

Management of Peristomal Pyoderma Gangrenosum

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PURPOSE: This study was designed to evaluate the presentation, management, and outcome of peristomal pyoderma gangrenosum at a specialist colorectal unit and develop a strategy for therapy. **METHODS:** Patients with peristomal pyoderma gangrenosum were identified from a prospectively accrued Institutional Review Board-approved stoma database. Data were collected regarding demographics, disease status, history of illness, time to healing, and treatments used from the database and by chart review. **RESULTS:** Sixteen patients presented between 1997 and 2002 with peristomal ulceration consistent with a diagnosis of peristomal pyoderma gangrenosum. Diagnosis was predominantly clinically based on a classic presentation of painful, undermined peristomal ulceration. The underlying diagnosis was Crohn's disease in 11 patients, ulcerative colitis in 3, indeterminate colitis in 1, and posterior urethral valves in 1. At the time of development of peristomal pyoderma gangrenosum, the underlying disease was active in 69 percent of patients. Stoma care, ulcer debridement with unroofing of undermined edges, and intralesional corticosteroid injection was associated with a 40 percent complete response rate and further 40 percent partial response rate. Of five patients who received infliximab, four (80 percent) responded to therapy. Complete response after all forms of therapy, including stoma relocation in seven patients, was 87 percent. **CONCLUSIONS:** Local wound management and enterostomal therapy are extremely important for patients with peristomal pyoderma gangrenosum. Infliximab may provide a useful option for those failing other forms of medical therapy. Relocation of the stoma is reserved for persistent ulceration failing other therapies, because

peristomal pyoderma gangrenosum may recur at the new stoma site. [Key words: Stoma; Pyoderma gangrenosum; Peristomal pyoderma gangrenosum; Infliximab; Peristomal ulcer]

Chronic ulcers in the peristomal region were first reported in Crohn's disease patients in 1970.¹ In the early postoperative period, such ulcers may be caused by abscess, infected hematomas, or mucocutaneous separation. Late after surgery they have been attributed to recurrent inflammatory bowel disease (IBD), enterocutaneous fistulas, face-plate pressure, trauma, and pyoderma gangrenosum (PG). Peristomal PG (PPG) was first reported in patients with Crohn's disease in 1984.² It is a rare condition, and most reports consist of small series of patients.³⁻⁵ It has been postulated that local skin trauma (pathergy) leads to the formation of ulcers in the region of the stoma, which can have a chronic and indolent course, but may also cause acute and persistent pain with difficulty applying pouches to the peristomal skin.

The rarity of the condition means that treatment has been based on conjecture and case reports or small series of patients collected over many years. We describe the clinical presentation, course of disease, and management of 16 patients with peristomal ulcers consistent with PPG that presented to this institution between 1997 and 2002 and describe a pathway for treatment.

PATIENTS AND METHODS

Sixteen patients presented to this institution between 1997 and 2002 with peristomal ulceration con-

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sistent with a diagnosis of PPG. After informed consent, patients were prospectively included into an Institutional Review Board-approved stoma database. Patients were identified by review of the stoma database. Data were collected regarding demographics, concurrent active disease, history of illness, time to healing, and treatments used. Patients were followed up by means of chart review, with confirmatory telephone interviews. Time from diagnosis and to healing is reported as median and interquartile range (IQR).

RESULTS

Eleven of 16 patients were female. The mean age at diagnosis of the PPG was 43 ± 14.7 years. Diagnosis was predominantly clinical and based on a classic presentation of painful, undermined peristomal ulceration. Biopsy of the ulcers was performed in 13 patients to rule out other associated diseases and causes of ulceration. Biopsy of the ulcer showed features of nonspecific acute and chronic inflammation with granulation tissue in most patients. One patient had mild squamous hyperplasia while another had pseudoepitheliomatous hyperplasia in addition to the ulcerative changes.

