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*Visual clues to the diagnosis of infectious disease***Recognizing Less Common Causes of Bacterial Cellulitis**Martin Van Dort, MD, Wael E. Shams, MD,
Patrick N. Costello, MD, and Felix A. Sarubbi, MD**Key words:** Cellulitis ■ *Enterobacter aerogenes* ■ Gram-negative bacteria

Cellulitis is an inflammatory response of the skin and subcutaneous tissue to noxious stimuli.¹ There are numerous causes of cellulitis, including infection; allergic dermatoses; drug reactions; and rheumatological diseases, such as systemic lupus erythematosus and gout. Cellulitis secondary to infection is a common cause of emergency department visits and hospitalizations.

Infectious cellulitis can be caused by bacteria, viruses, fungi, and parasites. *Staphylococcus aureus* and *Streptococcus* are the most common bacterial causes of cellulitis.¹ In data obtained from 5 series involving 284 patients and 86 bacterial isolates, Gram-positive organisms, including *S aureus*, groups A and B streptococci, and viridans streptococci, accounted for 79% of cases, while the remainder were caused by Gram-negative organisms.²

Cases of cellulitis caused by other, less common Gram-positive bacteria, such as *Erysipelothrix rhusiopathiae*, also have been reported (Figures 1 and 2).³ Although erysipeloid may resemble staphylococcal or streptococcal cellulitis, there are clues to distinguishing them. In erysipeloid, for example, suppuration and pitting edema are absent; also, erysipeloid has a distinctive violaceous color that is not typically seen in staphylococcal or streptococcal cellulitis.³

Although cellulitis occurs in persons of all ages, it is



Figure 1 – This resolving subacute cellulitis was caused by *Erysipelothrix rhusiopathiae*. The patient, a 54-year-old man, had been treated with doxycycline and ciprofloxacin. He probably acquired the infection while at his fishing camp. (From Durham HL et al. *Infect Med.* 2003.³)

more common at the extremes of age. Predisposing local factors include skin trauma, edema, dermatoses such as eczema, skin breakdown secondary to pressure ulcers or fungal infection, and chronic vascular insufficiency that predisposes to skin breakdown and ulceration.² Systemic predisposing factors include poorly controlled diabetes mellitus, immunodeficiency, liver cirrhosis, nephrotic syndrome, and heart failure.¹

Cellulitis can sometimes recur. Factors that may contribute to recurrent cellulitis include trauma, chronic venous stasis, tinea pedis, retained foreign bodies, anatomic abnormalities, underlying malignancy, radiation therapy, surgery, and immunosuppression.^{4,5} *S aureus* and groups B, C, and G streptococci may also cause recurrent cellulitis (Figure 3).⁶

The preferred treatment of patients with recurrent cellulitis is indefinite prophylaxis with a suitable antibiotic. In a patient with recurrent cellulitis caused by group A

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streptococci, long-term treatment with penicillin VK (500 mg twice daily) would be appropriate.⁶

Cellulitis caused by various species of Gram-negative bacteria, including *Escherichia coli*, *Proteus*, *Klebsiella*, *Enterobacter*, *Pseudomonas*, and *Serratia*, has been reported in patients with underlying diabetes, liver cirrhosis, penetrating injuries, surgical wounds, neutropenia, or immunosuppression.² In contrast, cellulitis secondary to *Aeromonas hydrophila* may occur in healthy persons after exposure of traumatized skin to freshwater.⁷

Gram-negative bacilli are rarely implicated as a cause of cellulitis in immunocompetent patients. These organisms are more often associated with skin infections from a penetrating injury, in persons with diabetes or cirrhosis, or in persons who are immunocompromised. Presented here is an uncommon case of severe cellulitis caused by *Enterobacter aerogenes* in an immunocompetent and otherwise healthy man.

Case report

A 37-year-old construction worker was hospitalized with a fever (temperature, 38.3°C [101°F]), chills, and left leg erythema. He had no other significant medical history. He stated that his left foot was exposed to sewage water while at a job site several days before the onset of symptoms.

