Ecthyma Gangrenosum Caused by *Escherichia coli* Bacteremia: A Case Report and Review of the Literature

Jitendrakumar K. Patel, MD; Oliver A. Perez, MD; Martha H. Viera, MD; Monica Halem, MD; Brian Berman, MD, PhD

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GOAL

To understand ecthyma gangrenosum (EG) to better manage patients with the condition

LEARNING OBJECTIVES

Upon completion of this activity, you will be able to:

1. Discuss the development of EG in patients with hematologic malignancies or an immunocompromised status.
2. Name organisms associated with the development of EG.
3. Diagnose EG based on clinical and histologic findings.

INTENDED AUDIENCE

This CME activity is designed for dermatologists and general practitioners.

CME Test and Instructions on page 252.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: October 2009.

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Dr. Patel was Clinical Research Fellow, Department of Dermatology, University of Miami, Miller School of Medicine, Florida, and currently is an intern, Jamaica Hospital Medical Center, New York. Dr. Perez is an advisory liaison, Dr. Viera is Senior Clinical Research Fellow, and Dr. Berman is Professor of Dermatology, all from the Department of Dermatology, University of Miami. Dr. Halem is Assistant Clinical Professor of Dermatology, Columbia University Medical Center, New York, New York. Correspondence: Jitendrakumar K. Patel, MD, 109-20 Queens Blvd, #5-I, Forest Hills, NY 11375 (drjitupatel@yahoo.com).

Ecthyma gangrenosum (EG) is a serious and well-recognized cutaneous condition. Development of EG is most commonly associated with Pseudomonas aeruginosa *septicemia. Other organisms, such as* Escherichia coli, *have been identified less often as the cause of EG. We describe a 50-year-old man previously diagnosed with acute myelogenous leukemia (AML) who developed an* E coli*–colonized EG lesion secondary to* E coli *bacteremia. This*

case represents the seventh of its kind in the literature and the first case in a patient with AML. In addition, a brief review of the etiopathology and management of EG is presented.

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Case Report

A 50-year-old man presented to the emergency department with chief concerns of fever, generalized weakness, fatigue, and bleeding gums of 2 days' duration. Six months prior, the patient had developed fever, nausea, abdominal pain, and gingival bleeding. A complete workup was performed. Results of a bone marrow biopsy showed 70% myeloblasts and normal cytogenetics consistent with a diagnosis of acute myelogenous leukemia (AML) (myelomonocytic [M4]). He received induction chemotherapy in the form of idarubicin (3 days) and cytarabine (7 days). After beginning induction chemotherapy, he intermittently developed various complications, such as *Aspergillus* pneumonia, septicemia, and thrombocytopenia, leading to a switch to consolidation chemotherapy with high-dose cytosine arabinoside. He had completed 4 cycles of high-dose cytosine arabinoside prior to presenting to the emergency department.

Prior to onset of AML, the patient did not have a remarkable medical or surgical history, and he did not have a history of trauma. Upon presentation, physical examination revealed a pale and cachectic appearance. Oral temperature was 38.8°C, and vital signs included the following: blood pressure, 100/56 mm Hg; heart rate, 162 beats per minute; respiratory rate, 20 breaths per minute; and oxygen blood saturation, 100% on room air. Intravenous fluids were started, and blood, urine, and stool cultures were obtained. The admission workup revealed leukopenia, thrombocytopenia, anemia, and elevated neutrophil band count. The patient received packed red blood cells, platelet transfusion, and human granulocyte colony-stimulating factor, as well as cefepime hydrochloride and gentamicin sulfate. An infectious disease specialist was consulted and therapy with daptomycin was started. Blood cultures were positive for gram-negative rods that later speciated as *Escherichia coli* sensitive to intravenous imipenem and cilastatin. Antibiotics were changed and voriconazole was added because of a prior complication of *Aspergillus* pneumonia. The chest x-ray showed right lung base scarring. Urine and stool cultures remained negative for bacteria and fungal organisms.

