Pyoderma Gangrenosum: A Review of Orthopedic Case Reports

Stephanie Chapman1, Daniel Delgadillo III1 and David T. Rispler2*

1Michigan State University College of Human Medicine, Grand Rapids, MI, USA
2Orthopedic Residency Program, Grand Rapids Medical Education Partners, Grand Rapids, MI, USA

*Corresponding author: David T. Rispler, MD, Grand Rapids Orthopedic Residency Program, 200 Jefferson Ave SE, Jefferson Building Suite 305, Grand Rapids, MI 49503, USA, Tel: 616-685-6615, 616-890-5658, Fax: 616-685-3033, E-mail: drispler@comcast.net

Abstract
Pyoderma gangrenosum (PG) is an uncommon disease characterized by necrotic ulcers that are often associated with underlying systemic disease. PG can occur at the surgical site following surgery, including orthopedic surgery, and may be commonly mistaken for postoperative infection, delaying diagnosis and resulting in wound deterioration and subsequent sequelae. Previously, 20 case reports of PG have been reported after orthopedic surgery. We reviewed these cases and found the majority (60%) were women. Forty percent had underlying evidence of systemic disease. Debridement was performed in 70%. Development of satellite lesions led to diagnosis of PG in 35%. These cases underscore the difficulty in diagnosis of PG and the use of inappropriate treatment, thereby highlighting the need for better awareness, diagnostic criteria, and clinical management of this disease.

Keywords
Pyoderma gangrenosum, Ulcers, Case report, Review, Orthopedic surgery, Postoperative infection

Introduction

PG was first described by Brocq [1] in 1916 and then by Brunsting et al. [2] in 1930. PG is a noninfectious neutrophilic dermatosis that manifests clinically as papules and pustules that enlarge and become undermined, painful necrotic ulcers with a bluish border and surrounding erythema and edema (Figure 1). The necrotic ulcers must be distinguished from bacterial infection, and this can be challenging as the ulcers may become secondarily infected and develop a purulent exudative cover. The peak incidence of disease is between the ages of 20 to 50 years with women being more often affected than men [3]. It is estimated that the disease affects somewhere between 3 and 10 patients per million [4]. In 50-70% of patients, PG occurs in association with an underlying systemic disease such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA) or seronegative arthritis, and hematologic disorders [3,5,6]. PG can develop in response to various medications or as a pathergic response at sites of skin damage after trauma and surgery [3].

We present an analysis of cases of PG reported in the orthopedic literature, and a review of the important clinical features of disease. The purpose of this report is to educate more health care providers on the possibility of PG in orthopedic surgery post-operative patients. A greater awareness of this condition may improve diagnostic accuracy and reduce patient morbidity.

Review of Individual Case Reports in the Orthopedic Literature

PG can occur following any kind of surgery including breast, abdominal, and orthopedic surgery [3]. A PubMed search was conducted to find case reports of PG following orthopedic surgery using the search term ‘pyoderma gangrenosum orthopedic surgery’. A total of 20 cases of PG following orthopedic surgery described in the English language were found and are shown in Table 1 [7-25]. Eight cases followed total knee replacement [7-14], 4 followed hip surgery [15-18], 2 after foot and ankle surgery [19,20], 1 after surgery on a rheumatoid hand [19], 1 followed meniscectomy [21], 1 followed patellar tendon repair [22], 1 after achilles tendon reconstruction [23], 1 after a traumatic tibial fracture [24], and 1 after rotator cuff repair [25]. In review, 60% affected women. In both cases of bilateral total knee arthroplasty, PG developed on both knees [8,12]. Forty
percent of patients had a significant past medical history including arthritis, myelodysplastic syndrome, and a vague history of wound complication. One patient had a history of both Crohn’s disease and RA and another had a prior history of PG following a dog bite.

In the postoperative period, PG can easily be confused with wound infection, delaying diagnosis and contributing to significant patient morbidity. Patients will often receive multiple treatments by debridement for suspected wound infection that exacerbate patient morbidity. Patients will often receive multiple treatments for wound infection, delaying diagnosis and contributing to significant morbidity.

