



Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Delayed diagnosis of post-surgical pyoderma gangrenosum: A multicenter case series and review of literature

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ARTICLE INFO

Article history:

Received 1 February 2018

Accepted 15 February 2018

Available online 19 February 2018

Keywords:

Post-surgical

Pyoderma gangrenosum

Necrotizing fasciitis

Case report

ABSTRACT

INTRODUCTION: Pyoderma gangrenosum is a chronic neutrophilic dermatosis which can occur following trauma or surgery and can mimic infection. Surgical intervention can lead to progression of disease.

PRESENTATION OF CASES: This case series describes 3 cases of post-surgical pyoderma gangrenosum with delayed diagnosis from two large medical centers.

DISCUSSION: Epidemiology, pathogenesis, clinical and histopathologic presentation, and management of post-surgical pyoderma gangrenosum are discussed with a review of the literature.

CONCLUSION: Post-surgical pyoderma gangrenosum (PSPG) can mimic ulcerative disorders including bacterial infection. The diagnosis should be suspected in post-operative wounds with negative bacterial cultures which progress despite broad-spectrum antibiotics and surgical debridement. Recognizing the clinical features of PSPG is fundamental to prevent severe destruction and deformity.

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1. Introduction

Pyoderma gangrenosum (PG) is a chronic, idiopathic, and rapidly evolving cutaneous ulcerative condition [1]. PG is considered a neutrophilic dermatosis that can affect any age group, however it has a peak incidence between ages of 20–50 [2]. It equally affects both sexes. Pathophysiology of the disease is not completely understood [3], however it is thought to involve up-regulation and aberrant trafficking of polymorphonuclear neutrophils (PMNs) with subsequent release of PMN-stimulating cytokines [4].

Although they can occur anywhere, the painful cutaneous lesions of PG most commonly occur on the lower extremities and trunk [3]. Typically, they begin as a tender pustule that becomes ulcerated with a raised, violaceous, undermined border and a cribriform base. Fever and malaise are often concurrent [5]. Although non-specific, common lab abnormalities in patients with PG can include leukocytosis, elevated erythrocyte sedimentation rate, and elevated C-reactive protein [3]. There have been a few reports of an elevated ANA titer [1]. A sterile incisional biopsy from the ulcer border including subcutaneous tissue is required to rule out an infectious etiology. Histopathology reveals mixed cellular

inflammation with neutrophil predominance [6]. A biopsy from erythematous skin adjacent to the ulcer may reveal superficial and deep vascular injury with necrosis and a dense lymphocytic infiltrate [6].

Pathergy plays a key role in the pathogenesis and development of PG [7]. Pathergy is the induction or exacerbation of skin lesion after trauma. More severe trauma, such as a surgical procedure, can result in induction of PG through the release of cytokines and PMN chemotaxis [8].

Herein, we present three cases of post-operative PG, whose course would likely have been curtailed by prompt diagnosis and initiation of appropriate treatment. This work has been reported in line with the SCARE criteria [9].

2. Presentation of cases

2.1. Case 1

A 41-year-old male presented to the hospital with progressive painful ulcerations on the left lower extremity and right arm following endovenous varicose vein ablation. The lesions progressively worsened over a 4-week period despite broad-spectrum antibiotics and surgical debridement. Physical exam revealed an ulcer on left lower extremity measuring 65 × 25 × 5 cm and on the right ventral forearm measuring 7 × 3.8 × 1.3 cm. Ulcerations exhibited deep violaceous undermined borders and granulation tissue and exposed muscle at base. The patient subsequently devel-

