# Pyoderma Gangrenosum Following Patellar Tendon Repair: A Case Report and Review of the Literature

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## Abstract

Postoperative pyoderma gangrenosum (PG) is an unusual and devastating complication following surgical procedures. This frequently misdiagnosed entity can progress rapidly if not identified and treated appropriately. A heightened awareness for the diagnosis of PG, coupled with a multidisciplinary approach to the disease, is essential to proper management of this entity. We report on a patient who developed postoperative PG following open repair of a patellar tendon rupture. The follow-up period was 2 years, and a review of the current literature is presented.

The diagnosis of PG was confirmed by tissue biopsy, and the condition was treated with high-dose prednisone and dapsone, with complete resolution of symptoms.

PG should be part of the differential diagnosis when evaluating patients with postoperative wound complications. Awareness of PG is the key to diagnosis and treatment of this potentially devastating complication.

Pyoderma gangrenosum (PG) is an uncommon neutrophilic dermatosis initially described by Brocq and colleagues in 1916.[1] Postoperative PG, which occurs following surgical procedures, is a rare and devastating variant of the condition and was first reported by Cullen in 1924.[2] Initially thought to have an infectious etiology that progressed to gangrene, the misnomer PG results from a noninfectious, inflammatory process.[3] The authors obtained the patient's written informed consent for print and electronic publication of this case report.

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## CASE REPORT

The patient, a 51-year-old healthy man, initially presented to Dr. Kelly's outpatient clinic with acute onset of pain in the right leg. Past medical history was only significant for a suspicion of Behçet disease based on history of poorly healing oral apthous ulcers and cutaneous pustules. The patient's family history was unremarkable, with no history of inflammatory disease. The patient reported that the pain started after playing a round of golf, without an acute traumatic injury.

On physical examination, the patient demonstrated exquisite tenderness over the tibial tubercle. He was able to perform a straight leg raise without evidence of an extensor lag. Plain radiographs, at this presentation, did not demonstrate any significant abnormality, thus magnetic resonance imaging (MRI) was obtained. MRI revealed edema within the tibial tubercle, consistent with a nondisplaced fracture. Given these findings, particularly the fact that the patient was able to perform a straight leg raise, conservative management was pursued, with crutches and a hinged knee brace limited to 45° of flexion with restriction of weight-bearing. The patient was doing well for almost 6 weeks with slow resolution of his leg pain.

Approximately 6 weeks following his initial injury, the patient presented to the emergency department (ED) after losing his footing and hyperflexing his right knee. The patient recalled sensing a "pop" in his knee as he fell. On physical examination, the patient again was found to have significant tenderness over his tibial tubercle. He was, however, unable to perform a straight leg raise. Radiographs obtained after this injury demonstrated a small cortical irregularity at the tibial tubercle and a mildly increased Insall-Salvati ratio of 1.26. MRI was subsequently obtained and demonstrated an acute, minimally displaced avulsion of the patella tendon from its insertion on the tibial tubercle (Figure 1). Given these findings, the decision was made to pursue operative management of his injury. Five days following the injury, the patient underwent an open repair of the patellar tendon with the use of suture anchors and nonabsorbable polyfilament suture placed through bone tunnels, utilizing the technique described by Krackow and colleaues.[4] The wound was closed with absorbable polyglactine suture (Vicryl; Ethicon, Somerville, New

**Table.** Differential Diagnosis of Pyoderma Gangrenosusm

**Early Stages**
Folliculitis
Necrotizing vasculitis
Erythema multiforme
Cutaneous abscesses
Tick bites

**Advanced Stages**
Rheumatic Diseases
    Wegener's granulomatosis, antiphospholipid antibody syndrome, Behcet's syndrome
Vascular Diseases
    Venouse ulcers, atherosclerosis-based ulcers, sensorineural-based ulcers, hyperhomocysteinemia, synergistic gangrene, Fournier's gangrene
Infections
    Ecthyma, gangrenous herpes, blastomycosis, cutaneous leishmaniasis, gummatous syphilis, atypical mycobacteriosis, cutaneous
    amebiasis, cutaneous tuberculosis, spider bites (brown recluse), misc mycoses
Malignancies
    Squamous cell carcinoma, basal cell carcinoma, lymphoma
Endocrine Diseases
    Necrobiosis lipoidica, calciphylaxis
Miscellaneous
    Bullous ulcerative contact dermatitis, halogenoderma (bromides, iodides), warfarin necrosis, dermatitis artefacta