On the fourth day of admission, the patient developed a 2×2-cm, large, erythematous, edematous lesion with bullae on the right upper extremity. Tenderness was present. The bullae ruptured the next day and became necrotic (Figure 1). There was no regional lymphadenopathy. To rule out an abscess, ultrasonography and computed tomography of the right upper extremity were performed. The results of these tests revealed soft tissue edema consistent with cellulitis without any focal fluid collections. A diagnosis of bullous hemorrhagic cellulitis versus ecthyma gangrenosum (EG) was initially considered. Swab cultures obtained from the base of the lesion and the fluid that drained from the bullae also were cultured and grew gram-negative rods that later speciated as *E coli*. Punch biopsy specimens obtained from the lesion on the

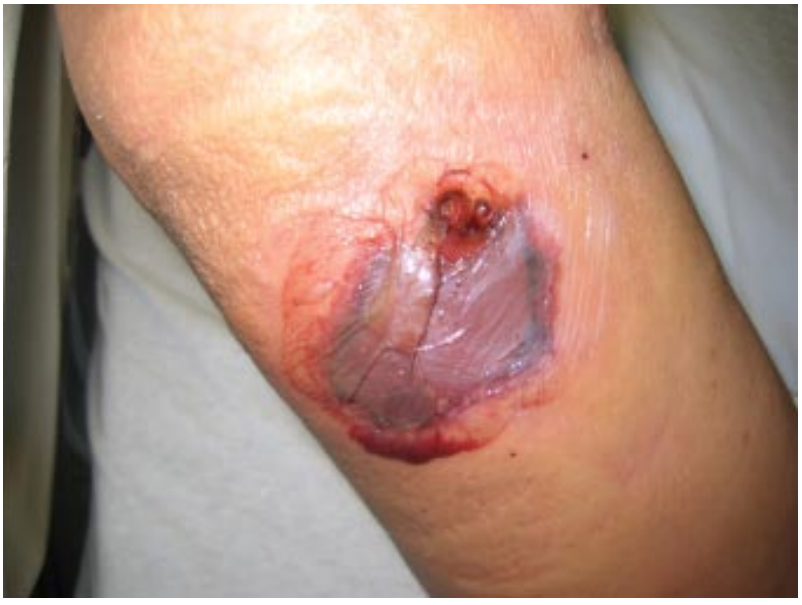

Figure 1. Ecthyma gangrenosum lesion with ruptured bullae at biopsy site.

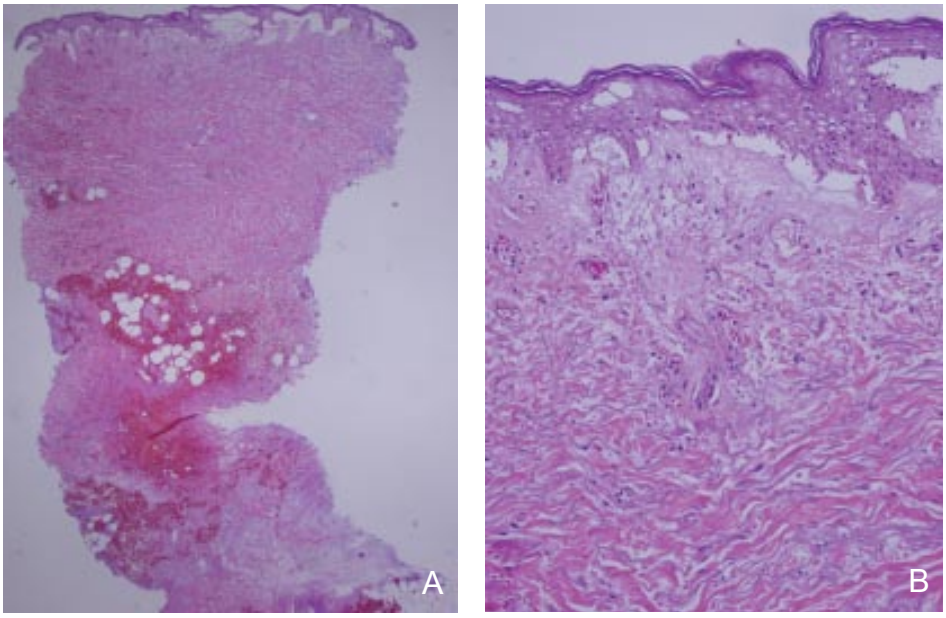

Figure 2. Biopsy of the ecthyma gangrenosum lesion revealed necrosis of the epidermis, dermis, and subcutaneous tissue (A and B)(H&E; original magnifications ×40 and ×100, respectively).

patient's right arm revealed necrosis of the epidermis, dermis, and subcutaneous tissue on histopathologic examination (Figure 2). Brown-Brenn stain identified gram-negative bacterial colonies in the subcutaneous tissue.

