Delayed Diagnosis of Pyoderma Gangrenosum: A Case Study

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Pyoderma gangrenosum (PD) is a rare, chronic, relapsing, ulcerative, neutrophilic cutaneous disease and may be difficult to recognize. It is not uncommon for PD to be mistakenly diagnosed as vascular occlusive or venous disease, vasculitis, cancer, infection, exogenous tissue injury, or other inflammatory disorders. A 55-year-old woman with a 5-year history of a very painful and enlarging ulcer presented at the authors’ clinic. Previously, based on an original diagnosis of venous ulcer, the wound had been surgically debrided and managed with saline-soaked gauze and compression therapy. After the authors secured a complete history (which included rheumatoid arthritis) and assessment, PD was suspected. A biopsy was performed for histological confirmation. Pyoderma gangrenosum treatment, including oral corticosteroids and topical 0.01% tacrolimus twice daily covered with non-adhesive gauze and compression wrapping, was started. After 4 weeks, the wound had improved noticeably and pain medications to manage wound pain were discontinued. The wound was completely healed after 4 months. The presence or absence of PD must be ascertained in all patients who present with a history of painful lower leg ulcers and PD risk factors, such as rheumatoid arthritis.

KEYWORDS: case study, pyoderma gangrenosum, skin ulcer, diagnosis


Pyoderma gangrenosum (PG) is a rare, chronic, ulcerative, cutaneous disease with recurrent relapses, one of the neutrophilic diseases that affect the skin. It was first described by Brocq in 1916 and later named by Brunsting in 1930.¹ The cause of PG remains unknown but results of a study¹ of biopsy specimens from patients with PG suggest that neutrophil chemotaxis is altered. Pyoderma gangrenosum has a worldwide distribution and can appear at any age in either gender but is most frequently diagnosed in women between 20 and 50 years old.²

In 50% of all cases, PG is associated with systemic disease, most commonly inflammatory bowel disease (30% to 60%).² A monoclonal gammopathy is present in approximately 10% of patients with PG; the frequency of malignant disease in patients with PG is uncertain, but 7% is a reasonable estimate.³ Pyoderma gangrenosum also has been described in patients with chronic active hepatitis, myeloma, polycythemia rubra vera, paroxysmal nocturnal hemoglobinuria, Takayasu’s arteritis, primary biliary cirrhosis, systemic lupus erythematosus, and HIV infection.³ Four One case

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of pyoderma gangrenosum associated with retinoid therapy has been reported.13

The purpose of this review and case study is to describe and illustrate clinical diagnostic and treatment strategies.

**Type and Course**

Clinically, PG may be designated as classic, atypical, and peristomal. The classic form is characterized by well-demarcated ulcers in the legs that begin as painful pustules or vesicles that become necrotic with overhanging borders. The pustules develop further necrosis and tend to grow and deepen over time. The base of the ulcer is suppurative and the borders undermined and violet. Loss of tissue may expose the underlying tendons. These ulcers may be unique or multiple and are located mainly on the legs. They often worsen after debridement (pathergy).

Atypical PG is usually found on the face, hands, or arms and is characterized by superficial ulcers with a blue-gray, bullous border. Peristomal PG occurs around stomas in patients with inflammatory bowel disease.14

The course of PG can be acute (uniphasic), relapsing, or chronic. Relapsing or chronic courses are more likely to be associated with underlying disease.14 Most descriptions of PG state that the ulcers grow rapidly.2

**Diagnosis**

Diagnosing PG can be difficult. A recent retrospective study of 240 patients found that 10% of PG patients can be misdiagnosed.15 Commonly, PG patients are grouped by comorbidity into vascular occlusive or venous disease, vasculitis, cancer, infection, exogenous tissue injury, and other inflammatory disorders.2,13-15 "The diagnosis of PG is based on presentation, complete clinical history, and a thorough physical exam emphasizing signs and symptoms of systemic diseases associated with PG along with a tissue specimen for histopathology. Routine laboratory evaluation is essential and should include a complete blood count, chemistry profile, hepatitis panel, serum and urine protein electrophoresis, urinalysis, antinuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factor, and antiphospholipid antibody assays14 to eliminate other possible conditions.

