Pyoderma Gangrenosum: A Diagnostic Challenge for the Surgical Consultant

AUTHORS:
Wakeley ME; Harrington DT

CORRESPONDING AUTHOR:
David T. Harrington, MD, FACS
Department of Surgery
Rhode Island Hospital
593 Eddy Street
Providence, RI 02905
Email: david.harrington@brownphysicians.org

AUTHOR AFFILIATION:
Department of Surgery
Brown University Warren Alpert Medical School
Providence, RI 02905

Background	Pyoderma gangrenosum is an inflammatory neutrophilic dermatitis characterized by the formation of small pustules which rapidly progress to ulcerating wounds. Strongly associated with systemic inflammatory conditions, including inflammatory bowel disease and underlying malignancy, pyoderma wounds most commonly occur on the anterior lower extremity and trunk and can be easily mistaken for infectious lesions.
Summary	We present a case of facial pyoderma gangrenosum confounded by concern for superinfection necessitating operative debridement.
Conclusion	Pyoderma gangrenosum is a sterile neutrophilic dermatitis that can appear similar to infectious abscesses; however, with the disease's predilection for pathergy, excessive debridement can lead to disfiguring wounds. Surgeons should be aware of the Delphi criteria for diagnosis and apply a high index of suspicion to ulcerative wounds in patients with systemic inflammatory diseases to minimize the risk of disfigurement.
Key Words	pyoderma gangrenosum; neutrophilic dermatitis; ulcerative colitis; autoimmune
Abbreviations	PG: Pyoderma gangrenosum IBD: Inflammatory bowel disease UC: Ulcerative colitis TNF: Tumor necrosis factor

DISCLOSURE STATEMENT:
The authors have no conflicts of interest to disclose.

FUNDING/SUPPORT:
The authors have no relevant financial relationships or in-kind support to disclose.

MEETING PRESENTATION:
Residents and Fellows Case Reviews Membership Meeting, Rhode Island Chapter of the American College of Surgeons, September 2019

RECEIVED: September 10, 2020
REVISION RECEIVED: January 6, 2021
ACCEPTED FOR PUBLICATION: February 1, 2021

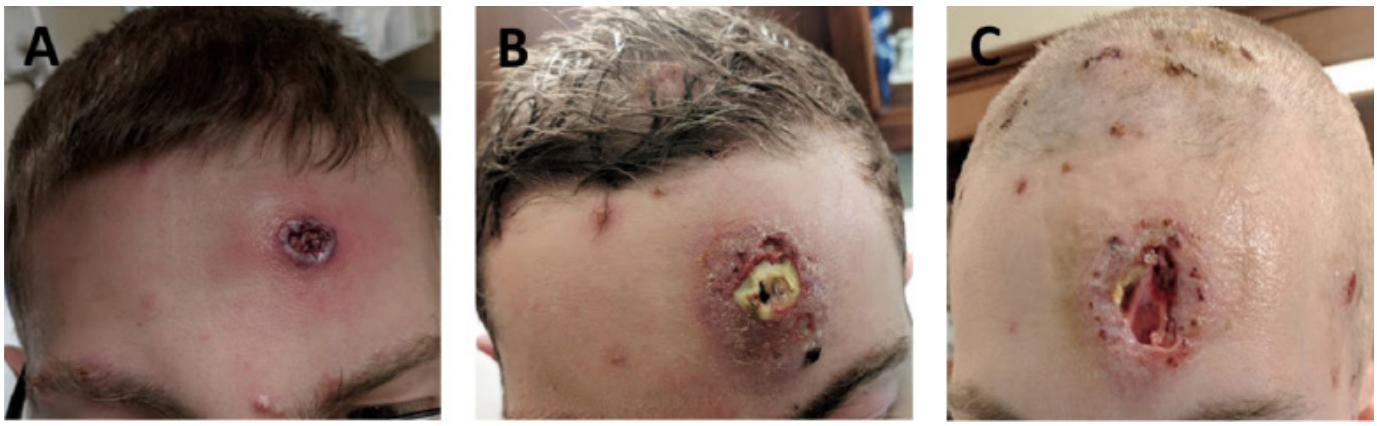
To Cite: Wakeley ME, Harrington DT. Pyoderma Gangrenosum: A Diagnostic Challenge for the Surgical Consultant. *ACS Case Reviews in Surgery*. 2023;4(1):82-86.

