

# Tender Annular Plaque on the Thigh

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A 58-year-old man who was receiving gilteritinib therapy for relapsed acute myeloid leukemia presented to the emergency department with a painful, rapidly enlarging lesion on the right medial thigh of 2 days' duration that was accompanied by fever (temperature, 39.2 °C) and body aches. Physical examination revealed a tender annular plaque with a dark violaceous halo overlying a larger area of erythema and induration. Laboratory evaluation revealed a white blood cell count of 600/ $\mu$ L (reference range, 4500–11,000/ $\mu$ L) and an absolute neutrophil count of 200/ $\mu$ L (reference range, 1800–7000/ $\mu$ L). A biopsy was performed.

## WHAT'S YOUR DIAGNOSIS?

- a. ecthyma gangrenosum
- b. erythema migrans
- c. leukemia cutis
- d. papulonecrotic tuberculid
- e. pyoderma gangrenosum

PLEASE TURN TO **PAGE E12** FOR THE DIAGNOSIS

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The authors report no conflict of interest.

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## THE DIAGNOSIS:

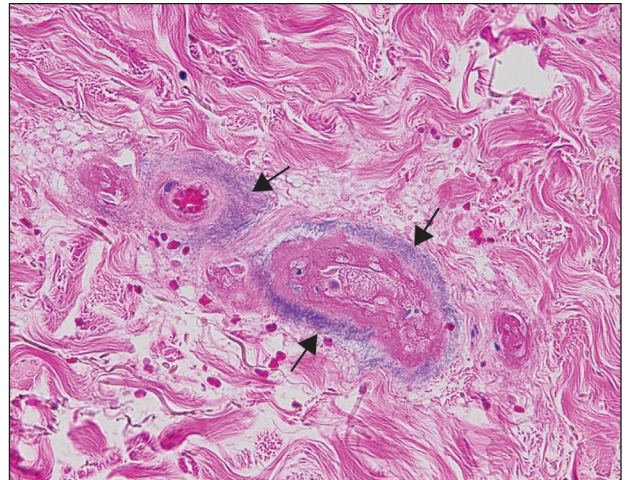
# Ecthyma Gangrenosum

**H**istopathology revealed basophilic bacterial rods around necrotic vessels with thrombosis and edema (Figure). Blood and tissue cultures grew *Pseudomonas aeruginosa*. Based on the histopathology and clinical presentation, a diagnosis of *P aeruginosa*–associated ecthyma gangrenosum (EG) was made. The patient's symptoms resolved with intravenous cefepime, and he later was transitioned to oral levofloxacin for outpatient treatment.

Ecthyma gangrenosum is an uncommon cutaneous manifestation of bacteremia that most commonly occurs secondary to *P aeruginosa* in immunocompromised patients, particularly patients with severe neutropenia in the setting of recent chemotherapy.<sup>1,2</sup> Ecthyma gangrenosum can occur anywhere on the body, predominantly in moist areas such as the axillae and groin; the arms and legs, such as in our patient, as well as the trunk and face also may be involved.<sup>3</sup> Other causes of EG skin lesions include methicillin-resistant *Staphylococcus aureus*, *Citrobacter freundii*, *Escherichia coli*, fungi such as *Candida*, and viruses such as herpes simplex virus.<sup>2,4-6</sup> Common predisposing conditions associated with EG include neutropenia, leukemia, HIV, diabetes mellitus, extensive burn wounds, and a history of immunosuppressive medications. It also has been known to occur in otherwise healthy, immunocompetent individuals with no difference in clinical manifestation.<sup>2</sup>