Diagnosis of EG secondary to *E coli* bacteremia was made. Therapy with daptomycin was discontinued; mupirocin ointment covered with perforated film absorbent dressing and gauze bandage roll was recommended. A surgeon was consulted and wound debridement was performed. The patient completed a 19-day course of intravenous imipenem and cilastatin with no fever and negative blood, urine, and stool cultures for bacteria and fungal organisms. The white blood cell count was within reference range. Subsequently, cadexomer iodine ointment was started and the patient was discharged after 29 days with wound care instructions.

Comment

Ecthyma is the term used to describe an ulcerative pyoderma of the skin that extends into the dermis; *gangrenosum* refers to necrotic tissue. The first cases of EG were described in 1897 by 2 different groups of investigators.[1,2] However, the nomenclature was introduced in 1930 by Brunsting et al.[3] Ecthyma gangrenosum is a known cutaneous manifestation of a gram-negative organism infection, mainly *Pseudomonas aeruginosa* septicemia. The development of EG lesions in patients with bacteremia occurs via perivascular invasion of numerous viable bacteria, while in patients without bacteremia, development of EG is believed to occur by direct inoculation of the infective organism into the skin site.[4] Most of the patients who have developed EG have been immunocompromised with a prior diagnosis of agammaglobulinemia, hypogammaglobulinemia, aplastic anemia, or AIDS.[5-9] Other underlying diseases related to development of EG include endocarditis, pneumonic plague, and gonorrhea.[10-12] One possible explanation for the development of EG in patients with hematologic malignancies or an immunocompromised status is that EG could be secondary to polymorphonuclear cell dysfunction and defects in T cell function.[13]

Although EG is considered pathognomonic for *Pseudomonas*, other organisms recently have been found to be associated with the development of EG (Table 1). However, only a few case reports of EG have been associated with *E coli* (Table 2). Infections most commonly associated with *E coli* include bacteremia, cellulitis, urinary tract infection, and meningitis.[36-39] The first case of EG associated with *E coli* was reported in 1979 in a 1-year-old child who had gastroenteritis and developed a circular necrotic lesion on the left nostril without bacteremia. *Escherichia coli* was isolated from the culture of the left nasal ulcer.[34] Rajan[16] later reported a case of EG secondary to *E coli* sepsis after spontaneous bacterial peritonitis in a patient with alcoholic cirrhosis. Patients with lung cancer undergoing chemotherapy also have been reported to develop *E coli*–associated EG lesions,[24] and Fuchshuber et al[35] described a case of EG in a patient with multiple myeloma who developed a lesion on the lower extremity secondary to a urinary tract infection caused by *E coli*. Based on a search of the literature using PubMed/MEDLINE for EG, *E coli* and

Table 1.

Ecthyma Gangrenosum Associations

Class	Organisms
Bacteria	*Aeromonas hydrophila*[9]
	Chromobacterium violaceum[14]
	Citrobacter freundii[4]
	Corynebacterium diphtheriae[15]
	Escherichia coli[16]
	Klebsiella pneumoniae[17]
	Morganella morganii[18]
	Neisseria gonorrhoeae[11]
	Pseudomonas aeruginosa[19]
	Pseudomonas cepacia[10]
	Pseudomonas maltophilia[20]
	Pseudomonas stutzeri[21]
	Serratia marcescens[22]
	Staphylococcus aureus[23]
	Streptococcus pyogenes[4,23]
	Xanthomonas maltophilia[24,25]
	Yersinia pestis[12]
Fungus	*Aspergillus fumigatus*[22]
	Candida albicans[26]
	Curvularia species[27]
	Exserohilum species[28]
	Fusarium solani[29]
	Metarhizium anisopliae[30]
	Mucor pusillus[31]
	Pseudallescheria boydii[27]
	Scytalidium dimidiatum[32]
Virus	Herpes simplex virus[33]

EG, and EG and *Pseudomonas*, our patient is the seventh reported case of an EG lesion associated with *E coli* bacteremia and the first case in a patient with AML.