Biopsy findings may not be specific; they must be correlated to the entire clinical picture. Histopathology will depend on the timing of the biopsy — if the specimen is taken from an early lesion, PG will appear as a dermal neutrophilic abscess that could progress to vasculitis and areas of thrombosis. If the specimen is taken from a chronic ulcer, it will usually show epidermal necrosis and ulceration, superficial dermal edema, and a dense, mixed dermal infiltrate that may extend to the panniculus.15

**Treatment**

The treatment of PG can be topical and/or systemic. Topical treatment with calcineurin inhibitors, such as tacrolimus and pimecrolimus, and high-potency steroids has been used to modulate the inflammatory response and inhibit the destructive skin inflammation characterizing PG.2,4,5

For patients with more widespread and progressive disease, systemic treatment must be added. Drugs like glucocorticoids, cyclosporin-A, sulfa, clofazimine, colchicine, azathioprine, mycophenolate mofetil, and cyclophosphamide have been used.1 Intravenous immunoglobulin has been used with success.18 Sulfones inhibit the myeloperoxidase-\(\text{H}_2\text{O}_2\) -halide-mediated cytotoxic system in polymorphonuclear leukocytes; dapsone may reduce tissue viscosity, thereby preventing edema and decreasing acute inflammatory reactions; and cyclosporine influences the early events in antigenic activation of helper T cells via inhibition of lymphokine production and secretion, thus

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**KEY POINTS**

- Because most lower leg ulcers are caused by venous insufficiency or arterial disease, the diagnosis of other conditions that can cause lower leg ulcers may be delayed.
- This case study illustrates the importance of obtaining a complete patient history and the need to consider common risk factors for pyoderma gangrenosum in patients with painful lower leg ulcers.
preventing the aggregation of lymphocytes at the periphery of PG lesion. Clofazimine mode of action is thought to relate to its anti-inflammatory, rather than antibacterial, effect. The treatment has to be continued and tapered based on clinical response. If steroids are used over long periods of time, steroid-sparing agents (eg, azathioprine) must be added and bone density, glucose, cholesterol, and other laboratory levels must be monitored. Recent case series and reports have shown promising results with biological therapy like etanercept and infliximab; however, in the authors’ setting, the cost of this therapy is too high.

Case Report

Presentation. Ms. G, a 55 year-old resident of Mexico City, was seen at the authors’ clinic with a history of a very painful ulcer of 5 years’ duration. The ulcer, located on the right leg, affected the external lateral aspect of the pretibial region, measured 16 cm x 10 cm, and featured well-defined overhanging violaceous borders (see Figure 1). Ms. G acknowledged exquisite pain that did not respond to conventional nonsteroidal anti-inflammatories (celecoxib, indomethacin, and diclofenac).

Ms. G reported that the ulcer had begun as a small abscess that spontaneously drained purulent material and grew progressively larger. Initially, her ulcer was treated with hydrocolloid dressings. When the ulcer enlarged, it was treated as a venous ulcer; it was debrided and covered with saline-moistened gauze and compression bandages. When the ulcer did not respond to this treatment, Ms. G was referred to the authors’ center.

Ms. G had a 14-year history of rheumatoid arthritis that was treated with nonsteroidal anti-inflammatories. Her most recent laboratory results showed only a positive rheumatoid factor and normocytic normochromic anemia. Antiphospholipid antibodies and cryoglobulins were negative.

Diagnosis and treatment. A biopsy showed a neutrophilic perivascular and interstitial infiltrate in the papillary and reticular dermis with necrosis characteristic of PG. Histopathology results along with the clinical history and presentation also were highly suggestive of PG. The decision was made to start Ms. G on topical 0.01% tacrolimus twice daily covered with nonadhesive gauze (Telfa, Covidien, Mansfield, Mass) and retained with a compression wrapping. Oral prednisone (1 mg/Kg/day) was slowly tapered over the next 8 weeks. At her follow-up visit 4 weeks later, remarkable improvement in the percentage of epithelialized surface, decrease in necrotic tissue, and decrease in wound size from 162 cm² to 83.05 cm² were noted (see Figure 2). Pain had decreased substantially, enabling Ms. G to stop taking pain medication and return to her normal activities. Improvement continued (see Figure 3) and the wound was completely healed 4 months after initiating therapy.

Discussion

Ms. G presented at the authors’ clinic with the classic variety of PG. Although a 5-year ulcer history is not
typical of classic variety PG, case studies of long-standing PG [21] have been published. Her clinical presentation and medical history — particularly, the presence of rheumatoid arthritis — contributed to the diagnosis and biopsy results supported the clinical findings. Ms. G responded quickly to glucocorticoid therapy and the use of tacrolimus used under the nonadhesive dressings, an approach that also helped decrease the pain associated with dressing changes. The rapid response to treatment was considered a confirmation of the accuracy of the authors’ diagnosis.

**Conclusion**

A diagnosis of PG must be considered in the presence of a very painful nonresponsive ulcer with a history of a pustule that ulcerates and increases in size in a patient positive for any of the comorbidities known to be associated with the disease. Assessment should include complete clinical history, thorough physical exam emphasizing signs and symptoms of systemic diseases associated with PG, laboratory evaluation, and a tissue specimen for histopathology.
Biopsy timing is a consideration. Proper treatment of the cause, including topical calcineurin inhibitors such as tacrolimus and pimecrolimus, as well as systemic steroids and anti-infective and anti-inflammatory treatments, facilitate wound healing and avoid further deterioration and subsequent suffering.

References