Case in Point

Neutrophilic Dermatoses in a Patient With Diabetes: An Easily Misdiagnosed Uncommon Variant

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Without an early diagnosis, pyoderma gangrenosum, often mistaken for an infection, can lead to unnecessary and detrimental treatments.

Pyoderma gangrenosum (PG) is a noninfectious, rare, but serious ulcerating skin disease, characterized by recalcitrant ulcers that spread rapidly. In as many as 70% of cases, PG may be associated with a variety of diseases, including inflammatory bowel disease (IBD), seropositive or seronegative arthritis, and multiple myeloma (MM).[1-6] Few cases have been reported in the literature of PG in patients with diabetes mellitus.[7] Early diagnosis may be challenging as there are no single pathognomonic histopathologic findings, and clinical features are often indistinguishable from other, more common ulcerative skin conditions. The diagnosis is one of exclusion and is based on clinical appearance and patient history. There are many reported cases in the medical literature of repeated, unsuccessful attempts at surgical closure and grafting in which the diagnosis of PG is delayed, all resulting in severe pathergic reactions, permanent scarring, and irreversible disfigurement.[8-11] We present a case of idiopathic atypical pyoderma gangrenosum (APG) in a man with diabetes who was initially misdiagnosed as having skin cellulitis.

CASE REPORT

A 61-year-old man with a medical history of type 2 diabetes mellitus, arterial hypertension, and a history of finger joint amputation, while gardening, noticed a small pustule with scant purulent secretions on his left hand. He presented to the Emergency Department (ED) with 1 day of left-hand swelling without systemic symptoms. He did not report a penetrating trauma. Left-hand cellulitis was diagnosed, and 7 days of moxifloxacin was prescribed. The patient did not improve and returned to the ER on 3 separate occasions for reevaluation. Moxifloxacin was changed to trimethoprim/sulfamethoxazole, but on the patient's fourth visit to the ED, his physical exam revealed a 6 cm x 7 cm bullous lesion with raised irregular violaceous borders on the dorsal aspect of the left hand (Figure 1) with associated similar smaller satellite lesions (1.4 cm) on the ipsilateral fifth digit (Figure 2), and 3 more on the right hand (Figure 3). The affected areas were warm, nontender, and oozing clear fluid, without evidence of lymphangitic spread. Laboratory results revealed leukocytosis, thrombocytosis, erythrocyte sedimentation rate (ESR) > 120 mm/h and normocytic normochromic anemia. The patient's bacterial and fungal cultures were

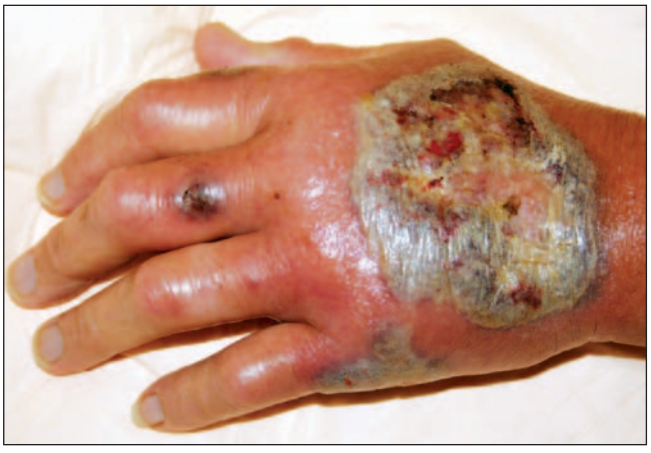

Figure 1. Large ruptured bullous ulcer measuring 6 cm x 7 cm with raised irregular violaceous borders on the dorsal aspect of the left hand.

FIGURES 1 THROUGH 6: COURTESY OF MEDICAL MEDIA OF VA CARIBBEAN HEALTHCARE SYSTEM.