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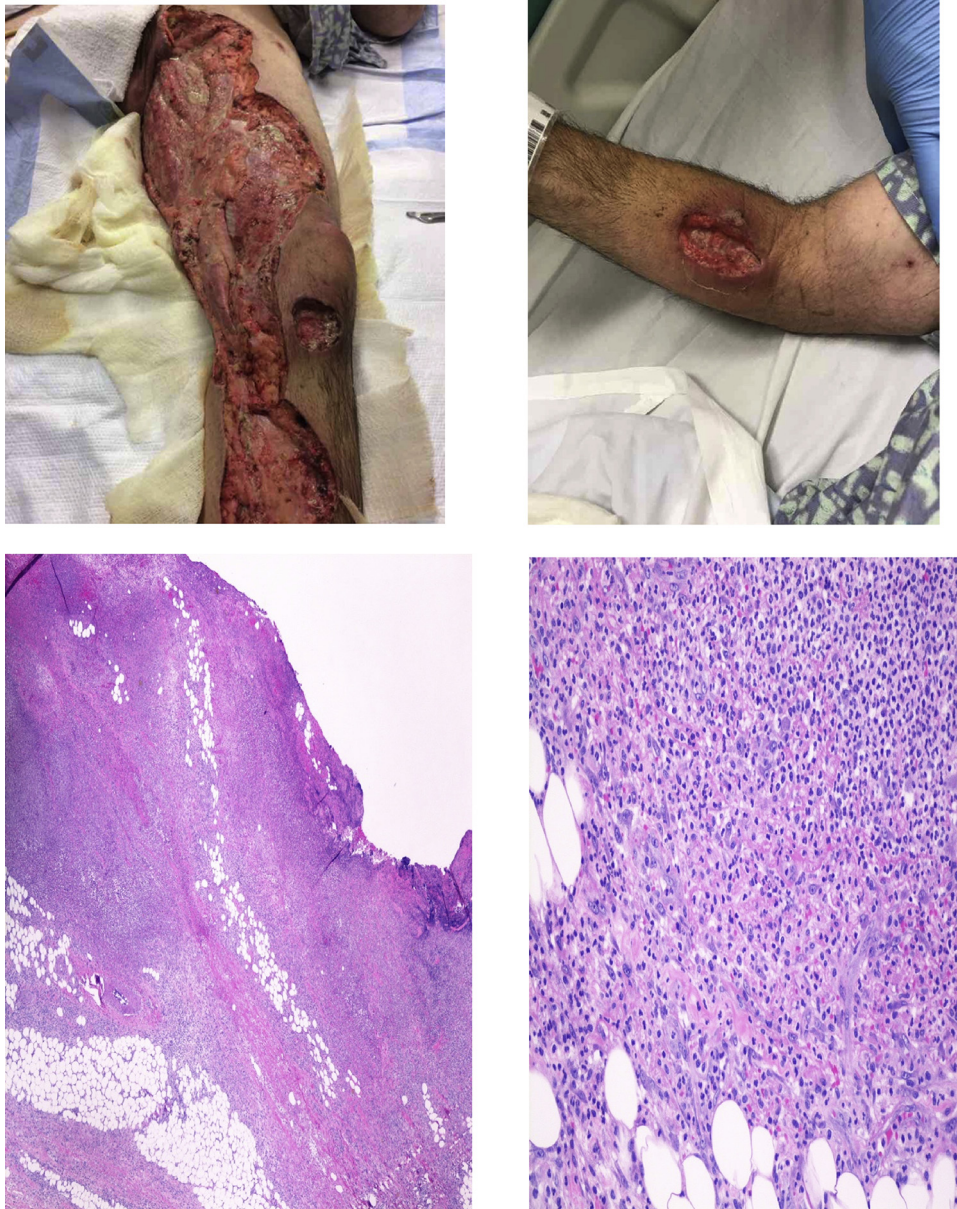


Fig. 1. Case 1. A: Ulceration shows violaceous undermined border B: Ulceration at site of venipuncture C: Histopathology at low magnification shows superficial and deep suppurative inflammation extending to deep subcutaneous tissue D: Histopathology at high magnification shows abundant neutrophils.

oped leukocytosis and fever. Blood, urine, and wound bacterial and fungal cultures didn't yield any infectious organisms. Four weeks after his initial endo-venous procedure, dermatology was consulted and performed an incisional skin biopsy. The histopathology showed epidermal ulceration with underlying superficial and deep neutrophilic inflammation extending to the deep subcutaneous adipose tissue lobules and connective tissue septae, findings suggestive of PG. Patient was managed with wound care, systemic steroids, and cyclosporine. Progression of ulcerations was quickly halted following initiation of treatment (Fig. 1).

2.2. Case 2

A 55-year-old Caucasian male with a history of multiple amputations of the right lower extremity due to peripheral vascular disease presented to the hospital with a progressive painful ulceration involving the right lower extremity stump following right below knee amputation. Physical exam revealed a 14×12 cm ulcer

with a rolled border, granulation tissue and a black eschar at the base. The ulceration was progressively enlarging despite antibiotic treatment, surgical debridement and negative tissue and blood cultures. One year after his initial amputation dermatology was consulted. Skin biopsy revealed a neutrophilic infiltrate and leukocytoclastic vasculitis suggestive of PG. Patient was immediately started on systemic steroids and noticed significant improvement of pain. The size of ulcer decreased gradually during treatment (Fig. 2).