The diagnosis is clinicopathologic, with initial evaluation including blood and wound cultures as well as a complete blood cell count once EG is suspected. An excisional or punch biopsy is performed for confirmation, showing many gram-negative, rod-shaped bacteria in cases of pseudomonal EG.<sup>7</sup> Histopathology is characterized by bacterial perivascular invasion that then leads to secondary arteriole thrombosis, tissue edema, and separation of the epidermis.<sup>7,8</sup> Resultant ischemic necrosis results in the classic macroscopic appearance of an erythematous macule that rapidly progresses into a central necrotic lesion surrounded by an erythematous or violaceous halo after undergoing a hemorrhagic bullous stage.<sup>1,9</sup> A Wood lamp can be used to expedite the diagnosis, as *Pseudomonas* bacteria excretes a pigment (pyoverdine) that fluoresces yellowish green.<sup>10</sup>

Ecthyma gangrenosum can be classified as a primary skin lesion that may or may not be followed by bacteremia or as a lesion secondary to pseudomonal bacteremia.<sup>11</sup> Bacteremia has been reported in half of cases, with hematogenous metastasis of the infection, likely in manifestations with multiple bilateral lesions.<sup>2</sup> Our patient's presentation of a single lesion revealed a positive blood culture result. Lesions also can develop by direct inoculation of



Histopathology showed basophilic bacterial rods around necrotic vessels (arrows) with thrombosis and edema (H&E, original magnification ×200).

the epidermis causing local destruction of the surrounding tissue. The nonbacteremic form of EG has been associated with a lower mortality rate of around 15% compared to patients with bacteremia ranging from 38% to 96%.<sup>12</sup> The presence of neutropenia is the most important prognostic factor for mortality at the time of diagnosis.<sup>13</sup>

Prompt empiric therapy should be initiated after obtaining wound and blood cultures in those with infection until the causative organism and its susceptibility are identified. Pseudomonal infections account for 4% of all cases of hospital-acquired bacteremia and are the third leading cause of gram-negative bloodstream infection.<sup>7</sup> Initial broad-spectrum antibiotics include antipseudomonal  $\beta$ -lactams (piperacillin-tazobactam), cephalosporins (cefepime), fluoroquinolones (levofloxacin), and carbapenems (imipenem).<sup>1,7</sup> Medical therapy alone may be sufficient without requiring extensive surgical debridement to remove necrotic tissue in some patients. Surgical debridement usually is warranted for lesions larger than 10 cm in diameter.<sup>3</sup> Our patient was treated with intravenous cefepime with resolution and was followed with outpatient oral levofloxacin as appropriate. A high index of suspicion should be maintained for relapsing pseudomonal EG infection among patients with AIDS, as the reported recurrence rate is 57%.<sup>14</sup>

Clinically, the differential diagnosis of EG presenting in immunocompromised patients or individuals with underlying malignancy includes pyoderma gangrenosum, papulonecrotic tuberculid, and leukemia cutis. An erythematous rash with central necrosis presenting in a

patient with systemic symptoms is pathognomonic for erythema migrans and should be considered as a diagnostic possibility in areas endemic for Lyme disease in the United States, including the northeastern, mid-Atlantic, and north-central regions.<sup>15</sup> A thorough history, physical examination, basic laboratory studies, and histopathology are critical to differentiate between these entities with similar macroscopic features. Pyoderma gangrenosum histologically manifests as a noninfectious, deep, suppurative folliculitis with leukocytoclastic vasculitis in 40% of cases.<sup>16</sup> Although papulonecrotic tuberculid can present with dermal necrosis resulting from a hypersensitivity reaction to antigenic components of mycobacteria, there typically are granulomatous infiltrates present and a lack of observed organisms on histopathology.<sup>17</sup> Although leukemia cutis infrequently occurs in patients diagnosed with leukemia, its salient features on pathology are nodular or diffuse infiltrates of leukemic cells in the dermis and subcutis with a high nuclear-to-cytoplasmic ratio, often with prominent nucleoli.<sup>18</sup> Lyme disease can present in various ways; however, cutaneous involvement in the primary lesion is histologically characterized by a perivascular lymphohistiocytic infiltrate containing plasma cells at the periphery of the expanding annular lesion and eosinophils present at the center.<sup>19</sup>

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