

Ecthyma Gangrenosum Due to *Pseudomonas fluorescens*

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PRACTICE POINTS

- Immunocompromised patients with a high exposure to agricultural products may be at increased risk for systemic infection by *Pseudomonas fluorescens*.
- *Pseudomonas fluorescens* is an opportunistic pathogen that can cause ecthyma gangrenosum, which necessitates rapid diagnosis and treatment to prevent mortality.

To the Editor:

A 50-year-old female farmer with diabetes mellitus, paroxysmal atrial fibrillation, and treatment-refractory systemic lupus erythematosus presented with worsening erythema, ecchymoses, edema, and tenderness in the bilateral legs of 3 weeks' duration. The patient was taking oral methylprednisolone 12 mg daily (8 mg in the morning, 4 mg in the evening) for systemic lupus erythematosus. She previously was treated with mycophenolate mofetil, mycophenolic acid, methotrexate, azathioprine, hydroxychloroquine, etanercept, and cyclosporine without success. Cyclophosphamide was helpful in the past, but the last dose was more than 1 year prior to the current presentation. Physical examination showed no fever and 1+ pitting edema to the mid shin. Multiple warm, tender, erythematous to gray plaques were present on the bilateral lower extremities, and a 2-cm ulcerated plaque with a violaceous border was present on the medial surface of the lower left leg (Figure 1). The surrounding erythematous tissue was markedly tender to palpation. No popliteal or inguinal lymphadenopathy was appreciated.



FIGURE 1. Ecthyma gangrenosum caused by *Pseudomonas fluorescens* in a patient with systemic lupus erythematosus. Warm, tender, erythematous to gray plaque on the patient's left leg before ulceration (A). Ulcerated plaque with a violaceous border on the medial surface of the lower left leg; the 2 circular defects represent the central and peripheral punch biopsies sites (B).

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Punch biopsies were obtained from the periphery and center of the ulcerated plaque on the left leg. Histopathologic analysis revealed an ulcerated necrotic epidermis with scant diffuse acute and chronic inflammation (Figure 2A). Leukocytoclastic vasculitis was present at the periphery of the lesion (Figure 2B). Colloidal iron stain revealed a marked increase in dermal mucin. Gram stain showed both gram-positive and gram-negative organisms (Figure 2C). Fungal and hyphal elements were seen in the superficial epidermis. Tissue cultures revealed a predominance of *Pseudomonas fluorescens*, along with *Candida albicans*, *Klebsiella oxytoca*, and *Staphylococcus* and *Enterococcus* species. Bacterial and fungal blood cultures were negative.

The patient was treated with ciprofloxacin, vancomycin, and voriconazole based on culture sensitivities. Although double coverage often is recommended for pseudomonal infections,¹ the patient could not be started on a second antipseudomonal agent due to multiple severe antibiotic allergies. She continued home

administration of methylprednisolone in the setting of active lupus; additional immunosuppression was avoided. Over the course of 1 week, the patient's preexisting ulcerated plaque on the medial surface of the lower left leg gradually improved, and no new lesions developed. Ciprofloxacin, vancomycin, and voriconazole were continued along with insulin, aspirin, warfarin, metoprolol, furosemide, and bumetanide at discharge. The patient subsequently was readmitted to the hospital several more times over the next 4 months for multiple bacterial infections and ultimately died of overwhelming septic shock several months later.

Ecthyma gangrenosum (EG) is a rare cutaneous infection that results from either direct inoculation or hematogenous dissemination. It classically is caused by infection with *Pseudomonas aeruginosa* in immunocompromised or neutropenic patients. However, other bacteria and fungi, mucormycosis, and herpes simplex virus also have been reported to cause EG.¹ Skin lesions often start as erythematous or purpuric macules, develop