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Table 1. Literature review of cases of pyoderma gangrenosum misdiagnosed as skin infection

Author; year	Age (y); gender	Affected area	Past medical history	Initial diagnosis	BC/TC	Management (1st degree)	Time to diagnosis	Management (2nd degree)	Response time
Tay YK; 1998[8]	38; F	Left palm and middle finger Sites of IV catheter	Crohn disease	Cellulitis Necrotizing fasciitis	Neg/Neg	ABX Debridement Amputation of digit	> 1 wk	MPSS × 3 days Prednisone sulfasalazine	12 h
Bennett; 1999[21]	25; F	Skin of metacarpo-phalangeal joints postrevision arthro-plasty and removal of silicone implants	Juvenile rheumatoid arthritis Crohn disease	Cellulitis Abscess	Neg/Neg	IV ABX Drainage Debridement	2 wks	MPSS × 3 days prednisone	24 h
Waterworth; 2004[22]	58; F	Right breast No history of trauma or surgery	Ulcerative colitis Deep vein thrombosis on chronic warfarin	Abscess Hematoma secondary to warfarin use Necrotizing fasciitis	Neg	Surgical exploration Later excision of necrotic skin and healing by secondary intention	2 d	Cyclosporin A Prednisone high dose	NS
Mahajan; 2005[23]	42; F	Skin necrosis post-laparascopic cholecystotomy IV catheter sites blistered with abscess formation Skin graft edge necrosis/ulceration (after 4 wks)	No relevant medical history	Necrotizing fasciitis	Neg	ABX Debridement Vacuum-assisted closure dressing Skin graft	4 wks	MPSS	Few hours
Barr; 2008[24]	70; F	Neck 2 wks after basal cell carcinoma excision	Crohn disease	Cellulitis Necrotizing faciitis Septic shock	Neg/Pos	ABX Multiple debridements	< 1 wk	IV steroids	7 d
Jaivsminsayna; 2009[25]	56; M	Postappendectomy surgical wound	None	Necrotizing fasciitis	Neg	ABX Debridement ICU care	NS	IV steroids	Instant

Ayestaray; 2010[26]	64; M	Right arm	Polycythemia vera	Cellulitis Necrotizing fasciitis	Neg	IV ABX Abscess excision Thin SSG with mesh	NS	IV steroids	48 h
Esteve-Martinez; 2011[27]	60; F	Thoracotomy wound after left upper lung lobectomy	Adenocarcinoma of the lung	Cellulitis secondary to fungal infection Necrotizing fasciitis	Neg	Broad spectrum ABX Antifungics	NS	Prednisone high dose	3 wk
Bisarya; 2011[11]	33; M	Right leg lateral aspect	Ulcerative colitis	Abscess Necrotizing fasciitis	Neg	PO and IV ABX Debridement	2 wk	Prednisone	48 h
Kasper; 2012[28]	51; M	Thoracic wall at automated implantable cardioverter-defibrillator site	Coronary artery disease Congestive heart failure	Necrotizing fasciitis	Neg	IV ABX Debridement	> 3 wk	Prednisone Cyclosporin A	Gradual over 6 mo

ABX = antibiotics; BC = blood culture; BKA = below knee amputation; ICU = intensive care unit; IV = intravenous; MPSS = methylprednisolone; NS = not specified; PO = oral; SSG = skin graft; TC = tissue culture.

negative. Diagnostic considerations included sporothricosis and refractory cellulitis due to community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA). Empiric antimicrobial therapy with itraconazole, vancomycin, and piperacillin/tazobactam was implemented but ineffective. A skin biopsy, taken from one of the lesions on the left hand, was remarkable for neutrophilic infiltration of the superficial and deep dermis without evidence of vasculitis, which was consistent with acute neutrophilic dermatosis (Figure 4). This histologic pattern, in association with the clinical presentation, suggested PG as the etiology.

Results from the workup for PG-associated conditions such as rheumatoid arthritis (RA), Wegener's granulomatosis, paraproteinemia, hepatitis, and IBD were negative. The diagnosis of idiopathic APG was established, and antimicrobial therapy was discontinued. High-dose intravenous (IV) methylprednisolone (1 g/d) was initiated, and after 3 days of therapy, there was significant improvement in the lesions (Figure 5). After 5 days of therapy, the lesions resolved (Figure 6). Systemic steroids were tapered and eventually discontinued. Over 2 months, the ulcer regressed without scarring, and no recurrence was reported.