The underlying diagnosis was Crohn's disease in 11 patients, ulcerative colitis in 3, indeterminate colitis in 1, and posterior urethral valves as an indication for ileal conduit formation in 1 patient (Table 1). The initial diagnosis in one of the Crohn's patients was diverticulitis requiring laparotomy and formation of stoma. PPG developed one year later and antedated the subsequent diagnosis of Crohn's disease after another year. The patient with an ileal conduit had no suggestion of IBD after eight months of follow-up. The other 15 patients developed PPG following surgery for IBD after a median duration of six months (IQR 1.25–10.5 months).

The association between disease activity and PPG was assessed. The three patients with ulcerative colitis and one patient with indeterminate colitis had residual disease in the rectum that may have predisposed them to the development of PPG. Eight of the 11 Crohn's disease patients had active disease in the colon, rectum, or perianal region at the time of appearance of the PPG, while three had no active disease. Three patients with Crohn's disease who did not have PPG around an initial stoma developed the condition after relocation of the stoma. While one of these patients had active disease in the ileum at the

time of relocation of the stoma, the other two patients did not have any evidence of active disease and underwent stoma relocation for parastomal hernias. In contrast, three other patients without PPG and with a prior history of PPG did not develop recurrence of lesions after subsequent relocation of stoma. Two of these patients did not have any evidence of active disease at the time of relocation, while one patient had disease in the rectum. Thus, no definite pattern was noted regarding an association between the development or recurrence of PPG with disease activity or residual disease.

All patients were followed up as outpatients at regular visits to ensure symptomatic control and healing of PPG. The median follow-up duration was six months (IQR 4–11.25). Patients were managed by a combination of local wound care, specialized enterostomal therapy, and medical and surgical treatment. Nonadherent dressings and pouching systems, transparent film (Biocclusive, Johnson & Johnson, Somerville, NJ), hydrogel, alginate, and foam dressings helped ensure adequate fitting of the stoma appliance while minimizing local trauma to prevent pathergy. Creating as dry a surface as possible despite the wetness of the wound helped maintain integrity of the appliance. In severe cases a "nonadherent system" was used. Using an absorbant-type dressing such as foam or calcium alginate was, however, usually adequate. A secondary dressing helped "seal in" the absorbant dressing thus creating a dry surface. Applying a semipermeable transparent film over the absorbant dressing allowed for gas and air exchange while maintaining a dry surface. The pouch could then be easily applied with a wear time of approximately one to three days depending on the size of the wound.

Fifteen patients underwent debridement under local anesthesia, with unroofing of the undermined ulcers followed by the intralesional injection of corticosteroids (Kenalog 40mg/ml, Bristol Myers Squibb, Princeton, NJ). Response could not be assessed in one patient who was lost to follow-up. There was complete clearing of the ulcers in six patients. Six patients had a partial response and required other therapies, while two patients had no response to this therapy, as outlined below (Fig. 1).

In addition to local therapy, systemic medication in the form of corticosteroids, pentoxifylline, 6-mercaptopurine, dapsone, antibiotics, cyclosporine, infliximab, or azathioprine were used in 14 patients (Table 1). Two patients with Crohn's disease did not receive any systemic medical treatment but had healing of

Table 1. Characteristics, Diagnosis, and Treatment of Patients with PPG, Showing Response to Different Forms of Therapy

