Serratia marcescens Necrotizing Fasciitis Presenting as Bilateral Breast Necrosis

Tayyab Rehman1, Thomas A. Moore2,3, Leonardo Seoane3,4

Running title: Serratia marcescens Necrotizing Fasciitis

1Section of Pulmonary & Critical Care Medicine, Louisiana State University Health Sciences Center, New Orleans, LA.

2Department of Infectious Diseases, Ochsner Clinic Foundation, New Orleans, LA.

3Multi-Organ Transplant Institute, Ochsner Clinic Foundation, New Orleans, LA.

4The University of Queensland School of Medicine, Ochsner Clinical School, New Orleans, LA.

Corresponding author: lseoane@ochsnser.org

Mailing address: 1514 Jefferson Highway, New Orleans, LA 70121.

ABSTRACT

Serratia marcescens is an extremely rare cause of necrotizing fasciitis. We report the first case of necrotizing fasciitis of the chest wall due to infection with S. marcescens that initially manifested as bilateral breast necrosis. The patient had a fulminant course leading to death within 72 hours of presentation. Literature pertinent to S. marcescens-mediated necrotizing fasciitis is also reviewed.

CASE REPORT

A 54-year-old woman with a history of lupus and end-stage renal disease requiring long-term dialysis presented with the chief complaint of bilateral mastalgia for 4 days. Eighteen months prior to presentation, the patient developed central venous catheter-related superior vena
cava (SVC) stenosis that proved refractory to angioplastic interventions. Subsequent clinical course was marked by progressive symmetric enlargement of her breasts from cup size B at baseline to larger than DD. A high-output left upper extremity arteriovenous (AV) fistula – originally created to provide hemodialysis access – appeared to be contributing to central venous congestion and breast engorgement. Five days prior to presentation, the AV fistula was ligated. The following day, the patient developed severe pain in both her breasts. There was no report of fever or chills. Home medications included prednisone 10 mg per day for immune thrombocytopenic purpura. The patient denied prior or current alcohol or intravenous drug use.

Initial vital signs were temperature 97.9°F, blood pressure 81/58 mmHg, heart rate 114 beats per minute, respiratory rate 22 breaths per minute, and arterial oxygen saturation 96% while breathing room air. General assessment was remarkable for facial plethora and bilateral upper extremity swelling. There was massive enlargement of both breasts with hyperpigmentation of overlying skin. The breasts were warm, tender, and edematous, without any palpable masses or a nipple discharge. The AV fistula ligation appeared uninfected. The patient was noted to have no indwelling vascular access catheters.

On laboratory work-up, a complete blood count revealed leukopenia with left shift (white blood cells $2.5 \times 10^3$ per mm$^3$, segmented neutrophils 74%, bands 9%, metamyelocytes 5%, myelocytes 3%, lymphocytes 5%, monocytes 5% and eosinophils 1%) and thrombocytopenia (52,000 per mm$^3$). A chemistry panel showed a metabolic acidosis with elevated lactic acid level (4 mmol/L). A test for human immunodeficiency virus (HIV) was negative.

The patient was diagnosed with severe sepsis. Management was initiated in accordance with the institution’s severe sepsis and septic shock protocol. Two sets of blood cultures were
obtained using separate venipuncture sites, and an empiric antibiotic regimen comprising vancomycin, piperacillin-tazobactam, and ciprofloxacin was instituted. Blood culture bottles (BD BACTEC™ Plus Aerobic/F and BD BACTEC™ Lytic/10 Anaerobic/F, 2 sets) were incubated in the BD BACTEC™ FX blood culture system. Fourteen hours later, the cultures turned positive. Gram staining revealed the presence of a gram-negative rod in 3 out of 4 culture bottles. Selective media were inoculated with the following results: MacConkey agar showed the growth of a lactose non-fermenting organism; triple sugar iron (TSI) agar showed an alkaline/acid reaction without gas formation; and phenylethyl alcohol (PEA) blood agar showed no growth. Subsequent identification and antimicrobial susceptibility testing was carried out using the automated SIEMENS MicroScan® WalkAway96 system. The organism was finally speciated as Serratia marcescens with susceptibility profile as shown in Table 1.

