</td>
<td>Prednisone (20 mg/d), topical clobetasone propionate</td>
<td>Resolved after third recurrence</td>
<td>Rheumatoid-like polyarthritis, pyoderma gangrenosum on the leg (10 y prior to peristomal lesion)</td>
</tr>
<tr>
<td>5/M/83 Bladder cancer</td>
<td>20 y</td>
<td>Triamcinolone acetonide, topical clobetasol propionate (6 wk)</td>
<td>None</td>
<td>Resolved</td>
<td>Hypertension, peptic ulcer disease</td>
</tr>
<tr>
<td>6/M/73 Bladder cancer</td>
<td>11 mo</td>
<td>Dapsone (11 mo for first occurrence), mycophenolate mofetil (8 mo)</td>
<td>Prednisone (20 mg/d), topical cromolyn sodium, clobetasol propionate</td>
<td>Still active</td>
<td>Steroid-induced diabetes, diverticulitis</td>
</tr>
<tr>
<td>7/M/64 Rectal adenocarcinoma</td>
<td>22 y</td>
<td>Triamcinolone acetonide, topical clobetasol propionate (3 mo)</td>
<td>None</td>
<td>Resolved</td>
<td>Hypertension, gout, hyperlipidemia</td>
</tr>
</tbody>
</table>

*Triamcinolone acetonide is usually administered intralesionally as 3 mg/mL every 3 to 4 weeks.

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Patient 4 had a lesion of classic pyoderma gangrenosum on her leg 10 years prior to the development of PPG and has had chronic polyarthritis. She had no colon or rectum at the time of either ulcerative lesion and has had no evidence of active IBD since her colectomy, yet PPG occurred. Three of the 4 patients with IBD had active bowel disease in association with the occurrence or recurrence of PPG. Patient 3 had a subtotal colectomy; following proctotectomy her lesions promptly healed and have not recurred for more than 3 years, unlike the situation in patient 4. In patients 1 and 2, systemic antibiotics that improved the intestinal symptoms did not lead to improvement of PPG. Patient 1 was treated with infliximab and had a prompt and sustained response of her bowel disease. Her PPG almost completely resolved after the third month’s infusion, but recurred within 4 weeks. Five patients have had multiple episodes of PPG.

Therapy was empiric and the responses varied (Table). All patients had been treated with 1 or more courses of broad-spectrum antibiotics for a presumed skin infection prior to the diagnosis of PPG. Topical clobetasol propionate (a class I topical corticosteroid) used in conjunction with intralesional (dermal) injection of triamcinolone acetonide was effective in 3 patients, ineffective in 2 patients, and possibly useful as adjunctive therapy in 2 patients. Topical 2% cromolyn sodium solution was effective in 1 patient and ineffective in another. Three patients required the addition of an immunosuppressive agent (cyclosporine [n = 2] or mycophenolate mofetil [n = 1]) because of systemic corticosteroid failure or adverse effects. Patient 4 had repeated responses to oral dapsone with each of her 3 relapses (Figure); in contrast patient 6’s initial episode responded to dapsone, but a relapse failed to respond.

**COMMENT**

Classic pyoderma gangrenosum is associated with systemic disease in half of such patients, whereas all of our small group of patients with PPG had a systemic disorder. Inflammatory bowel disease occurs in 15% to 20% of patients with classic pyoderma gangrenosum, and until recently accounted for almost all patients with PPG. Tumors of the colon, bladder, prostate, bronchus, ovary, breast, and adrenal gland have been associated with sporadic cases of classic pyoderma gangrenosum. Malignancies were the reason for stoma creation in 3 of our patients.

There was wide variability in the time from formation of the enterostomy/colostomy to the onset of PPG (2 months to 25 years). Dermatologists consider pathergy to be a process whereby, in susceptible persons, trauma to the skin results in pustules and/or ulcers. Pathergy may have functioned with the debridement, grafting, and relocation of the stoma in our patients to cause PPG. A seemingly insignificant degree of trauma related to irritation of the adhesive of the appliance or leakage of urine or feces may invoke pathergy, resulting in PPG in predisposed persons. Pathergy has been suspected in up to 30% of patients with pyoderma gangrenosum, and occurs in other neutrophilic dermatoses including Behçet disease, Sweet syndrome, and the blind loop syndrome.

The PPG in 2 of our 7 patients responded to topical superpotent corticosteroids and intralesional injection of triamcinolone acetonide. However, the majority (6/7) required some form of systemic therapy, including dapsone, cyclosporine, mycophenolate mofetil, or infliximab. The latter agents allowed discontinuation of systemic corticosteroids in 4 patients with corticosteroid-induced diabetes mellitus, cataracts, glaucoma, or facial swelling.

The approach to treatment of patients with PPG is empiric. In patients with active IBD, measures to treat the underlying disease must be started along with conservative local wound care and topical application of a potent or superpotent corticosteroid. Patients without active bowel disease may try a topical corticosteroid. In cases that fail to respond, topical cromolyn sodium solution or tacrolimus ointment may be effective. After 2 to 4 weeks of local therapy without response, systemic therapy should be considered. Prednisone, 0.5 to 1.0 mg/kg per day, is standard therapy for pyoderma gangrenosum, whether peristomal or on other sites; however, we often consider other agents because of the adverse effects that commonly accompany use of systemic corticosteroids. A variety of agents can be tried, but our first-line therapy is dapsone for 4 to 6 weeks, then cyclosporine or mycophenolate mofetil.

Peristomal pyoderma gangrenosum may cause serious morbidity in patients who require placement of a stoma. The majority of our patients were initially misdiagnosed as having a skin infection, tending to confirm our belief that PPG is underreported.

**REFERENCES**