Age	Gender	Current Diagnosis	Type of Stoma	Wound Treatment	Medications Used	Response to Therapy			
						Corticosteroid Injections/unroofing	Immunosuppression	Infliximab	Stoma Relocation
63	F	Crohn's	Colostomy	CA, transparent film, hydrogel	Pentoxifylline, prednisone	Partial	Partial	Partial	Complete
45	M	Crohn's	Ileostomy	NP, xeroform gauze, hydrogel	6-MP, INF, prednisone, Dapsone, Bactrim, cyclosporine, topical corticosteroids	Complete	None	Complete	Complete
14	F	Crohn's	Ileostomy	NP, nonadherent topper dressing	Dapsone, INF, corticosteroid spray	Complete	None	Complete	Complete
44	F	Crohn's	Ileostomy	Transparent film, gauze, NP, CA	Dapsone, INF, corticosteroid spray	None	None	Partial	Complete
51	F	Crohn's	Ileostomy	CA, telfa	INF, 6-MP	Partial	Partial	Complete	Recurred
39	F	Crohn's	Ileostomy	CA, telfa, FP, Tegaserb (hydrocolloid), gel	Ciprofloxacin, flagyl	Partial	Partial	Complete	Recurred
30	F	Crohn's	Ileostomy	CA, allewyn	antibiotics, azathioprine	Complete	Partial	None	Partial/recurred
30	F	Crohn's	Ileostomy	Durahesive, CA, allewyn	antibiotics, azathioprine	Complete	Partial	None	Partial/recurred
30	F	Crohn's	Ileostomy	CA, transparent film, foam, gauze	antibiotics, azathioprine	Complete	Partial	None	Partial/recurred
39	F	Crohn's	Ileostomy	HCD, CA, transparent film	antibiotics, azathioprine	None	None	Complete	Complete
35	M	Crohn's	Ileostomy	CA	antibiotics, azathioprine	Complete	Complete	Complete	Complete
51	F	IC	Ileostomy	Marlex flexible convexity, CA, hydrogel on telfa, flat pouch	antibiotics, azathioprine	Partial	Partial	Complete	Complete
34	M	PUV	Ileostomy	Powder, CA, foam	antibiotics, azathioprine	Partial	None	Complete	Complete
67	M	MUC	Ileostomy	CA, foam	antibiotics, azathioprine	No followup	No follow-up	Complete	Complete
37	M	MUC	Ileostomy	CA, allewyn, Eakin washer, flat one piece	antibiotics, azathioprine	Complete	No follow-up	Complete	Complete
70	F	MUC	Ileostomy	NP, duoderm, CA, transparent film	antibiotics, azathioprine	Complete	Complete	Complete	Complete

INF = infliximab, 6-MP = 6-mercaptopurine, CA = calcium alginate, NP = nonadherent pouch, FP = flexible pouch system, HCD = hydrocolloid. PPG = peristomal pyoderma gangrenosum; IC = indeterminate colitis, MUC = mucosal ulcerative colitis, PUV = posterior urethral valves. Response to treatment graded as none, partial, complete, and unsure.

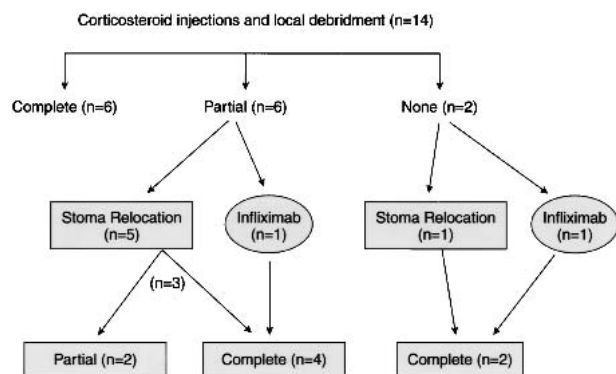


Figure 1. Results of intralesional injection of corticosteroids in peristomal pyoderma gangrenosum (PPG).

PPG after a median duration of five months (IQR 7.25–13.25) in response to debridement and intralesional injections of corticosteroids.

Four of five patients (80 percent) responded to treatment with infliximab. Two of these patients had not had any response to debridement with injection of corticosteroids—one responded completely to infliximab, but the other ultimately required relocation of the stoma. Of the six patients who had partial response to local debridement and intralesional corticosteroids, one was treated with infliximab and had a complete disappearance of the lesions. One patient was treated with infliximab before treatment with other modalities and had complete resolution of the ulcers. The patient who did not respond to initial therapy with infliximab had complete resolution of the ulcers with debridement and local injection of corticosteroids.

Seven patients with indolent PPG, including five patients with a partial response to debridement and intralesional corticosteroids, did not respond to any treatment and so underwent stoma relocation. Five relocation patients had an underlying diagnosis of Crohn's disease. Complete resolution of PPG was noted following relocation of the stoma in three patients, but it recurred in two patients 9 and 14 months after surgery. PPG resolved following stoma relocation in the patient with indeterminate colitis and the patient with posterior urethral valves. The final complete response rate after all forms of therapy was 87 percent.