DISCUSSION

PG is an ulcerative, necrotic dermatosis of unknown etiology.[12] It was first described in 1930 by Brunsting and colleagues, who believed that streptococcal infection was a major component leading to secondary cutaneous gangrene.[13] This theory later was disproved, but because of the clinical appearance of the disease, the name pyoderma gangrenosum has persisted.[14] There are 3 distinct clinical variants of PG described: classical, atypical, and peristomal. The classical variant can occur anywhere on the body but is usually localized to the lower extremities. Atypical PG is characterized by superficial lesions that involve mostly the upper extremities in 75% of the cases, with the presence of hemorrhagic bullous formation, as seen in our patient.[15]

A diagnosis of PG is made clinically as no specific histopathologic or immunofluorescent patterns are present. Diagnosis can be challenging and depends on recognition of the wide spectrum of clinical features. The lesions of PG characteristically have an acute, rapid, painful development, usually beginning as red papules. Within hours, the lesions become pustular, spread rapidly, and undergo central necrosis with purulent bases and irregular, erythematous borders with a purple hue. Our patient developed a large bullous ulcer in 4 days. Although histopathologic features are not diagnostic, a skin biopsy

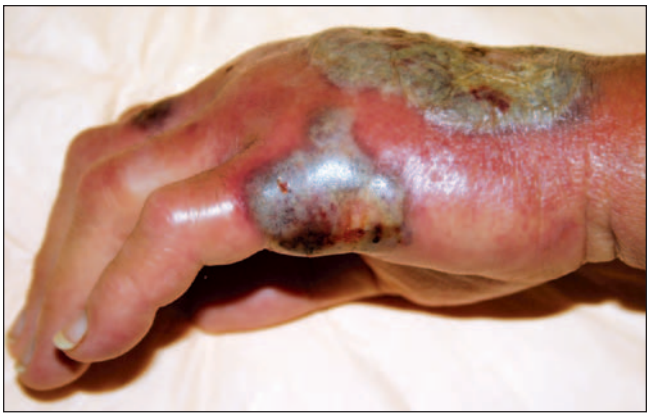

Figure 2. Similar smaller satellite lesions (1.4 cm) on the ipsilateral fifth digit with associated edema, erythema up to the wrist.

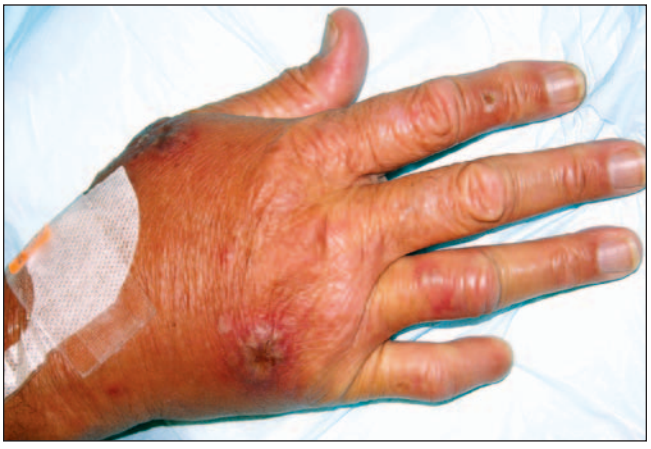

Figure 3. He had similar satellite lesions on his contralateral hand. Also notice the fifth DIP joint amputation.

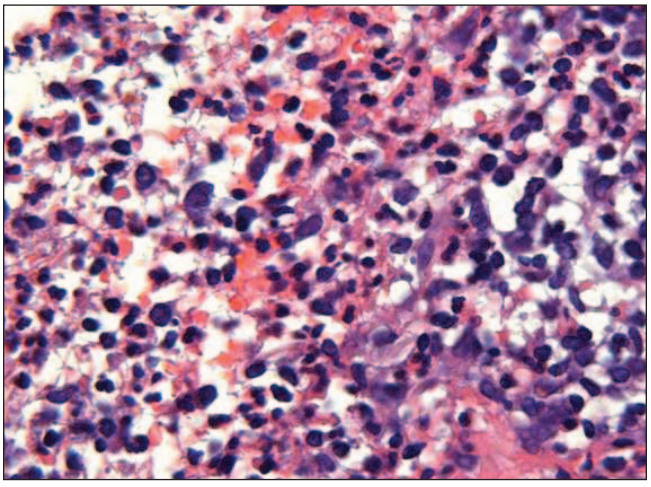

Figure 4. Photomicrograph of biopsy over the bullous lesion on the left hand, showing a nonspecific diffuse, neutrophilic infiltration in the superficial dermis, accompanied by inflammatory cells (hematoxylin-eosin).