### Discussion

PG is a neutrophilic dermatosis characterized by papules and pustules that rapidly progress to undermined necrotic ulcerations that can occur following surgery [3,5]. Several clinical variants of PG have been described in the literature: ulcerative, pustular, bullous

### Table 1: Cases of Pyoderma Gangrenosum Following Orthopedic Surgery.

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Procedure</th>
<th>Age/sex</th>
<th>Past medical history</th>
<th>Number of debridements before accurate diagnosis</th>
<th>Satellite lesions (Y/N)</th>
<th>Amputation (Y/N)</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong/1999</td>
<td>Total hip arthroscopy</td>
<td>69/M</td>
<td>Pyoderma gangrenosum</td>
<td>2</td>
<td>Y</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Bennett/1999</td>
<td>Tarsal tunnel release, release of deep fascia overlying abductor hallucis muscle, and plantar fasciectomy</td>
<td>32/F</td>
<td>Not significant</td>
<td>9</td>
<td>N</td>
<td>Y (partial amputation of third toe)</td>
<td>Prednisone</td>
</tr>
<tr>
<td></td>
<td>Revision arthroplasty of the third, fourth, and fifth metacarpophalangeal joints</td>
<td>25/F</td>
<td>Juvenile rheumatoid arthritis and Crohn’s disease</td>
<td>2</td>
<td>Y</td>
<td>Methylprednisolone sodium succinate</td>
<td></td>
</tr>
<tr>
<td>Jain/2000</td>
<td>Total knee arthroplasty</td>
<td>63/M</td>
<td>Osteoarthritis</td>
<td>1</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Mandal/2006</td>
<td>Total knee arthroplasty</td>
<td>72/F</td>
<td>Not given</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>Debridement, wound VAC, skin graft</td>
</tr>
<tr>
<td>Wadia/2007</td>
<td>Bilateral total knee arthroplasty</td>
<td>80/F</td>
<td>Not significant</td>
<td>None</td>
<td>Y</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Madsen/2009</td>
<td>Arthroscopic partial meniscectomy</td>
<td>50/M</td>
<td>Not given</td>
<td>Multiple</td>
<td>N</td>
<td>N</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Verma/2009</td>
<td>Total Knee Arthroplasty</td>
<td>72/F</td>
<td>Not given</td>
<td>None</td>
<td>Y</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>de Thomasson/2010</td>
<td>Hip arthroscopy</td>
<td>65/F</td>
<td>Arthritis Adenocarcinoma of colon and pancreas</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>Prednisone</td>
</tr>
<tr>
<td>Attar/2010</td>
<td>Bilateral Total Knee Arthroplasty</td>
<td>80/F</td>
<td>History of wound problem after prior surgery</td>
<td>4</td>
<td>N</td>
<td>N</td>
<td>Latissimus flap, free fasciocutaneous anterolateral thigh flap, gastrocnemius flap</td>
</tr>
<tr>
<td>Steenbrugge/2011</td>
<td>Tibial plateau fracture of knee following trauma</td>
<td>55/F</td>
<td>Not given</td>
<td>Unclear</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Hill/2011</td>
<td>Total knee arthroplasty</td>
<td>63/F</td>
<td>Sjogrens Disease</td>
<td>Multiple</td>
<td>Y</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Nakajima/2011</td>
<td>Total knee arthroplasty</td>
<td>80/F</td>
<td>Type 2 diabetes mellitus</td>
<td>Multiple</td>
<td>Y</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Suarez/2011</td>
<td>Hip surgery</td>
<td>81/M</td>
<td>Myelodysplastic Syndrome</td>
<td>1</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Waniich/2012</td>
<td>Patellar tendon repair</td>
<td>51/M</td>
<td>Not significant</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Fang/2013</td>
<td>Midfoot fusion and ipsilateral achilles tendon reconstruction</td>
<td>74/F</td>
<td>History of wound complication</td>
<td>5</td>
<td>Y</td>
<td>Y</td>
<td>Polyclonal immunoglobulin</td>
</tr>
<tr>
<td>Grollmus/2013</td>
<td>Right ankle arthroscopy with debridement and microfracture</td>
<td>48/F</td>
<td>Not significant</td>
<td>1</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Reid/2014</td>
<td>Elective rotator cuff repair and Bankart repair</td>
<td>55/M</td>
<td>Not significant</td>
<td>8</td>
<td>N</td>
<td>N</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Nizamoglu/2015</td>
<td>Hip surgery</td>
<td>82/M</td>
<td>Not significant</td>
<td>1</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Jing Hui/2015</td>
<td>Total Knee Arthroplasty</td>
<td>56/M</td>
<td>Not given</td>
<td>4</td>
<td>N</td>
<td>N</td>
<td>Prednisolone</td>
</tr>
</tbody>
</table>
and vegetative [3,5,6]. Ulcerative type classically presents on the legs, although it can occur anywhere and is associated with IBD and arthritis. The evolution of ulcerative PG involves pustules that enlarge and necrose, forming ulcers with a blue, damaged border and surrounding erythema. Pustular type commonly presents on the limbs as discrete, superficial pustules that coalesce and ulcerate, and is commonly associated with IBD. Bullous type typically occurs in association with hematologic malignancy and is characterized by painful vesicles that enlarge into bullae with a necrotic center. Vegetative type typically presents on the trunk with a superficial, solitary ulcer. Vegetative PG is considered to be less aggressive and is usually not associated with an underlying systemic disease [5].