DISCUSSION

First described in 1930,⁶ pyoderma gangrenosum is a chronic, painful, debilitating ulceration of the skin,

which occurs as an extraintestinal manifestation in 2 percent of patients with IBD⁷ but can also be seen with other disorders. It classically occurs on the lower extremities (usually tibia) but can involve other areas.⁸ Erythematous papules or pustules first appear, which coalesce into superficial ulcers with surrounding induration, undermined violaceous edges, and a bright outer halo of erythema. Healing results in atrophic, hypopigmented, and wrinkled scars with a cribriform pattern. The ulcers may be serpiginous and can be destructive and debilitating within hours or days of onset. The skin lesions may sometimes antedate the appearance of the associated systemic disorder⁹ and may occur at a surgical incision site.⁸ The rapidity of development is considered by some to be the hallmark of the disease.^{10–12} The diagnosis of PPG is based on clinical appearance alone in up to 83 percent of cases¹³ after the exclusion of other processes such as infection and malignancy. The condition is likely underdiagnosed as a result of lack of awareness,¹⁴ and it has been suggested that any patient who develops peristomal ulcers may well have PPG.^{13,15,16} However, it is important to assess any patient with a diagnosis of PG carefully because reconsideration and review may reveal a different cause for the ulceration rather than pyoderma gangrenosum.¹⁷

Review of current literature indicates that the clinical course of PPG may be indolent despite the use of various treatment modalities. In addition to attentive wound and stoma management that is a crucial adjunct to any medical therapy, various treatments have been used. Local therapies used include debridement, hydrophilic occlusive dressings, and topical agents such as antimicrobial agents, corticosteroids, 5-ASA, sodium cromoglycate, and nitrogen mustard. Intralesional injection of corticosteroids or cyclosporine has also been used (Table 2). Response to topical tacrolimus has recently been reported.²²

Lesions resistant to local therapy and those with more aggressive or severe initial disease have been treated with systemic corticosteroids or other immunosuppressive agents and immunomodulators. Therapy with corticosteroids and antimicrobials like sulphas, clofazimine, and minocycline appears to yield variable results. Hyperbaric oxygen, thalidomide, potassium iodide, cyproheptadine, nicotine, and radiation therapy and electron beam irradiation have also been used.

There was a female preponderance in our series of patients as with other reports.¹³ Most of the PPG occurred in association with IBD, especially with

Table 2.
Previous Reports of Peristomal Pyoderma Gangrenosum

Author (yr)	No. Cases	Years to Accrue	UC/CD/ Other	Therapy Used	Intralesional Corticosteroids	Association with Disease Activity	Stoma Relocation
Tjandra <i>et al.</i> ⁴ (1994)	5	N/a	3/2/0	Prednisolone, topical corticosteroids, cyclosporine, proctectomy	Yes	Yes, 5 of 5 patients	N/a
McGarity <i>et al.</i> ² (1984)	3	N/a	3/0/0	Prednisolone, sulfasalazine	No	yes	2 cases
Sheldon <i>et al.</i> ¹⁸ (2000)	20	13	13/7/0	Prednisone, metronidazole, cyclosporine, infliximab	No benefit	Yes, 12 of 13 CD patients	5 cases
Hughes <i>et al.</i> ⁵ (2000)	7	11	2/2/3	Topical corticosteroids, topical cromolyn Na, infliximab, Dapsone, cyclosporine, sulfasalazine, metronidazole	Effective in 2	3 of 4 patients with IBD	1 case
Lyon <i>et al.</i> ¹⁹ (2000)	26	4	11/6/6	Topical corticosteroids, prednisolone, Dapsone, clofazimine, minocycline, tacrolimus	Effective in 1	N/a	2 cases
Ng <i>et al.</i> ²⁰ (1992)	5	8	4/1/0	Sulfasalazine, metronidazole, prednisone, topical corticosteroids	No	4 of 5 patients	N/a
Wolfson <i>et al.</i> ²¹ (1990)	5	8	2/3/0	Sulfasalazine, metronidazole, prednisone, topical corticosteroids	No	N/a	N/a
Kiran (current article)	16	5	3/11/1	6-MP, INF, prednisone, Dapsone, Bactrim, topical corticosteroids, pentoxifylline	Yes	12 of 15 patients	7 cases

N/a = data not available; CD = Crohn's disease; IBD = inflammatory bowel disease.