2.3. Case 3

A 30-year-old Caucasian male presented to the hospital with a history of recurrent wounds and abscesses on his face and prior surgical sites on his trunk over a period of 3.5 years. Ulcers continued to progress despite broad spectrum antimicrobial coverage, multiple attempts of incision and drainage and surgical debridement. He subsequently underwent successful skin grafting; however, sur-

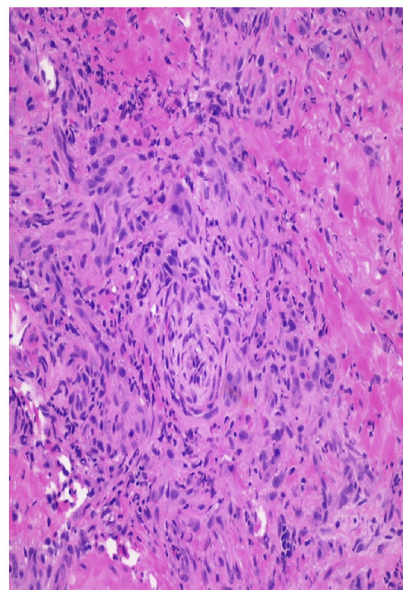
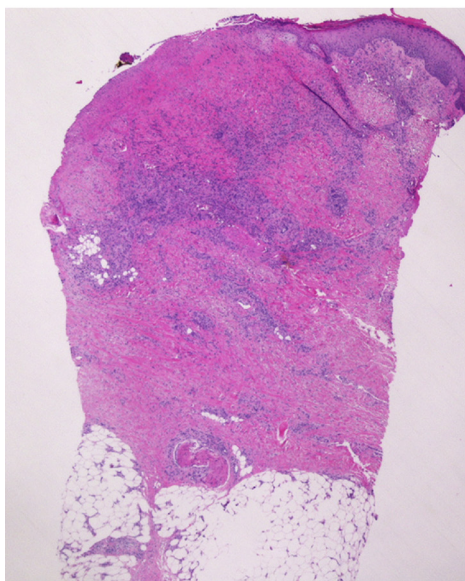


Fig. 2. Case 2. A: Ulceration at stump site shows undermined erythematous border and a cribriform base B: Histopathology at low magnification shows superficial and deep suppurative inflammation extending to subcutaneous tissue C: Histopathology at high magnification shows mainly neutrophils and leukocytoclastic vasculitis.

gical sites still remained complicated by non-healing ulcerations. Physical exam revealed large ulcers with undermined wound edges and surrounding violaceous, blue grey erythema on the mid sternum, left flank, and bilateral pre-auricular regions. Tissue aspirates and blood cultures only grew staphylococcus epidermidis, which was considered a contaminant. Three and a half years after developing his initial lesions, dermatology was consulted. A tangential biopsy was performed and showed a diffuse neutrophilic infiltrate consistent with PG. He was then started on systemic steroids with subsequently rapid improvement of his condition. Colonoscopy was performed and the patient was diagnosed with IBD. Patient was successfully managed with Adalimumab for both his PG and IBD (Fig. 3).

3. Discussion

Post-surgical PG (PSPG) has been noted to develop at the site of surgery within 7–11 days of surgical intervention [1,10]. It may be mistaken for necrotizing fasciitis due to the initial erythema and

disproportional pain [11–15]. Both misdiagnosis, most commonly as infection, and aggressive surgical intervention lead to rapid progression of PSPG [12]. Baranska-Rybak et al. found that 5 out of 12 patients underwent surgical intervention before the diagnosis of PSPG was made [13].

In over 50% of cases, PG is associated with systemic diseases such as inflammatory bowel disease, rheumatoid arthritis, and myeloproliferative disorders [16]. PSPG, on the other hand, has been found to be associated with systemic disease in 22%–35% of cases, the most common comorbidity being myeloproliferative disorders [9]. This leaves the majority of patients with no predisposing comorbidity other than surgery.

Correctly and promptly diagnosing PSPG is of the utmost importance in reducing its often destructive course. Ahronowitz et al. [17] advised obtaining a complete patient history and physical examination, culturing the tissue to exclude infectious causes, and collecting skin biopsies containing the active border of the ulcer and penetrating deep into the subcutaneous tissue. Histology of the wound will show a non-specific inflammatory infiltrate without bacteria,