The patient's vital signs were a blood pressure of 107/66 mm Hg, pulse rate of 98 beats per minute, and respiration rate of 22 breaths per minute. The physical examination findings revealed bilateral tinea pedis and a nontender, mildly swollen, and erythematous left leg with small bullae that contained yellow purulent fluid. He also had tender left-sided inguinal adenopathy. The findings from the remainder of the physical examination were normal.

The patient's white blood cell (WBC) count was 8800/μL, with 54% bands; hemoglobin level was 16.3 g/dL; and platelet count was 153,000/μL. Results of a comprehensive metabolic panel were normal. Blood cultures were obtained, and the patient was given ceftriaxone empirically. A Doppler ultrasonogram of the legs ruled out deep venous thrombosis.

Over the next 48 hours, the patient's condition deteriorated. He became lethargic, confused, and short of breath. The systolic blood pressure decreased to 90 mm Hg, and both his respiration and pulse rates increased (30 breaths per minute and 130 beats per minute, respectively). The left leg erythema extended to involve the entire left lower extremity with several confluent bullae (Figure 4).

Fluid from a bulla was aspirated, and a Gram stain showed some WBCs but no organisms. The patient's therapy was switched to vancomycin, clindamycin, gentamicin, and fluconazole. Intravenous immunoglobulin

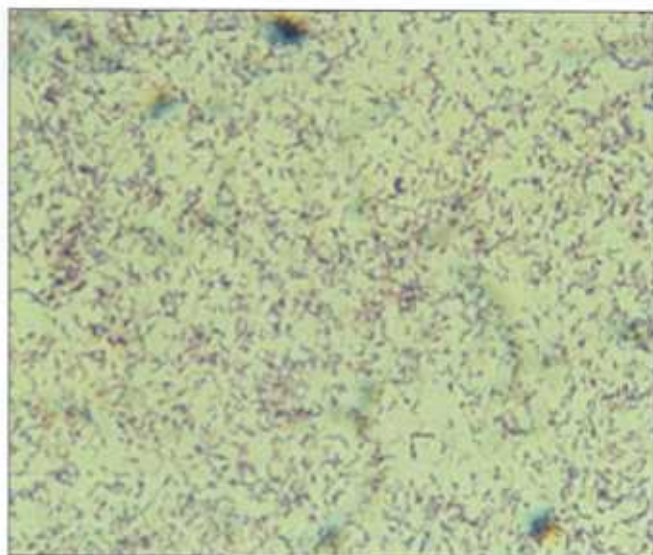


Figure 2 – A Gram stain of the organism identified on culture as *Erysipelothrix rhusiopathiae* is shown here (original magnification $\times 1000$). (From Durham HL et al. *Infect Med.* 2003.¹)



Figure 3 – This 41-year-old indigent woman had a 12-year history of recurrent cellulitis. In this episode, group A streptococcus was identified as the cause. Although she received antibiotic therapy during some episodes, she had never been on a constant therapeutic regimen. Residual lymphedema developed, and she was lost to follow-up. (From Vincent AL et al. *Infect Med.* 2005.⁶)



Figure 4 – Within 48 hours of hospitalization, the cellulitis had spread to involve the patient's entire left leg.



was also administered.

A skin biopsy specimen showed nonspecific inflammatory changes suggestive of acute cellulitis. An MRI scan of the left lower extremity showed no evidence of abscess or necrotizing fasciitis. The patient's condition improved over the next few days.

The culture of the bulla fluid grew *E aerogenes* susceptible to ceftriaxone, gentamicin, and levofloxacin. Blood cultures remained negative. The patient was discharged home and given a 2-week course of oral levofloxacin, 750 mg/d. He fully recovered.

