

PYODERMA GANGRENOSUM

Background:

- Pyoderma gangrenosum (PG) is an uncommon ulcerative cutaneous condition of uncertain etiology.
- PG was first described in 1930.
- 50% of patients with PG have an underlying systemic disease such as UC, Crohn's, chronic active hepatitis, myeloproliferative disorders and RA.
- The diagnosis of PG is one of exclusion—conditions such as diabetes, malignancy, and collagen vascular diseases must all be ruled out.

Pathophysiology:

- The pathophysiology of PG is poorly understood
- dysregulation of the immune system is believed to be involved.
- The initial lesion may be precipitated by trauma to the area (pathergy), but may also occur spontaneously.

Demographics:

- In the US: PG occurs in about 1 person per 100,000 people each year.
- The incidence of PG in individuals with IBD is 1-2%. (15-20% of those with PG also have IBD.)
- Affects all racial backgrounds equally. Possible mild female predominance.
- Any age may be affected; although most predominant in 4th to 5th decades

Presentation:

- Patients with PG usually describe the initial lesion as a bitelike reaction, with a small, red papule or pustule changing into a larger ulcerative lesion. Often, patients give a history of a brown recluse or other spider bite, but they have no evidence that a spider actually caused the initial event. Although any area of the body can be affected (including bones, liver, CNS, GI tract, and spleen), the skin of lower extremities is most commonly involved.

- Peristomal pyoderma gangrenosum is frequently mistaken for an abscess due to sutures, contact dermatitis, irritation from leaking feces or urine, extension of underlying Crohn disease, or a wound infection
- The lesions tend to be very painful.
- Arthralgias and malaise may often be present, often consistent with the underlying systemic disease process.

Physical:

- Two main variants of PG exist: classic and atypical. Several other variants may exist.
 - Classic PG : characterized by a deep ulceration with a violaceous border that overhangs the ulcer bed. May occur anywhere on the body; but most commonly found on the legs
 - Classic PG may occur around stoma sites; this type is known as peristomal PG. This form is often mistaken for a wound infection or irritation from the stoma appliance, a suture abscess, contact dermatitis, irritation from leaking feces or urine, or an extension of underlying Crohn disease.
 - Atypical PG: has a vesiculopustular component only at the border, is erosive or superficially ulcerated, and most often occurs on the dorsal surface of the hands, the extensor parts of the forearms, or the face.
 - PG may occur on the genitalia; this form is termed vulvar or penile PG. This variant must be differentiated from sexually transmitted diseases.
 - An intraoral form of the disease, known as pyostomatitis vegetans, has been reported and occurs primarily in patients with inflammatory bowel disease.
 - Extracutaneous neutrophilic disease may be evident on ocular examination.

Lab Studies:

- R/O systemic diseases: Routine blood work includes a complete blood count; a comprehensive chemistry profile, including a liver function test; and a urinalysis.
- R/O hepatitis: A hepatitis profile.
- R/O hematologic malignancies: Serum and/or urine protein electrophoresis, peripheral smear, and bone marrow aspiration should be performed if indicated to evaluate for hematologic malignancies.
- Other serum studies include a Venereal Disease Research Laboratory (VDRL) test, antineutrophil cytoplasmic antibody test, partial thromboplastin time test, and antiphospholipid antibody test to rule out Wegener granulomatosis, vasculitis, and antiphospholipid antibody syndrome.

Imaging Studies:

- In patients with symptoms, consider barium enema or an upper GI series to exclude associated inflammatory bowel disease. The study of asymptomatic individuals is controversial.
- May consider angiography or doppler studies in patients with suspected vascular insufficiency.

Other Tests:

- The following tests may be performed:
 - Flexible sigmoidoscopy or colonoscopy in selected patients
 - Bone marrow aspiration or biopsy in selected patients
 - Culture of the ulceration and possibly of the biopsy material. Cultures of PG are non-specific and may show many different colonizing bacteria and other organisms.

Procedures:

- A skin biopsy should be performed. Aside from a central zone of necrosis, the histological changes in PG are also not specific, but may include neutrophilic or mononuclear cell infiltrates, endothelial swelling, necrosis of the epidermis, and/or fibrinoid necrosis. Long-standing disease may show granuloma formation, especially if associated with Crohn's disease, but this is generally not considered an element of PG. Most common histological feature, however, is dermal infiltration of neutrophils.

Medical Care: Therapy is variable for patients with PG. In patients with an associated underlying disease, the effective therapy of the associated condition may be associated with a control of the cutaneous process as well.

- Local care: debridement, intralesional injection of steroids or cyclosporin, topical agents to alter immune response (nitrogen mustard, steroids, acetic acid, 5-aminosalicylic acid) or inhibit infection.
- Systemic care: *Glucocorticoids (prednisone)* -- These agents have anti-inflammatory properties and cause profound and varied metabolic effects. In addition, these agents modify the body's immune response to diverse stimuli. *Immunosuppressives (Cyclosporine, Azathioprine, Mycophenolate, Cyclophosphamide, Tacrolimus, Chlorambucil)* -- These agents have immunomodulatory effects. *Blood products (IVIg immune globulins)* -- These agents are used to improve the clinical and immunologic

aspects of the disease. They may decrease autoantibody production and increase solubilization and removal of immune complexes. *Immunomodulators* (Thalidomide, Clofazimine) -- These agents have effects on the activity of the immune system.

- Other therapy includes hyperbaric oxygen.

Surgical Care:

- Due to the pathergic phenomenon that may occur with surgical manipulation or grafting, resulting in wound enlargement, surgery should be avoided as a mode of treatment if possible. In some patients, grafting has resulted in the development of PG at the harvest site.
- Some patients with ulcerative colitis have responded to total colectomy; however, in others, the disease is peristomal and occurs following bowel resection. Relocation of the stoma should be avoided, as it may be associated with a new ulceration.

Prognosis:

- Generally a positive outcome; however, recurrences may occur, and residual scarring is common.
- Many patients with PG improve with initial immunosuppressive therapy and require minimal care afterwards; however, many patients follow a refractory course and multiple therapies fail. These patients require frequent follow-up and long-term care. Some patients demonstrate pathergy, and, in such instances, protection of the skin from trauma may prevent a recurrence.

Michael Wolfeld, M.D.
Marja Samenfeld-Specht MSIII