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). Few cases have been reported in the literature of PG in patients with diabetes mellitus. 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. 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 ED 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
Table 1. Literature review of cases of pyoderma gangrenosum misdiagnosed as skin infection

<table>
<thead>
<tr>
<th>Author; year</th>
<th>Age (y); gender</th>
<th>Affected area</th>
<th>Past medical history</th>
<th>Initial diagnosis</th>
<th>BC/TC</th>
<th>Management (1st degree)</th>
<th>Time to diagnosis</th>
<th>Management (2nd degree)</th>
<th>Response time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tay YK; 1998</td>
<td>38; F</td>
<td>Left palm and middle finger Sites of IV catheter</td>
<td>Crohn disease</td>
<td>Cellulitis Necrotizing fasciitis</td>
<td>Neg/Neg</td>
<td>ABX Debridement</td>
<td>&gt; 1 wk</td>
<td>Prednisone sulfasalazine</td>
<td>12 h</td>
</tr>
<tr>
<td>Bennett; 1999</td>
<td>25; F</td>
<td>Skin of metacarpophalangeal joints postrevision arthroplasty and removal of silicone implants</td>
<td>Juvenile rheumatoid arthritis Crohn disease</td>
<td>Cellulitis Abscess</td>
<td>Neg/Neg</td>
<td>IV ABX Drainage</td>
<td>2 wks</td>
<td>MPSS x 3 days prednisone</td>
<td>24 h</td>
</tr>
<tr>
<td>Waterworth; 2004</td>
<td>58; F</td>
<td>Right breast No history of trauma or surgery</td>
<td>Ulcerative colitis Deep vein thrombosis on chronic warfarin</td>
<td>Abscess Hematoma secondary to warfarin use Necrotizing fasciitis</td>
<td>Neg</td>
<td>Surgical exploration Later excision of necrotic skin and healing by secondary intention</td>
<td>2 d</td>
<td>Cyclosporin A Prednisone high dose</td>
<td>NS</td>
</tr>
<tr>
<td>Mahajan; 2005</td>
<td>42; F</td>
<td>Skin necrosis postlaparoscopic cholecystotomy IV catheter sites blistered with abscess formation Skin graft edge necrosis/ulceration (after 4 wks)</td>
<td>No relevant medical history</td>
<td>Necrotizing fasciitis</td>
<td>Neg</td>
<td>ABX Debridement Vacuum-assisted closure dressing Skin graft</td>
<td>4 wks</td>
<td>MPSS</td>
<td>Few hours</td>
</tr>
<tr>
<td>Barr; 2008</td>
<td>70; F</td>
<td>Neck 2 wks after basal cell carcinoma excision</td>
<td>Crohn disease</td>
<td>Cellulitis Necrotizing fasciitis Septic shock</td>
<td>Neg/Pos</td>
<td>ABX Multiple debridements</td>
<td>&lt; 1 wk</td>
<td>IV steroids</td>
<td>7 d</td>
</tr>
<tr>
<td>Jaivsminsayna; 2009</td>
<td>56; M</td>
<td>Postappendectomy surgical wound</td>
<td>None</td>
<td>Necrotizing fasciitis</td>
<td>Neg</td>
<td>ABX Debridement ICU care</td>
<td>NS</td>
<td>IV steroids</td>
<td>Instant</td>
</tr>
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<th>Management</th>
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<tr>
<td>Tay YK; 1998</td>
<td>Crohn disease</td>
<td>Sites of IV catheter</td>
<td>8</td>
<td>Prednisone</td>
<td>12 h</td>
<td>2nd degree</td>
<td>Debridement</td>
</tr>
<tr>
<td>Bennet; 1999</td>
<td>Cellulitis</td>
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<td>42</td>
<td>Prednisone</td>
<td>2 wks</td>
<td>Neg/Neg</td>
<td>Drainage</td>
</tr>
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<td>Waterworth; 2004</td>
<td>Abscess</td>
<td>Cellulitis fasciitis</td>
<td>22</td>
<td>Prednisone</td>
<td>2 d</td>
<td>NS</td>
<td>Debridement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hematoma</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Abscess</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Debridement</td>
</tr>
<tr>
<td>Ayestaray; 2010</td>
<td>Cellulitis</td>
<td>Necrotizing fasciitis</td>
<td>56</td>
<td>Prednisone</td>
<td>&gt; 3 wk</td>
<td>NS</td>
<td>Debridement</td>
</tr>
<tr>
<td>Esteve-Martinez; 2011</td>
<td>Adenocarcinoma of the lung</td>
<td>Necrotizing fasciitis</td>
<td>60</td>
<td>Prednisone</td>
<td>NS</td>
<td>NS</td>
<td>Debridement</td>
</tr>
<tr>
<td>Bisanya; 2011</td>
<td>Ulcerative colitis</td>
<td>Necrotizing fasciitis</td>
<td>33</td>
<td>Prednisone</td>
<td>42 h</td>
<td>NS</td>
<td>Debridement</td>
</tr>
<tr>
<td>Kasper; 2012</td>
<td>Coronary artery disease</td>
<td>Necrotizing fasciitis</td>
<td>51</td>
<td>Prednisone</td>
<td>over 6 mo</td>
<td>NS</td>
<td>Debridement</td>
</tr>
</tbody>
</table>

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.

*CASE IN POINT*

PG is an ulcerative, necrotic dermatosis of unknown etiology. It was first described in 1930 by Brunsting and colleagues, who believed that streptococcal infection was a major component leading to secondary cutaneous gangrene. This theory later was disproved, but because of the clinical appearance of the disease, the name pyoderma gangrenosum has persisted. There are 3 distinct clinical variants of PG described: classical, atypical, and periostomal. 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.

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 negative. Diagnostic considerations included sporothrixosis 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. It was first described in 1930 by Brunsting and colleagues, who believed that streptococcal infection was a major component leading to secondary cutaneous gangrene. This theory later was disproved, but because of the clinical appearance of the disease, the name pyoderma gangrenosum has persisted. There are 3 distinct clinical variants of PG described: classical, atypical, and periostomal. 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.

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is necessary to exclude other causes of acute skin ulcerations, particularly infections and necrotizing fasciitis. 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. APG also may be associated with myelodysplastic disorders and IgA paraproteinemia. Vasculitis, infections, malignancy, and factitious ulcers can mimic lesions of PG and need to be excluded before making a diagnosis.

On diagnosis of PG, prompt implementation of therapy is essential. Treatment involves a combination of...
local wound care and systemic therapy. Systemic therapies include corticosteroids, cyclosporine, mycophenolate mofetil, azathioprine, cyclophosphamide, chlorambucil, and tumor necrosis factor-alpha (TNF-alpha) inhibitors. 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. 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
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REFERENCES