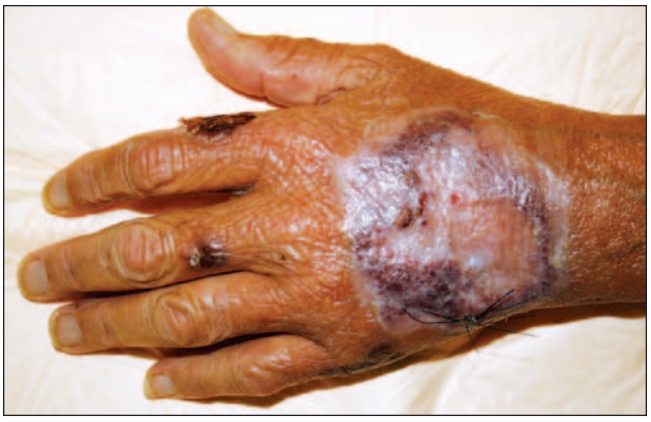

Figure 5. Significant improvement after 3 days of systemic corticosteroid therapy.

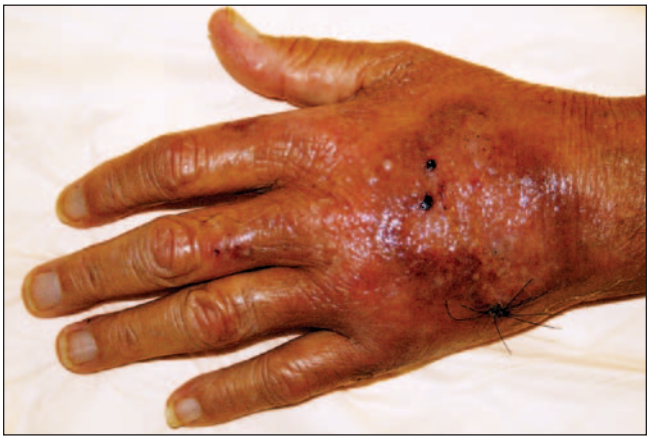

Figure 6. Almost complete resolution after 5 days of therapy.

is necessary to exclude other causes of acute skin ulcerations, particularly infections and necrotizing fasciitis.[16] As in our case, PG initially may be mistakenly diagnosed as a skin infection such as skin cellulitis or necrotizing fasciitis (Table 1). However, the borders of necrotizing fasciitis are usually poorly defined and rapidly progressive over hours; as opposed to PG, which has a well-defined violaceous ulcer edge and progresses more slowly over days. Moreover, cultures in PG are often negative and respond poorly to systemic antibiotics. The most distinctive feature of PG is its rapid and dramatic response to corticosteroids.

The most common systemic diseases associated with PG include IBD, inflammatory arthritis, myeloproliferative disorder, and chronic active hepatitis.[17] APG also may be associated with myelodysplastic disorders and IgA paraproteinemia.[18] Vasculitis, infections, malignancy, and factitious ulcers can mimic lesions of PG and need to be excluded before making a diagnosis.[19]

On diagnosis of PG, prompt implementation of therapy is essential. Treatment involves a combination of

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local wound care and systemic therapy. Systemic therapies include corticosteroids, cyclosporine, mycophenolate mofetil, azathioprine, dapsone, tacrolimus, cyclophosphamide, chlorambucil, and tumor necrosis factor-alpha (TNF-alpha) inhibitors.[20] IV therapies include pulsed methylprednisolone, pulsed cyclophosphamide, infliximab, and IV immune globulin. Our patient showed a dramatic clinical response after 3 days of methylprednisolone pulse therapy.

Pathergy is a feature of PG with new lesions arising at sites of minor trauma; therefore, surgical debridement should be avoided since it can incite the disease process. Repeated attempts at surgical closure and grafting of wounds result in severe pathergic reactions, permanent scarring, and deformities.[8-11] In this case, a minimal laceration was likely the incitant activating the pathergic reaction. In the patient's contralateral left hand, 2 years prior, an unhealed traumatic ulcer led to amputation of his right fifth distal interphalangeal (DIP) joint after a surgical debridement, suggesting a severe pathergic reaction induced by surgical manipulation (Figure 3).

In summary, as reported in the literature and as demonstrated by this case, PG is often mistaken for an infection and is treated with operative debridement and administration of antibiotics. Operative treatment is overwhelmingly contraindicated because of its well-documented propensity to exacerbate the condition. A high index of suspicion is, therefore, essential to diagnose PG clinically, because failure to do so in the early stages of the disease can lead to disfigurement, amputation, or unnecessary and detrimental surgery. ●

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

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