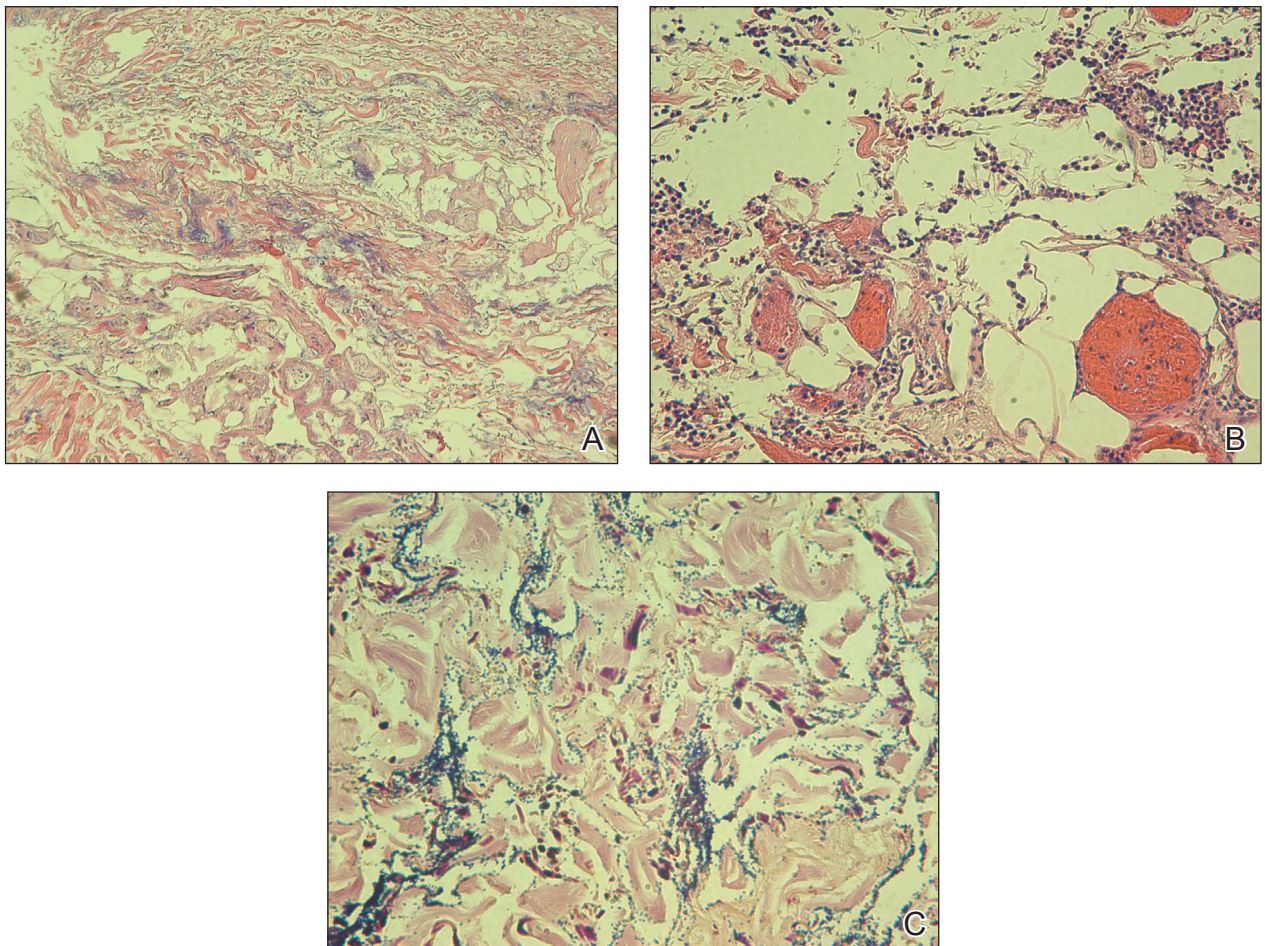


FIGURE 2. Biopsy from the center of the lesion showed an ulcerated necrotic epidermis with scant diffuse acute and chronic inflammation (A) (H&E, original magnification $\times 100$); biopsy from the periphery of the lesion showed leukocytoclastic vasculitis (B) (H&E, original magnification $\times 100$). Gram stain showed both gram-positive and gram-negative organisms (C) (original magnification $\times 100$).

into vesicles and bullae, and eventually become necrotic ulcers with central eschars.² Histopathologic findings reveal necrotizing hemorrhagic vasculitis; gram-negative rods often are found in the medial and adventitial walls of deeper vessels.^{3,4} The case mortality rate is high, ranging from 15% in nonbacteremic patients to 38% to 96% in patients with bacteremia.³

The leukocytoclastic vasculitis seen on biopsy in our patient was a reaction pattern, likely a direct result of the soft tissue infection. Biopsy showed hyphal or pseudohyphal elements in the superficial epidermis, corresponding to the positive *C albicans* growth on fungal culture. *Candida albicans* has been reported to cause lesions that mimic bacterial EG.¹ However, the marked predominance of *P fluorescens* on biopsy and culture suggests that the *Candida* likely were opportunistic and managed to invade secondary to the vascular damage caused by *P fluorescens*.

Pseudomonas fluorescens is an aerobic gram-negative rod-shaped bacterium found in soil that rarely is implicated in human disease. This bacterium is unable to ferment lactose and grows best on MacConkey agar between 30°C and 37°C but also can grow at temperatures as low as 4°C.⁵ The ability of *P fluorescens* to rapidly proliferate at low temperatures (ie, in refrigerated blood products, saline solutions, water dispensers, ice baths, humidifier water) is thought to explain a number of reported clinical consequences, ranging from asymptomatic colonization to fatal bacteremia.⁶⁻¹⁰ This opportunistic pathogen also has been linked to Crohn disease and has been reported to cause pelvic inflammatory disease with the use of intrauterine contraception devices and nosocomial respiratory tract infections due to contaminated spirometers.¹¹⁻¹⁴ In our case, the patient was part of a family of farmers and worked in an agricultural setting. She often handled the produce and worked at the family's produce stand at the local farmer's market. Her exposure to soil and soil pathogens may have been the source of the *P fluorescens* infection.

This case introduces *P fluorescens* as a causative agent of EG, suggests that exposure to agricultural products

may predispose an immunosuppressed patient to this type of infection, and emphasizes the importance of timely diagnosis through tissue culture and histopathology so that immunosuppressive medications can be withheld and appropriate antibiotics can be initiated.

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