Case Description

Pyoderma gangrenosum (PG) is a rare, sterile, neutrophilic dermatosis occurring in 0.3–1.0 per 100,000 persons.[1] The disease can present anywhere on the body but most typically involve the anterior lower extremity and trunk. Wounds begin as a pustule or nodule and rapidly progress to painful ulcers.[2] Diagnosis is made based on clinical signs, including erythema, undermined borders, multiple ulcers, and history of inflammatory bowel disease (IBD), along with biopsy characteristics, as defined in the Delphi criteria.[3] Treatment is multimodal, involving wound care, topical therapies, and immunosuppression, and wound resolution occurs slowly, with an average of 20.37 weeks to complete healing.[1] The predilection of this disease for pathergy, or propagation into traumatic wounds, including surgical incisions, as well as the frequency of superinfection and the commonality of peristomal disease in IBD patients, lead to surgical involvement in care. However, traditional interventions such as incision and drainage can result in larger wounds and delay healing. Here we present a case in which concern for infection precipitated surgical involvement prior to diagnosis of PG.

A 31-year-old male with a history of hereditary angioedema and a recent diagnosis of ulcerative colitis (UC) presented to the emergency department, reporting a 48-hour history of tender nodules across his face and scalp (Figure 1A), which began spontaneously draining that morning, as well as a painful rash along his right hip. He denied fevers and reported starting mesalamine therapy three days prior but was not receiving systemic immunosuppressive therapy for his UC. He also reported persistent GI symptoms, including 8 to 10 bloody bowel movements daily and a 20-pound weight loss over the preceding month. A physical exam revealed two distinct cutaneous processes, with ulcerated areas on the scalp and forehead draining purulent material and grouped vesicles in a band around his hip. Workup, including wound cultures, CBC, BMP, and blood cultures, revealed a leukocytosis to 16.7 but no evidence of bacteremia or organisms in the wound. The patient was diagnosed with shingles and a facial infection and discharged with a course of Valtrex and doxycycline.

Figure 1. Initial Presentation, Doxycycline Course, and Operative Debridement. Published with Permission



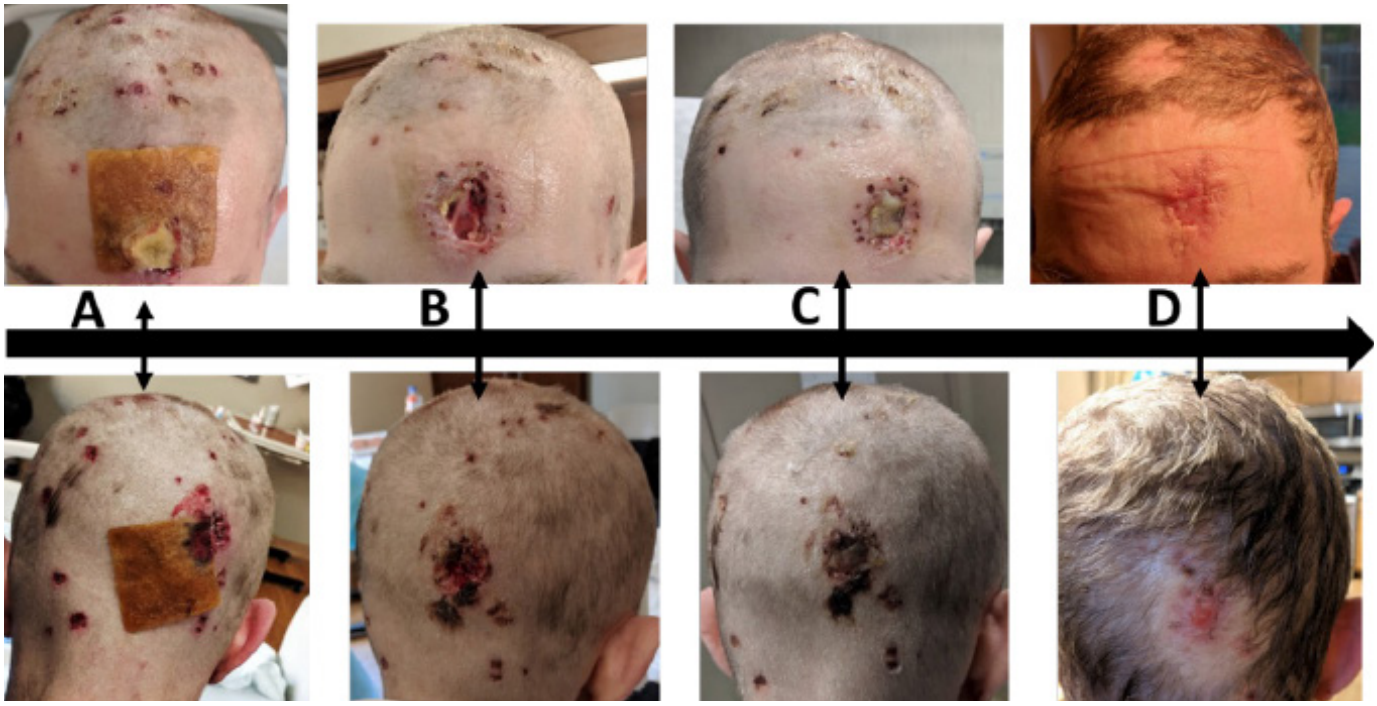
A) Initial appearance of largest ulcerating wound upon initial presentation to emergency department; B) wound appearance 48 hours after initial presentation during doxycycline management; and C) seven days after initial presentation, two days after operative debridement.