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Jersey) and a nonabsorbable monofilament for the subcuticular layer (Prolene; Ethicon). The patient was discharged home without incident.

At the patient's first postoperative visit, 10 days following surgery, the wound was noted to be "poorly healing" with distal ulceration. Cellulitis was presumed, and empiric, oral antibiotic therapy (cephalexin) was initiated. Seven days later, his wound continued to worsen and oral ciprofloxacin was added to broaden antimicrobial coverage. His wound failed to respond and continued to develop ulcerations with the formation of hemorrhagic bullae with expansion of his cellulitis. Consequently, on postoperative day 26, he was advised to return to the ED for admission and intravenous antibiotic therapy. At that time, he had a temperature of 39.3 °C/102.74°F, a white blood cell count of 12,700 cells/μL, an erythrocyte sedimentation rate (ESR) of 117 mm/h, and a C-reactive protein level of 36.6 mg/L. At this time, his wound had extended to a 15x15-cm shaggy-based ulcer with violaceous, overhanging borders. His hemorrhagic bullae had ruptured and sloughed off, revealing the underlying epidermal and dermal necrosis surrounded by blanching erythema (Figure 2). MRI upon admission revealed only superficial edema and no evidence of an abscess or deep space infection. He was started on intravenous vancomycin and imipenem, pending the results of a superficial wound culture. Consultations were obtained from the infectious disease, plastic surgery, rheumatology, and dermatology departments.



**Figure 1.** Sagittal T1-weighted MRI obtained preoperatively demonstrating avulsion of the patellar tendon from the tibial tubercle.



**Figure 2.** Clinical radiograph taken on postoperative day 26 demonstrating ulceration of the operative site with epidermal and dermal necrosis.
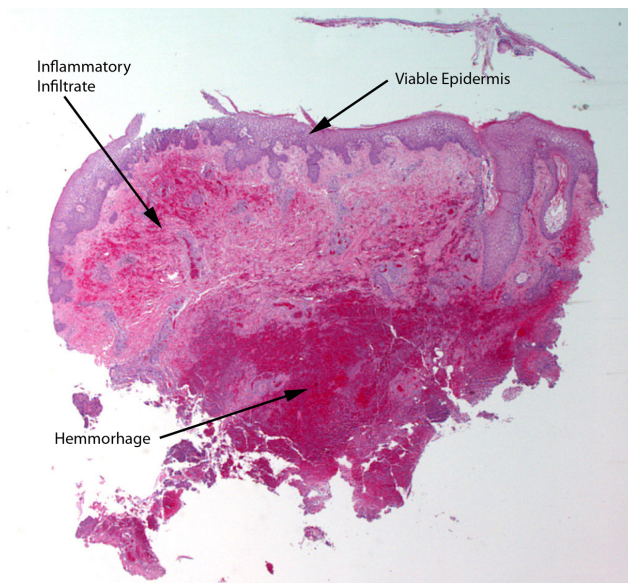
**Figure 3.** H&E staining of a punch biopsy obtained from the site of ulceration revealing an inflammatory infiltrate and hemorrhage beneath the epidermis.



**Figure 4.** Clinical radiograph taken on postoperative day 40, following 2 weeks of treatment with intravenous antibiotics, prednisone, and dapsone.