Discussion

Gram-negative cellulitis can be severe and may sometimes represent one of several skin and soft tissue manifestations of Gram-negative bacillary sepsis.⁸ Edema, tissue ischemia, bleb formation, and gangrene may occur after thrombosis of blood vessels. However, underlying muscle is usually spared.¹

E aerogenes is a facultative, anaerobic, motile, short

Gram-negative rod that has a relatively small capsule. It is a member of the Enterobacteriaceae family, whose natural habitat is the intestinal tract of humans and animals. However, the organism may be free-living as well. *E aerogenes* is a lactose fermenter forming colored viscous colonies on differential eosin-methylene blue agar (Figure 5).⁹

Cellulitis secondary to infection with *Enterobacter* species has been rarely reported in immunocompetent hosts. In one case report, bullous hemorrhagic cellulitis developed in a 45-year-old otherwise healthy man.¹⁰ *Enterobacter cloacae* was isolated from bullae fluid, and the patient responded to a course of gentamicin.¹⁰

Another case of cellulitis caused by *E cloacae* was reported in an immunocompetent patient who presented with bilateral paronychia infections of both great toes.¹¹ The patient recovered after treatment with antibiotics and local debridement.

Prolonged cellulitis and abscess caused by *E cloacae* developed after a plant thorn injury to the wrist in a healthy 5-year-old boy.¹² The child did well after abscess drainage

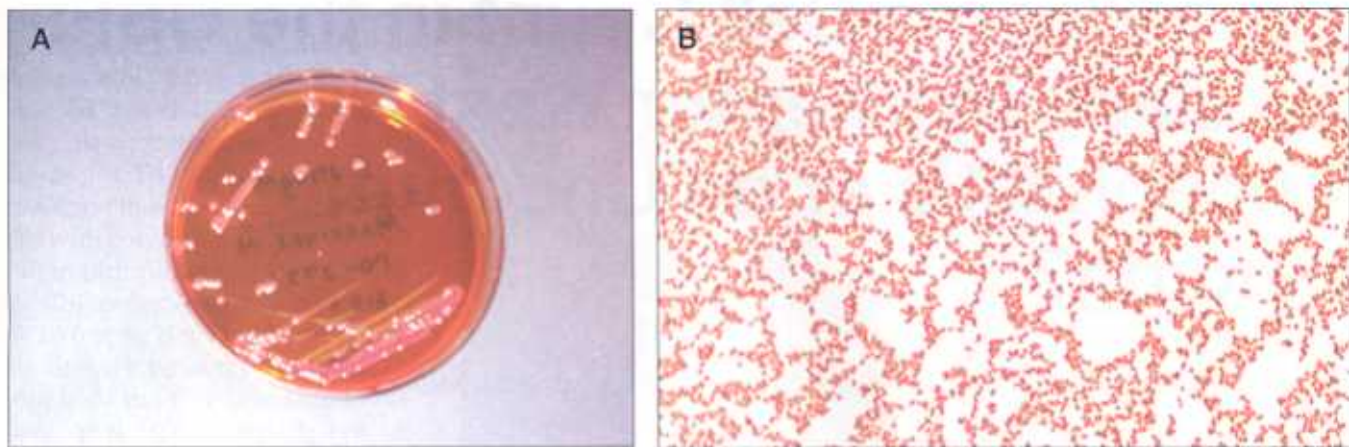


Figure 5 – This culture (A) of fluid aspirated from a bulla on the patient's leg shows growth of *Enterobacter aerogenes* (culture medium, cosin-methylene blue agar). A Gram stain (B) of a colony swab from the culture plate shows the characteristic morphology of *E. aerogenes*.

and thorn removal.

Two cases of crepitant cellulitis caused by *E. aerogenes* in patients with diabetes have been reported. One of the patients died despite surgical intervention and antibiotic therapy.¹³ The other patient, who had diabetes with vascular disease, was treated successfully with a 10-day course of intravenous loramphenicol.¹⁴

Gram-negative cellulitis caused by *E. aerogenes* in a nondiabetic immunocompetent patient has not been reported previously. The patient described in our case report probably acquired the *E. aerogenes* infection after his feet were contaminated with sewage water while he was working at a construction site. Skin breakdown secondary to tinea pedis probably served as the portal of entry for the bacteria.

Empiric therapy for acute cellulitis should be based on the possible causative organisms, the patient's predisposing factors, and the circumstances in which the infection occurred. Failure to account for these factors may result in poor outcomes related to delays in appropriate treatment of patients with these uncommon yet serious infections.

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