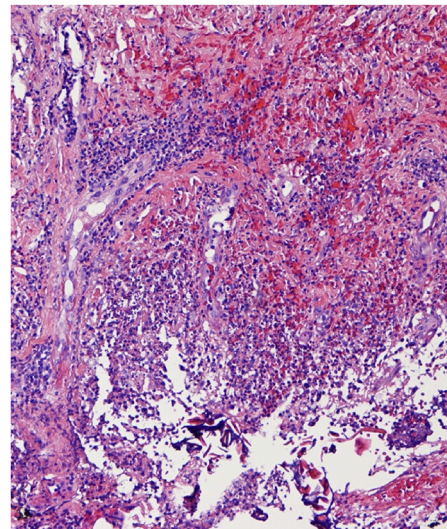
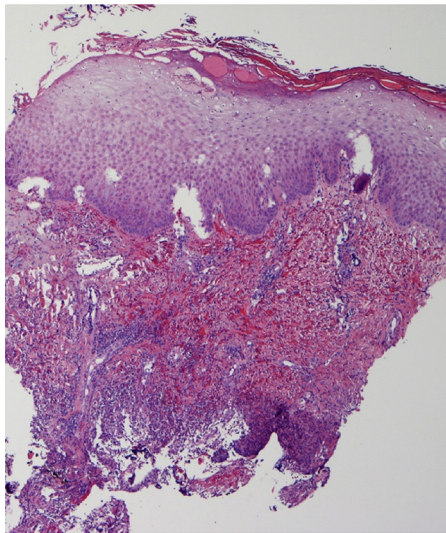


Fig. 3. Case 3. A: Ulceration at previous surgical sites show undermined erythematous ulcers with surrounding violaceous, blue grey erythema B: Histopathology at low magnification shows suppurative inflammation extending into the deep subcutaneous tissue C: Histopathology at high magnification shows sheets of neutrophils with focal necrosis and hemorrhage.

however it is important to remember that there may be colonization of the wound or secondary bacterial infection that can make it challenging to differentiate from primary infection [12]. Binus et al. demonstrated that 74 patients with PG had tissue samples evaluated and 30% contained at least one single colony of bacteria [7]. A lack of response to antibiotics and surgical debridement along with repeated negative bacterial cultures should prompt consideration of PG.

Management of PSPG is similar to classic PG. Surgical debridement is not generally recommended because it may induce pathergy and persistence and/or expansion of the ulcers. In addition to wound care and pain management, systemic corticosteroids and cyclosporine alone or in combination are considered first-line therapies [10]. Hyperbaric oxygen, cyclophosphamide, methotrexate, mycophenolate mofetil, sulfasalazine, and azathioprine are considered other treatment options [14]. More recently targeted therapies are proven effective in management of PG, namely the tumor necrosis factor alpha antagonists, infliximab and adalimumab [18]. There have been few reports in the literature of successful grafts and flaps

to cover primary defect after institution of immunosuppression. However, this treatment option remains highly controversial [15].

4. Conclusion

PG remains a diagnosis of exclusion and one not often seen by surgical specialties outside of Dermatology. It can mimic many other cutaneous conditions including bacterial infection, vascular occlusive disease and chronic non-healing wounds, which often lead to misdiagnosis and aggressive surgical debridement. The diagnosis is often delayed despite inadequate response to antibiotics, surgical debridement, and negative bacterial cultures. Recognizing the clinical features of PG and its pathogenic nature while ensuring timely management is fundamental to preventing severe destruction and deformity.

Conflict of interest

No conflict of interest for any of the authors.

Funding

No funding provided.

Ethical approval

Ethical approval was obtained from Ochsner Health Care System and University of Texas Medical Branch Health Care System.

Consent

Written consent was obtained from all three patients reported in this case series to have their case and pictures published in the journal.

Author contribution

Rawaa Almkhtar, M.D. contributed to study concept, collection of clinical history, physical exam, biopsy, any other investigations, interpretation of data, and manuscript writing and review.

Julie Martin, M.D. contributed to study concept, collection of clinical history, physical exam, interpretation of data, and manuscript review.

Bethany Vincent, M.D. contributed to study concept, interpretation of data, and manuscript review.

Brain Lee, M.D. contributed to study concept, interpretation of data, and manuscript review.

Andrew Armenta contributed to study concept, collection of clinical history, physical exam, biopsy, any other investigations, interpretation of data, and manuscript writing and review.

Brandon Goodwin collection of clinical history, physical exam, biopsy, any other investigations, interpretation of data, and manuscript review.

Mara M. Dacso contributed to study concept, collection of clinical history, physical exam, biopsy, any other investigations, interpretation of data, and manuscript writing and review.

Guarantor

Rawaa Almkhtar, Andrew Armenta, Brain Lee, Julie Martin, Brandon Goodwin, Bethany Vincent, and Mara M. Dacso.

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