Two days after admission, the patient underwent a punch biopsy of the wound edge by the dermatology service. The specimen was hemisected; one piece was sent for histology, and the remaining tissue was sent for microbiologic culture. Histopathology demonstrated hemorrhage and a mild superficial lymphocytic inflammatory infiltrate (Figure 3).

The epidermis showed spongiosis, while the deep dermis was filled with massive numbers of neutrophils. No cutaneous malignancy or vasculitis was identified. The clinicopathologic picture supported a diagnosis of PG with super-imposed acute bacterial cellulitis. Bacterial cultures of the wound demonstrated mix skin flora while results of acid fast bacilli and fungal cultures were negative. The patient was immediately started on high-dose systemic corticosteroids (prednisone 60 mg orally twice per day) and dapsone (50 mg orally every day). The patient had remarkable improvement in his wound over the next several days. Antibiotic therapy was discontinued after 7 days; tapering of his steroid therapy and increasing of his dapsone (50 mg daily) began upon discharge home, 9 days after admission. The patient's ulcer continued to granulate and contract toward the center. At the patient's first follow-up visit, 1 week following discharge, the patient was found to have complete resolution of the erythema without further expansion of the ulceration (Figure 4).

The central area of ulceration evolved into a dry, necrotic base. The dapsone (50 mg daily) remained stable until completion of the prednisone taper following 12 weeks of treatment, at which point both medications were discontinued. Although part of the patient's inpatient evaluation revealed a serum paraproteinemia, subsequent study results revealed this had reverted to normal.

At the patient's 2-year follow-up visit, he demonstrated complete healing of his wound with minimal scarring (Figure 5). The patient does have a residual extensor lag of 10°.

## EPIDEMIOLOGY AND ETIOLOGY

PG can occur in patients of all ages, but appears primarily to affect patients between 30 and 50 years of age.[3] In one study, the authors estimate the incidence to be 3 per million.[5] In 50% to 80% of cases, PG is associated with an underlying systemic disease.[5,6] Most often, PG is associated with inflammatory bowel disease. Other associated systemic illnesses include hematologic dyscrasias, collagen vascular disease, immune system disorders, neoplasms, chronic active hepatitis, and human immunodeficiency virus. PG resulting from trauma or surgery has become an increasingly reported entity.[7-16] While there have been several cases of postoperative PG following abdominal, gynecologic, and plastic surgical procedures, there have only been 7 reported cases of PG following orthopedic surgery.[8,17-21] It is estimated that between 20% and 30% of new PG lesions are the result of trauma.[22]

The pathogenesis of PG remains unknown. An immunologic etiology has been suggested, since it is often associated with disorders such as inflammatory bowel disease and rheumatic diseases like lupus, antiphospholipid antibody syndrome, and Behçet disease. Results of numerous studies have demonstrated defects in both humoral and cell mediated immunity, as well as alterations in the complement system and circulating immunoreactants.[23-28] There has been evidence of increased immunoglobulin M, C3, and fibrin deposition in the perivascular region, as well as fibrin thrombi within vessels of PG lesions.[23] Other studies, however, have failed to demonstrate simi-

**Figure 5.** Clinical radiograph taken at last follow-up 2 years following index surgical procedure.

lar findings.[29] Anergy to particular fungal antigens support a defect in cell-mediated immunity.[25] Furthermore, some patients have been found to have altered neutrophil chemotaxis.[25-27] Certain cytokines have been implicated in the pathogenesis of PG. Interleukin-8 (IL-8) appears to be upregulated in these patients.[29] One animal model demonstrated that overexpression of IL-8 led to formation of PG-like lesions.[24] Pathergy is a central defining feature of PG.[30] Pathergy is an abnormally exuberant response to localized trauma that leads to skin breakdown and subsequent ulceration, and may be the result of an underlying immunologic defect. Unfortunately, most studies have a limited sample size and are not appropriately powered to detect a common defect or alteration to unify the majority of cases.

