

Necrotizing Cellulitis With Multiple Abscesses on the Leg Caused by *Serratia marcescens*

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PRACTICE POINTS

- *Serratia marcescens* skin infection should be considered in cases of cellulitis in immunocompromised patients when conventional antibiotics are not effective.
- Broad-spectrum antibiotics such as third-generation cephalosporins, fluoroquinolones, or imipenem-cilastatin are indicated in cases of *S marcescens* skin infections, and surgery should be promptly considered.

Serratia marcescens is an unusual cause of severe skin infection initially described in immunocompromised patients. We report a case of necrotizing cellulitis of the leg caused by *S marcescens* in a 68-year-old woman with diabetes mellitus and a history of chronic lymphoedema of the leg. We reviewed the literature and found 49 cases of severe skin infections from *S marcescens* that included 20 cases of necrotizing fasciitis (NF) as well as 29 cases of severe skin infections without NF (non-NF cases). Patients were immunocompromised in 59% to 70% of cases. The mortality rate was high in NF cases (60%) versus non-NF

cases (3%). Surgery was required in 95% of NF cases and in 24% of non-NF cases. The other clinical manifestations of *S marcescens* skin infection reported in the literature included disseminated papular eruptions in patients infected with human immunodeficiency virus with folliculitis on the trunk. *Serratia marcescens* is naturally resistant to amoxicillin alone and amoxicillin associated with clavulanic acid. Broad-spectrum antibiotics are indicated to treat *S marcescens* skin infections, and surgery should be promptly considered in cases of severe skin infections if appropriate antibiotic therapy does not lead to rapid improvement.

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A gram-negative bacillus of the Enterobacteriaceae family, *Serratia marcescens* is an organism known to cause bacteremia, pneumonia, urinary tract infection, endocarditis, meningitis, and septic arthritis.¹ Unusual cases of cellulitis and necrotizing fasciitis (NF) caused by *S marcescens* also have been reported.^{2,3} This entity has been initially described in immunocompromised and nonimmunocompromised patients.⁴ Both community and nosocomial cases also have been reported.³

Case Report

A 68-year-old morbidly obese woman with high blood pressure, diabetes mellitus, chronic renal insufficiency, chronic venous insufficiency, and left leg lymphoedema was referred to our emergency unit. She had pain and circumferential erythema with multiple abscesses of the left leg of 2 weeks' duration. No history of trauma, ulcer, injection, or animal bite was noted. At the time of presentation she had no fever and vital parameters were normal. Empirical treatment with oral amoxicillin (6 g daily) and amoxicillin-clavulanate (375 mg daily) was started. Forty-eight hours later, inflammation, pain, and abscesses worsened (Figure 1A). Laboratory tests showed an elevated white blood cell count ($15.9 \times 10^9/L$ with 86% neutrophils [reference range, $4.5\text{--}11.0 \times 10^9/L$]) and an elevated C-reactive protein level (322 mg/L [reference range, <2 mg/L]). Human immunodeficiency virus serology was negative. Needle aspiration

of an abscess yielded *S marcescens*. A second aspiration confirmed the presence of the same organism, wild-type *S marcescens*, which was resistant to amoxicillin and clavulanic acid, first-generation cephalosporin, and tobramycin but sensitive to piperacillin, third-generation cephalosporins, amikacin, ciprofloxacin, and co-trimoxazole. Intravenous cefepime, a third-generation cephalosporin, was started. During the next 48 hours the patient developed severe sepsis with confusion, acute renal failure (creatinine: $231 \mu\text{mol/L}$ vs $138 \mu\text{mol/L}$ at baseline [reference range, $53\text{--}106 \mu\text{mol/L}$]), and worsening of skin lesions. Blood cultures were negative and amikacin was added. Magnetic resonance imaging showed a diffuse inflammatory process involving the skin and subcutaneous tissue that extended to the soleus fascia with no other muscle involvement or deep collection (Figure 2). Surgical debridement of infected tissues was performed (Figure 1B). Histologic examination revealed spreading suppurative inflammation



Figure 1. Erythema with multiple abscesses on the left ankle and leg at presentation (A), day 1 following surgical debridement of infected tissues (B), and 2 months later with complete healing following a skin graft (C).

Immunologic Factors Predisposing to *Serratia marcescens* Severe Skin Tissue Infections

Immunologic Factor	No. of Cases (%)		
	NF (n=20)	Non-NF Severe Skin Infection (n=29)	Total (N=49)
Renal insufficiency ^{3,17,20,22,24,26,27,39,a}	6 (30)	4 (14)	10 (20)
Chronic granulomatous disease ^{29,34,44,45}	0 (0)	8 (28)	8 (16)
Immunosuppressive drugs (eg, nonsteroidal anti-inflammatory drugs, corticosteroid, cyclosporine, chemotherapy) ^{3,12,17,19,20,25,31}	5 (25)	2 (7)	7 (14)
Diabetes mellitus ^{3,22,23,26,30,40}	4 (20)	3 (10)	7 (14)
Heart failure ^{3,15,22,27,30,37}	4 (20)	2 (7)	6 (12)
Lupus ^{3,17,20}	3 (15)	0 (0)	3 (6)
Solid tumor or hemopathy ^{13,25}	2 (10)	0 (0)	2 (4)
Nephrotic syndrome ^{12,20}	2 (10)	0 (0)	2 (4)
Hepatic cirrhosis ^{32,33}	0 (0)	2 (7)	2 (4)
Agranulocytosis ^{25,36}	1 (5)	1 (3)	2 (4)

Abbreviation: NF, necrotizing fasciitis.