Pathogenesis is multifactorial and thought to involve abnormalities in neutrophil function and inflammatory mediators as well as a genetic predisposition [4]. Defects in neutrophil migration, chemotaxis, and phagocytosis have been reported in patients with PG. Increased activity of neutrophils is thought to contribute to pathergy, an aberrant immune response to skin antigens altered by surgery or trauma responsible for causing PG in about 20-30% of patients. Various pro-inflammatory cytokines and other inflammatory mediators have also been implicated in pathogenesis. Immunohistochemical studies have demonstrated high levels of IL-8, a chemoattractant for neutrophils, in PG ulcers. Studies have also shown that IL-17, IL-23, TNF-alpha, and matrix metalloproteinases are overexpressed in PG lesions and that there is an imbalance of T-regulatory cells and Th17 cells in patients with PG. A number of genetic mutations have been reported, and in some cases a constellation of diseases occur in concert with PG. PAPASH syndrome is characterized by pyogenic arthritis, PG, hidradenitis suppurativa, and acne as a result of a mutation in the PSTPIP-1 gene. Genetic mutations implicated in IBD susceptibility have also been correlated with the development of PG [4].

Diagnosis is based predominantly on clinical findings. Obtaining a detailed past medical history of PG or an underlying systemic illness may help lead to the appropriate diagnosis. Diagnosis is made challenging by the fact that there is no laboratory parameter diagnostic of PG and biopsies of skin lesions demonstrate non-specific acute inflammatory changes with a preponderance of neutrophils [3,7] (Figure 2). Additionally, PG may mimic infection. Important clues to the diagnosis include sterile wound cultures, failure of ulcerative lesions to respond to antibiotic therapy, and provocation of disease after wound debridement [7]. In practice, the development of satellite lesions distant to the site of surgery has proven to aid diagnosis. Major and minor diagnostic criteria have been proposed and may serve as a useful tool to the clinician when considered together [26,27]. Major criteria include: 1) a rapidly progressing, painful, and necrolytic cutaneous ulcer, 2) exclusion of other cutaneous diseases. Minor criteria include: 1) a history of pathergy, 2) presence of an underlying systemic disease associated with PG, 3) characteristic histopathologic findings, 4) rapid response to steroids [27].

Approach to treatment involves both local and systemic therapies [5,28]. Local therapy is centered on proper wound care and prevention of secondary infection. Topical corticosteroids may also be used alone or as an adjunct to systemic therapy [6]. Skin grafting is typically unsuccessful and has been associated with the formation of new lesions at the donor site [19]. However, in this review we found surgery was performed successfully after appropriate treatment had been employed. Options for systemic therapy include corticosteroids such as oral prednisone at a dose of 1mg/kg/day until lesions significantly improve followed by a taper. Intravenous pulse administration of high dose methylprednisolone can be used for rapid relief in refractory cases. Other systemic treatment options include TNF-alpha antagonists such as infliximab (which has the highest level of evidence), adalimumab, or etanercept, and calcineurin inhibitors such as cyclosporine, antimicrobials such as dapsone, and chemotherapeutic agents such as cyclophosphamide and methotrexate [19,27].

In conclusion, prompt identification and treatment of PG is imperative to decrease patient morbidity. This comprehensive analysis of individual case reports of PG in the orthopedic literature highlights the challenge of diagnosis in the postoperative period and the need for increased education amongst clinicians. In cases where cutaneous lesions develop postoperatively, PG should be considered in the differential, especially among patients with strong risk factors. Efforts to increase awareness of this disease should be taken to prevent misdiagnosis of infection and aggressive treatment by debridement that only exacerbates this condition.

Acknowledgements

Robert S. Kirsner, MD

Department of Dermatology, University of Miami, Miami, FL, USA

References