## CLINICAL FEATURES

PG is typically categorized into 4 different types: classic (ulcerative), bullous, pustular, and vegetative.[5] The characteristic lesion of PG typically begins as a follicular-based, erythematous papule or pustule, an inflammatory nodule, or a hemorrhagic bulla on an erythematous base.[31] Bullae are more commonly seen in patients with an underlying leukemia (usually acute myeloid leukemia). As the lesion evolves, it develops into a necrotic ulcer with a purulent base and a peripherally expanding, erythematous border. Typically, the ulcer expands in the dermis causing an undermined or overhanging, violaceous edge.[32] The disease can begin with single or multiple lesions that can occur anywhere on the body but typically affect the anterior legs, a frequent site of insignificant trauma. The lesions heal with the formation of a cribiform scar. These ulcers are exquisitely painful, though the discomfort improves rapidly once appropriate therapy is instituted.

## DIAGNOSIS

Given the characteristic appearance of PG, along with its development following localized trauma or surgery, it often is mistaken for an infectious process. This con-

fusion results not only in delayed treatment but also in possible debridement, which exacerbates the process due to pathergy. Furthermore, the lack of any specific histologic or laboratory findings further complicates the diagnosis. PG is often a diagnosis of exclusion in the proper clinical setting.

Once the diagnosis has been established based on the clinical features of the disease, it is helpful to pursue a multidisciplinary approach to the problem. This includes the involvement of dermatology, rheumatology, and in some instances, plastic surgery. Since PG often is associated with systemic illnesses, a thorough investigation should be performed to exclude any underlying conditions. Useful laboratory studies include a complete blood count, ESR, liver and kidney profiles, colonoscopy, peripheral blood smear, protein electrophoresis of serum and urine, bone marrow examination, chest x-ray, coagulation panel (including antiphospholipid antibody), antineutrophil cytoplasmic antibodies, and cryoglobulins.[33] While nonspecific, a biopsy of the lesion is essential, and normally demonstrates inflammatory infiltrates with significant neutrophil accumulation and areas of necrosis.[5] A biopsy also helps to rule out other etiologies of ulceration, including such primary cutaneous neoplasms as squamous cell carcinoma and lymphoma, vasculitis, or chronic viral infection with either herpes simplex or cytomegalovirus. Cultures of the lesion typically are sterile initially but can become secondarily superinfected as the disease progresses. The differential diagnosis of PG is summarized in the Table.

## TREATMENT

There is no standard treatment for PG except to avoid aggressive debridement. Therapy should be tailored according to the extent of the disease, presence of underlying illnesses, and existence of any medical comorbidities. PG treatment can be divided into local versus systemic therapy.

Local therapy includes local wound care, topical steroids and immunomodulators, intralesional steroids and cyclosporines. Gentle dressing changes may be performed by cleansing the skin with normal saline, sterile water, Burrow solution, 0.5% silver nitrate, or potassium permanganate.[34] Cleansing is followed with nonadherent dressings, such as Xeroform gauze or Telfa. Hydrocolloid dressing and bovine collagen matrices may be helpful in promoting re-epithelialization.[28,35] The use of topical steroids has not been found to be effective in the majority of cases.[36] There have been reports of success with topical 5-aminosalicylic acid, but this experience is rather limited.[37] For small, early lesions, or as an adjunct to systemic therapy, intralesional injections of corticosteroids have been useful.[31] Injections are undertaken cautiously, since even simple needle sticks for blood draws can incite a new lesion.

