Pretibial erythematous plaque in a young male

**Case study**

A healthy 17-year-old male presented with a 2-week history of an erythematous, slightly painful plaque on the right lower leg that was preceded by an injury to the area. He was otherwise asymptomatic and appeared well. Medical history was unremarkable.

Physical examination revealed an erythematous plaque with cribriform erosions on its surface and a crusty edge (*Figure 1*). Laboratory tests were normal, except for the erythrocyte sedimentation rate (ESR) which was slightly high (31 mm/hr; normal range for men: 0–22 mm/hr). A skin biopsy was performed and showed a perivascular and perifollicular mixed infiltrate of neutrophils and lymphocytes from the epidermis to the subcutis. No bacterial or fungal microorganisms were identified on culture.

The patient was treated empirically with topical antifungal therapy and followed up the next day. By this time, the superficial erosions were more pronounced and crusts had appeared on the surface of the lesion (*Figure 2*). After 3 days, the lesion was completely necrotic with a deeply ulcerated centre (*Figure 3*).

**Question 1**

What is the most likely diagnosis?

**Question 2**

What differential diagnoses should be considered?

**Question 3**

Why did the necrotic ulceration appear after the biopsy?

**Question 4**

What are the treatment options for pyoderma gangrenosum?
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Answer 1
Pyoderma gangrenosum (PG) is a painful, ulcerative, necrotic skin lesion with distinctive clinical features. The aetiology is uncertain and the pathophysiology is poorly understood, but dysfunction of the immune system is believed to play a role. Approximately one-half of cases are associated with an underlying systemic disease (Table 1), most commonly inflammatory bowel disease, arthritis, or a lymphoproliferative disorder. The diagnosis is made by excluding differential diagnoses (see Question 2). The lesions may be single or multiple; they are usually chronic and/or recurrent. They occur most commonly on the legs, especially the pretibial area, but can develop on any area of the body (eg, the abdominal wall adjacent to a stoma following a colectomy).

Answer 2
The differential diagnoses of PG include deep mycoses, bacterial infections (including mycobacteria), chronic ulcerative herpes simplex virus, vasculitis and insect bite reaction among others (Table 2). Histopathologic findings may help distinguish between these disorders, but there are no investigation results that are pathognomonic for PG.

Answer 3
This event is explained by the phenomenon of pathergy that was first described by Blobner in 1937. Pathergy refers to the formation of a papule, sterile pustule or ulceration 24–48 hours after a needleprick to the skin. It has long been used in the diagnosis of Behçet disease, but the phenomenon is also associated with PG, eosinophilic pustular folliculitis, cutaneous ulcerative lichen planus, bowel-associated dermatitis-arthritis syndrome, rheumatoid arthritis, leukocytoclastic vasculitis, non-Hodgkin lymphoma and chronic myeloid leukaemia treated with interferon alfa. Many patients with PG report previous trauma to the sites of their lesions, however, pathergy, in the absence of other clinical criteria, is not sufficient to make a diagnosis of PG.

Answer 4
Treatments for PG include local and systemic approaches (Figure 4). Local or topical therapies include colloidal membrane occlusive dressings, whirlpool baths, topical antiseptics (benzoyl peroxide, silver sulfadiazine), topical or intralesional glucocorticoids and topical tacrolimus ointment. Where systemic treatments are required, systemic glucocorticoids are generally first line (eg, prednisolone 0.5–2.0 mg/kg/day). For lesions that are refractory to oral glucocorticoids alone, additional treatment options include azathioprine (50–150 mg/day), mycophenolate mofetil (1–2 g twice daily), cyclophosphamide (2–3 mg/kg/day), cyclosporin (5 mg/kg/day, with target trough serum levels of 150–350 ng/mL), high dose intravenous immunoglobulin has been reported to be effective in some cases. In addition, biologic agents have shown efficacy in the treatment of PG. Infliximab therapy was superior to placebo in a randomised trial of 30 patients. Clinical improvement has also been reported in several patients treated with adalimumab and in one patient who received ustekinumab.

Table 1. Systemic diseases associated with pyoderma gangrenosum

<table>
<thead>
<tr>
<th>Inflammatory bowel disease: ulcerative colitis, Crohn disease</th>
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<tbody>
<tr>
<td>Arthritis: classic rheumatoid arthritis (RA), seronegative RA-like syndrome, non-destructive monoarticular arthritis of large joints</td>
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<tr>
<td>Monoclonal gammopathy: 75% IgA, 25% IgG, rarely myeloma</td>
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<tr>
<td>Immunologic dysfunction: leukaemia, transplants, HIV infection, congenital and acquired hypogammaglobulinaemia</td>
</tr>
<tr>
<td>Haematologic and malignant: leukaemia, IgA myeloma, myelofibrosis, polycythaemia rubra vera, lymphoma, solid tumours of colon, adrenal gland, bladder, breast, lung, ovary</td>
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<tr>
<td>Others: acne conglobate, Behçet disease, chronic active hepatitis, gastric ulceration, Hashimoto thyroiditis, Hidradenitis suppurativa, hyperthyroidism, primary biliary cirrhosis, sarcoidosis, systemic lupus erythematosis, Wegener granulomatosis</td>
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Table 2. Differential diagnosis of pyoderma gangrenosum

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Non-infectious</th>
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<tbody>
<tr>
<td>Bacterial infections (including mycobacteria)</td>
<td>Halogenodermas</td>
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<tr>
<td>Syphilis</td>
<td>Drugs</td>
</tr>
<tr>
<td>Deep fungal infections</td>
<td>Antiphospholipid syndrome</td>
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<tr>
<td>Necrotising fasciitis</td>
<td>Insect bite: spider</td>
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<tr>
<td>Amoebiasis</td>
<td>Factitial</td>
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<tr>
<td>Viral infections (herpes simplex virus, varicella-zoster virus in immunosuppressed patients)</td>
<td>Neoplasms: – lymphoma – systemic vasculitis</td>
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<td>Cutaneous leishmaniasis</td>
<td>Warfarin skin necrosis</td>
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References


Figure 4. Treatment algorithm for pyoderma gangrenosum