Crohn's disease and ulcerative colitis as previously reported.¹³ It is, however, important to be aware that PPG is known to occur with other conditions.^{2,4,5,19}

None of the patients in our series had the histologic features of peripherally located lymphocytic vasculitis with associated immune complex deposits or a centrally located necrotic polymorphonuclear infiltrate, both of which have previously been reported.^{10,11} Most of our patients had nonspecific acute and chronic inflammation as discussed earlier.

At the time of development of PPG, underlying disease was active in 69 percent of patients in our series, and only 28 percent of patients who developed recurrence of PPG had evidence of active disease elsewhere at the time of recurrence. Interestingly, the three patients with UC and the patient with indeterminate colitis had residual disease, which may have contributed to the development of PPG. It is known that PPG may not appear for some time after total colectomy,^{23,24} and other authors also report that cutaneous manifestations of IBD do not always mirror disease in the bowel.^{25,26} However, Tjandra *et al.* report that the clinical outcome of PPG may be related to the activity of the underlying IBD or low-grade perineal sepsis.⁴

Previous reports are conflicting with regard to healing of PPG after relocation. While some^{5,13} have suggested that relocation results in recurrence of the lesions, others² suggest that relocation may, in fact, result in healing of indolent lesions. We found that relocation of the stoma may not result in healing of the peristomal ulcers, and lesions may recur at the new site as was seen in two patients. It was not possible to predict which patients would develop PPG, and patients with previous PPG did not always develop relapse or recurrence after subsequent relocation or revision of stoma. Conversely, patients were found to develop PPG only at the time of relocation for other reasons, although this did not occur at the time of first stoma formation.

The patients in this series were managed with intensive local wound management and enterostomal therapy. Undermined wounds were unroofed under local anesthesia, and enterostomal nurses were integrally involved in wound management and fitting the optimal stoma appliance to prevent further local trauma and pathergy. The principles of wound management included reduction or elimination of causative factors and debridement of ulcers and unroofing of all undermined areas. Factors considered when selecting skin care and ostomy products included main-

tenance of a moist environment, creation of a barrier to protect skin and absorb exudates, general comfort, simplicity of application, cost effectiveness, and pressure reduction. The use of nonadhesive stoma appliances was found to be particularly useful for this patient cohort.

Treatment with intralesional corticosteroids after debridement of ulcers and unroofing of all undermined areas resulted in a response in 40 percent of patients in our series. The effect of debridement on pathergic conditions such as PPG is not really known. Whether the use of intralesional corticosteroids balances out the effect of trauma from debridement and resulted in improvement in our patients is difficult to ascertain. Previous studies report conflicting results. While some report response of PPG to intralesional injection of corticosteroids^{16,27} and topical corticosteroids,¹⁹ Sheldon *et al.*¹⁸ did not notice any response. Two patients who did not respond or responded only partially to treatment with intralesional corticosteroids were treated with infliximab and responded. Although pentoxifylline may be beneficial in some patients because it helps to control the disease, this was not a consistent finding in all patients and it was difficult to identify which patients benefited from the medication.^{20,21}

CONCLUSIONS

In conclusion, PPG is a rare condition that is difficult to treat and requires a variety of treatment options to be available. Recommended management includes attentive wound care and the assistance of experienced enterostomal nursing care. Debridement under local anesthesia, with injection of intralesional corticosteroids, may result in complete or partial healing of lesions. Infliximab may be useful to improve healing in patients who fail to respond or partially respond to appropriate complete medical therapy, including antibiotics, systemic corticosteroids, and immunosuppression. Relocation of the stoma is avoided unless all other options have been exhausted. Such an approach allows for healing of PPG in 87 percent of patients.

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