Systemic therapy is the mainstay of treatment for PG. First-line treatment is systemic corticosteroids. Typically, lesions respond rapidly to prednisone 40 mg to 120 mg daily (15 mg/kg/day to 1.5 mg/kg/day divided dose).[5,38] The course of steroids is continued until the disease is controlled, and then is slowly tapered off.[31] Intravenous pulse methylprednisolone 1 g daily for 3 days to 5 days has been used in some cases for lesions unresponsive to oral steroids or for extensive disease.[39]

Second-line therapy includes cyclosporin, azathioprine, mycophenolate mofetil, dapsone, chlorambucil, sulfasalazine, minocycline, cyclophosphamide, infliximab, thalidomide, tacrolimus, and intravenous immunoglobulin. Cyclosporine, as monotherapy, or in combination with corticosteroids, has demonstrated excellent efficacy in the treatment of PG.[15] Typical doses are 2 mg/kg/day to 6 mg/kg/day for 7 months and then tapered over 3 months.[40] Cyclosporine, however, has limited use in the treatment of PG that is associated with chronic conditions as cyclosporine's adverse effect profile restricts long-term therapy. Dapsone may be used as a steroid-sparing agent, and thalidomide is thought to be especially useful in patients with underlying Behçet disease.

Intravenous immunoglobulin also has been shown to be efficacious in the treatment of classic PG with potentially less adverse effects than immunosupressants.[41] Widespread use of intravenous immunoglobulin is limited by the costs and demands of monthly infusions.

There has been increasing interest in the use of biologic agents including tumor necrosis factor-$\alpha$ inhibitors and T-cell modulators such as infliximab, etanercept, adalimumab, efalizumab, and alefacept.[42] While results of several clinical studies have demonstrated efficacy with the use of the aforementioned biologics, the study involving infliximab was the only placebo-controlled trial.[43]

Surgical management of PG is controversial. It is felt that surgical modalities will exacerbate the disease, given its pathergy.[30] Others have found a role for wound debridement and skin grafting.[44] If surgical management is considered, it should only be performed in conjunction with immunosuppressive therapy for stable, controlled lesions.[45] It has been reported that the recurrence rate of PG is as high as 50%; however, there is no information regarding the recurrence rate with future surgical procedures.[6] It has been suggested that patients with a history of PG undergoing surgery should be treated prophylactically with immunosuppressive therapy for a period of 6 months following surgery, although this recommendation is based solely on anecdotal data.[46]

## Conclusion

PG is a rare and difficult diagnosis that can lead to serious complications following surgical procedures. Great care must be taken when considering surgery in patients with a history of active PG. Elective procedures should be avoided if possible. In patients with underlying diseases requiring surgery, prophylactic immunosupression should be considered and surgery should be performed during quiescent periods with close postoperative observation in order to rapidly initiate therapy at the earliest signs of recrudescence.[30] Furthermore, skin closure with subcuticular stitches has been found to reduce the severity and development of lesions.[30]

This is the first reported case of PG following a patellar tendon repair. Previous cases following orthopedic surgery include knee arthroscopy, knee replacement, hip replacement, spinal fusion, tarsal tunnel release, and metacarpophalangeal arthroplasty.[8,17-21] This case demonstrates the difficulty in diagnosing this unusual entity. The patient's suspected history of Behçet disease should have prompted a high suspicion for the diagnosis of PG. As previous case reports have demonstrated, a delay in diagnosis is quite common.[8-10,12,16-21] In the case reports of PG following orthopedic surgery, the majority of cases resolved after 2 months to 5 months of high-dose steroid therapy.[8,17,19-21] The one exception was the case of PG following knee arthroscopy.[18]

This case illustrates the potential complications following a delayed PG diagnosis. After undergoing routine arthroscopy for a meniscal tear, the patient developed a purulent arthritis and underwent multiple repeat arthroscopies, followed by an open synovectomy, ultimately requiring an arthrodesis with an Ilizarov. This patient remains on immunosuppressive therapy after 2 years due to recurrent ulceration upon withdrawal of medication. He also has developed steroid-induced diabetes as a result of his treatments.

There is usually a heightened awareness for infection in the setting of wound problems following surgery, and PG must be close behind in the differential. As discussed above, a mistaken diagnosis of infection followed by surgical debridement can exacerbate and worsen the problem. When PG is considered diagnostically, a multidisciplinary approach should be utilized to quickly control this rapidly progressive disease.

## Authors' Disclosure Statement

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