Clinically, EG typically presents as single or multiple grayish black eschars with surrounding erythema and necrosis. Ecthyma gangrenosum lesions caused by bacteremia may induce a disseminated infective vasculitis that is characterized as macules, papules, or nodules. These lesions may have a central hemorrhagic vesicle or bulla that when ruptured leaves a punched out indurated ulcer with elevated edematous edges and central necrosis.[40] The spread of the initial lesion usually takes place within the first 12 hours, as in our patient, and requires immediate attention. The most common sites for EG presentation are the extremities and gluteal, axillary, and perineal regions.[6] The diagnosis of EG is difficult and usually is based on history and clinical examination as well as blood and lesion cultures. A definitive diagnosis can be made by skin biopsy and stains (eg, Brown-Brenn stain, Grocott-Gomori methenamine-silver stain, Warthin-Starry silver stain) to detect bacteria and fungi.[41] Our patient had positive blood and wound swab cultures for *E coli*, and necrosis of the epidermis, dermis, and subcutaneous tissue were identified with a skin biopsy. In addition, the Brown-Brenn stain was positive for gram-negative bacteria. All of these results were suggestive of a diagnosis of EG secondary to *E coli* bacteremia.

Early diagnosis and prompt treatment of EG are crucial for decreasing mortality and preventing complications associated with long-term sequelae, which can be possible by controlling underlying conditions with broad-spectrum antibiotics and/or supportive therapy. The choice of antimicrobial treatment depends on the site, severity of infection, and in vitro antimicrobial sensitivity tests. Antibiotics should cover the gram-negative organism and can include carbenicillin indanyl sodium, gentamicin sulfate, imipenem, mezlocillin, and piperacillin sodium. Usually a combination of antipseudomonal β-lactam penicillin and aminoglycoside is recommended; however, a combination of quinolone and antipseudomonal β-lactam penicillin also can be effective.[42] Surgical drainage of localized abscesses and debridement of all necrotizing tissues may be needed to prevent the spread of infection and septicemia. Resultant large tissue defects may require reconstructive surgery.[43] Granulocyte-macrophage colony-stimulating factor and immunoglobulin may be required in patients with severe neutropenia and hypogammaglobulinemia or agammaglobulinemia.[6,7,44] Despite aggressive therapy, the mortality rate is very high in patients with EG, specifically when associated with shock and multisystem organ failure.[45]

Table 2.

Ecthyma Gangrenosum Caused by *Escherichia coli:* Reports in the Literature

Case Report	Year	No. of Cases	Presenting Site	Preceding Bacteremia	Underlying Disease
Anderson[34]	1979	1	Left nostril	No	Gastroenteritis
Rajan[16]	1982	1	Upper extremity and lower extremity	Yes	Alcoholic cirrhosis
Edelstein and Cutting[24]	1986	3	Lower extremity and perianal skin	Yes	Lung cancer
Fuchshuber et al[35]	1998	1	Lower extremity	Yes	Multiple myeloma
Present case	Reported in 2007	1	Upper extremity	Yes	Acute myelogenous leukemia

Prognosis also depends on the patient's general health and immunologic status and is poor in patients with an underlying malignancy, neutropenia, or bacteremia.[40,46,47] If the source of *P aeruginosa* sepsis is the lung or abdomen, the mortality rate has been reported to be as high as 100%.[45] Also, a delay of 1 to 2 days in the administration of appropriate antibiotic therapy has been reported to increase the mortality rate from 46% to 74%.[48] However, in patients with EG but without bacteremia, prognosis usually is better and the reported mortality rate is 15%.[49] Because of fewer reported cases, prognosis of EG associated with *E coli* bacteremia is unknown.

Conclusion

We report an unusual manifestation of EG that developed secondary to *E coli* bacteremia. Our patient had an underlying malignancy and was immunocompromised, both associated with a poor prognosis. However, after prompt and appropriate systemic antibiotic therapy, local debridement at the EG site, and supportive medical management, our patient was discharged from the hospital 29 days after admission. Even though EG is considered pathognomonic for *Pseudomonas*, other infectious agents, including fungal and viral organisms, should be considered. Early diagnosis and prompt treatment of EG are crucial for decreasing mortality and preventing complications associated with long-term sequelae.

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