After 48 hours, the wounds continued to progress (Figure 1B), cultures demonstrated rare coagulase-negative staphylococcus and few cutibacterium, and the patient was directly admitted for IV vancomycin therapy. At the time of admission, the patient's leukocytosis had resolved, and he remained afebrile, though he continued to have active UC symptoms, including five or more bloody bowel movements daily. Surgery was consulted for incision and drainage of his multiple scalp wounds, and a biopsy of the ulcer edge was obtained. The infectious disease team managed the patient's antibiotic regimen. On hospital day 5, following two additional sets of negative blood cultures and wound cultures as well a biopsy deemed consistent with PG, the patient received an IV induction of corticosteroids and was started on an oral prednisone taper. He was transitioned to daptomycin and discharged with a PICC line to complete a two-week course. Gastrointestinal symptoms and wound healing improved dramatically after steroid administration; however, healing plateaued after a week, and his dose of oral prednisone was increased. Due to persistent GI symptoms and pathergy, with the conversion of his shingles wounds into PG, the patient was started on infliximab therapy six weeks after discharge and was subsequently tapered off corticosteroids. At 20 weeks postoperatively, the patient has achieved complete healing of his large anterior and posterior scalp ulcerations and continues to utilize a topical steroid for two small facial lesions (Figure 2).

Discussion

PG is a neutrophilic dermatosis representing the second most common dermatological extraintestinal manifestation of inflammatory bowel disease (IBD).[2] Characterized by leukocyte infiltration and abnormal neutrophil function, PG pathogenesis is associated with an overproduction of IL-8, precipitating exuberant neutrophil chemotaxis. The subsequent IL-1β release drives inflammatory cytokine release and perpetuates further neutrophil chemotaxis.[2] Some studies have associated this with imbalanced T-helper and suppressor T-cells, matrix metalloproteinase production, and mutations in the PSTPIP1/CD2BP1 gene.[4] PG is associated with various systemic inflammatory conditions, including IBD, autoimmune arthropathies, hematologic malignancies, HIV, diabetes mellitus, and thyroid disease.[4,5]

Figure 2. Postoperative Debridement and Steroid Therapy. Published with Permission



A) Appearance of largest ulcerations the morning after operative debridement: B) 72 hours after initiation of broad-spectrum antibiotic therapy; C) after 48 hours corticosteroid therapy; and D) one month after corticosteroid administration, just before infliximab induction.

There are four subtypes of pyoderma (ulcerative, pustular, bullous, and vegetative), characterized by their initial wound appearance and behavior.[5] Ulcerative disease is most common, characterized by necrolytic cutaneous ulcers with violaceous and irregular borders. Pustular and ulcerative PG is associated with inflammatory bowel disease and arthropathies, while bullous PG is distinctly associated with hematologic malignancies. The vegetative form is more limited, beginning as a purple plaque or abscess and healing with a distinctive cribriform pattern. PG wounds have been described to occur in any location on the body, including the torso, back, face, perianal area, and extremities.[6] Most patients present with at least one lower extremity ulcer; however, peristomal and truncal ulcers are also quite common, especially in the surgical patient.[5-7] Facial disease, as demonstrated in this case, is uncommon, but multiple instances of facial ulcerations have been described before.[8]

Historically, diagnosis of PG was one of exclusion; however, in 2018, a panel of experts released a Delphi consensus of diagnostic criteria consisting of one major and eight minor criteria.[3] This panel determined the single major criteria for diagnosis to be the presence of neutrophilic infiltrate on a biopsy taken from an ulcer edge. Minor criteria focus on more clinical findings, including the exclusion of infection, presence of pathergy, history of IBD or inflammatory arthritis, peripheral erythema and undermining violaceous borders, and decreased ulcer size within one month of immunosuppressive initiation. In testing criteria against a series of known cases and mimickers, these criteria demonstrated an 86% sensitivity and a 90% specificity. The patient, in this case, not only met the major criteria upon biopsy but also demonstrated four of the eight minor criteria at the time of presentation and, following initiation of treatment, demonstrated all eight except for an ulcer on the anterior leg.