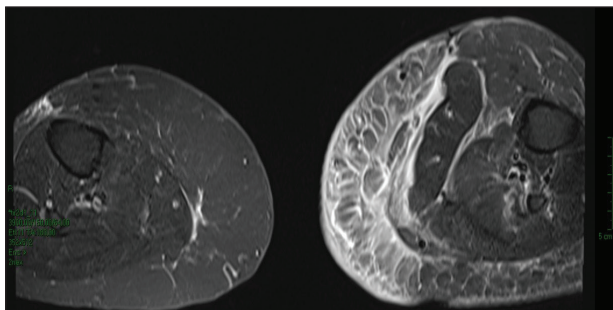


Figure 2. Magnetic resonance imaging showed a diffuse inflammatory process involving the skin and subcutaneous tissue that extended to the soleus fascia with no other muscle involvement or deep collection.

involving the dermis and subcutaneous tissues. Clinical healing was obtained after 21 days of antimicrobial therapy. The debrided area required skin grafting 2 months later (Figure 1C).

Comment

The most common causative bacteria of cellulitis are *Staphylococcus aureus* and group A β -hemolytic streptococci. *Serratia marcescens* is a rare but increasingly recognized pathogen of skin and soft

tissue infections.⁵ The proposed pathogenic mechanism for skin necrosis during *S marcescens* infection is the bacterial production of large proteases (eg, deoxyribonuclease, lipase, gelatinase).⁶ Injection of purified proteinase from *S marcescens* into rat skin leads to increased vascular permeability, necrosis of epidermal tissue, dermal inflammation and edema, and infiltration of polymorphonuclear leukocytes into the subcutaneous fat and muscle.⁷ *Serratia marcescens* is ubiquitous in soil and water and it also may colonize the respiratory, urinary, and digestive tracts in humans. Cellulitis due to *S marcescens* secondary to iguana bites^{8,9} and snake bites¹⁰ or leech-borne cellulitis¹¹ suggest that the oral cavity of these animals may be colonized. To date, 49 cases of severe *S marcescens* skin infections have been described, according to a search of PubMed articles indexed for MEDLINE using the terms *Serratia marcescens* and skin, cutaneous, soft tissue, and cellulitis or necrotizing fasciitis: 20 cases with NF^{3,12-28} and 29 non-NF cases^{8-11,29-46} (typical cellulitis presentation [n=8]^{9,11,35-38,40}; abscesses, gumma, or pyoderma gangrenosum-like lesions associated with chronic granulomatous disease in childhood [n=7]^{29,44,45}; painful nodules with secondary abscesses [n=6]^{31-34,46}; acute bullous cellulitis [n=4]^{8,10,30}; secondary infections of ulcers

[n=2]^{35,40}; abscesses in immunocompetent patient [n=1]⁴¹; and necrotizing skin ulceration [n=1]³⁶). Lower extremities were frequently involved (NF cases, n=13; non-NF cases, n=16). Underlying immunosuppression was observed in 14 NF cases and in 17 non-NF cases. Predisposing immunologic factors are summarized in the Table. Local risk factors, including chronic leg edema, trauma, surgical wound, filler injection, and ulcer, were frequently reported in NF and non-NF cases,^{16,20,26-28,31,32,34,35,37,38,40,46} including our case. Surgery was required in 19 NF cases and in 7 non-NF cases. *Serratia marcescens*-mediated NF led to higher mortality (n=12) than non-NF cases (n=1). Other nonsevere clinical manifestations of *S marcescens* infection reported in the literature included disseminated papular eruptions with human immunodeficiency virus infection⁴² and trunk folliculitis.⁴³ Our patient had many risk factors, including chronic edema, diabetes mellitus, chronic renal insufficiency, and chronic venous insufficiency. The potential presence of abscesses and necrotic tissue hinders antibiotic penetration at the infection site, and surgery should be systematically considered as early as possible in view of the high mortality rate of *S marcescens* cellulitis.

Conclusion

Although uncommon, an *S marcescens* skin infection may be suspected in cases of cellulitis in immunocompromised patients, especially when conventional antibiotics are not effective. *Serratia marcescens* naturally produces a cephalosporinase that confers resistance to amoxicillin and to amoxicillin associated with clavulanic acid. Broad-spectrum antibiotics such as third-generation cephalosporins, fluoroquinolones, or imipenem-cilastatin are indicated in cases of *S marcescens* skin infections, and surgery should be promptly considered if appropriate antibiotic therapy does not lead to rapid clinical improvement.

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