Treatment of PG focuses on reducing ongoing inflammation, limiting pain, and preventing infection and often includes a mix of wound care, topical therapies, and systemic immunosuppressive therapies.[2] Given the frequency with which pathergy is associated with PG, wound care must avoid adherent dressings and irritating solutions. Further, any unnecessary manipulation of the ulcer bed should be avoided.[2] Topical therapy, such as steroid application, is often a useful adjunct, and intralesional injections, such as Kenalog, also facilitate healing in these complex wounds. Systemic immunosuppressive therapy with oral corticosteroids or cyclosporine is commonly employed as first-line therapy. However, tumor necrosis factor (TNF) inhibitors, including infliximab, adalimumab, and enteracept, have all been reported to demonstrate greater than 85% response rate and nearly 70% complete response rate leading some to suggest their use early in treatment of PG.[1] One review of 356 cases managed from 2000 to 2016 at two centers noted that TNF inhibitors were used in 32% of cases while 73.3% of patients were treated with oral steroids, and topical steroids were used in 61.5% of cases.[7]

Surgeons will often be involved in the care of patients with PG. Peristomal location is a common site for PG wounds in IBD patients requiring operative management, and pathergy also allows PG to occur in traumatic wounds. Further, as pyoderma wounds present with erythema, purulence, and pain, they can mimic abscesses in their earliest phases. Patients often undergo serial treatment with antibiotics or incision and drainage procedures before obtaining the appropriate diagnosis. One study, conducted before the Delphi criteria consensus was published, found that appropriate treatment was delayed nearly eight months for PG patients.[2] Significant mortality in PG patients is associated with overwhelming sepsis, varying from 1.12% to 21.7% in different cohorts.[1]

Conclusion

Pyoderma gangrenosum is a sterile neutrophilic dermatitis that can appear similar to infectious abscesses; however, with the disease's predilection for pathergy, excessive debridement can lead to disfiguring wounds. Surgeons should be aware of the Delphi criteria for diagnosis and apply a high index of suspicion to ulcerative wounds in patients with systemic inflammatory diseases to minimize the risk of disfigurement.

Lessons Learned

Concern for pathergy must not interfere with obtaining tissue samples for diagnosis. Further, providers should always treat infections whenever reasonable consideration for their presence exists.

References

1. Ben Abdallah H, Fogh K, Bech R. Pyoderma gangrenosum and tumour necrosis factor alpha inhibitors: A semi-systematic review. *Int Wound J*. 2019;16(2):511-521. doi:10.1111/iwj.13067
2. Plumptre I, Knabel D, Tomecki K. Pyoderma Gangrenosum: A Review for the Gastroenterologist. *Inflamm Bowel Dis*. 2018;24(12):2510-2517. doi:10.1093/ibd/izy174
3. Maverakis E, Ma C, Shinkai K, et al. Diagnostic Criteria of Ulcerative Pyoderma Gangrenosum: A Delphi Consensus of International Experts. *JAMA Dermatol*. 2018;154(4):461-466. doi:10.1001/jamadermatol.2017.5980
4. Al Ghazal P, Herberger K, Schaller J, et al. Associated factors and comorbidities in patients with pyoderma gangrenosum in Germany: a retrospective multicentric analysis in 259 patients. Orphanet J Rare Dis. 2013;8:136. Published 2013 Sep 8. doi:10.1186/1750-1172-8-136
5. Vacas AS, Torre AC, Bollea-Garlatti ML, Warley F, Galimberti RL. Pyoderma gangrenosum: clinical characteristics, associated diseases, and responses to treatment in a retrospective cohort study of 31 patients. *Int J Dermatol*. 2017;56(4):386-391. doi:10.1111/ijd.13591
6. Weizman AV, Huang B, Targan S, et al. Pyoderma Gangrenosum among Patients with Inflammatory Bowel Disease: A Descriptive Cohort Study. *J Cutan Med Surg*. 2015;19(2):125-131. doi:10.2310/7750.2014.14053
7. Ashchyan HJ, Butler DC, Nelson CA, et al. The Association of Age With Clinical Presentation and Comorbidities of Pyoderma Gangrenosum [published correction appears in JAMA Dermatol. 2018 May 1;154(5):630]. *JAMA Dermatol*. 2018;154(4):409-413. doi:10.1001/jamadermatol.2017.5978
8. Tomioka T, Soma K, Sato Y, Miura K, Endo A. Pyoderma gangrenosum on the nose. *Auris Nasus Larynx*. 2018;45(5):1130-1134. doi:10.1016/j.anl.2018.04.004