With worsening breast examination and rising lactic acid levels, the patient was taken to the operating room where both breasts were confirmed to be nonviable and were removed. The chest wall underneath the breasts demonstrated evidence of necrotizing fasciitis and pectoral myonecrosis. A radical chest wall debridement was performed that included the pectoral fascia and the bulk of the pectoralis major and pectoralis minor muscles bilaterally. Intraoperative cultures from the deep pectoral fascia also grew back S. marcescens with a susceptibility profile similar to the organism growing from the blood (Table 1). The antibiotic regimen was modified to doripenem to cover multidrug resistance. However, the patient continued to deteriorate clinically and despite maximal supportive care died of overwhelming septic shock.
Necrotizing fasciitis is an uncommon life-threatening soft tissue infection (7). The clinical syndrome is characterized by widespread subcutaneous fascial and fat necrosis associated with severe systemic toxicity. Early debridement, intravenous antibiotics, and supportive care are the cornerstones of therapy (12, 17). A variety of microorganisms—gram-positive cocci, gram-negative rods, and anaerobes—have been implicated as etiologic agents. \( S. \) \textit{marcescens} is an extremely rare cause of necrotizing fasciitis.

\( S. \) \textit{marcescens} is a gram-negative aerobic bacillus belonging to the family \textit{Enterobacteriaceae}. \textit{Serratia} species are widely distributed in nature, hospitals and may even be found as commensal in the human gut microbiota. In recent years, \( S. \) \textit{marcescens} has been increasingly recognized as an important and frequent opportunistic pathogen. \textit{Serratia} species rank among the 10 most common causes of bacteremia (3), and skin and soft tissue infections (13), accounting for 1.4% and 2.0% of cases respectively. Epidemiologic studies have shown an incidence rate of 1.3 cases of \textit{Serratia} bacteremia per 100,000 of population (6). A substantial proportion (47%) of these events originates in the community. Thus, \textit{Serratia} is not a strict nosocomial pathogen and frequently causes disease in non-hospital settings. Around a third of patients with \textit{Serratia} bacteremia are not alive 6 months after diagnosis (6). While non-\( marcescens \) \textit{Serratia} species may be pathogenic, more than 90% of isolates in humans are \( S. \) \textit{marcescens} (9). A high rate of antimicrobial resistance has not been shown in epidemiologic studies, though a few reports do indicate the presence of multidrug-resistant strains (1, 6, 9).

The exact mechanisms underlying the virulence of \( S. \) \textit{marcescens} in humans are not completely known. Culture filtrates prepared from \( S. \) \textit{marcescens} are toxic to mammalian cells (4) including human fibroblasts (14). \( S. \) \textit{marcescens} secretes a broad array of factors, including a...
hemolysin, a nuclease, a metalloprotease, serine proteases, siderophores, and lipases (1).

Molecular studies have shown a secreted 56-kDa metalloprotease (common to all *S. marcescens* strains) to be a critical mediator of cytotoxicity *in vitro* (11). Whether neutralization of this metalloprotease *in vivo* has any therapeutic utility remains to be explored.

To identify previously reported cases of *S. marcescens*-mediated necrotizing fasciitis, a Medline search was performed using search terms necrotizing fasciitis, *Serratia*, and *Serratia marcescens*. The search was limited to the English-language literature published between January 1966 and September 2011. Reference lists of identified reports were also reviewed to find additional cases of *S. marcescens* necrotizing fasciitis. As a result, 9 previously reported cases were identified (Table 2) (2, 5, 8, 10, 15, 16, 19, 21). Overall, the lower extremity was the most common site of infection, being involved in 7 out of 10 (70%) patients. The present case constitutes the first report of *S. marcescens* causing necrotizing fasciitis of the chest wall.

A known immunocompromised state was not always identified in previous reports. None of the patients were infected with HIV, even though all cases emerged after 1985. Several comorbidities and risk factors were noted that might have contributed to enhanced susceptibility to infection with *S. marcescens*. Advanced renal disease was present in 4 out of 10 patients, with 3 patients receiving scheduled hemodialysis. Corticosteroid use was reported in 3 out of 10 patients. Three patients had diabetes mellitus, 2 had lupus, and 1 had received chemotherapy for lung cancer. The antibiotic susceptibility profile of the isolated *S. marcescens* was reported only by Curtis et al. (5) who found their isolate to be resistant to ampicillin, cefazolin, and cefuroxime but susceptible to ceftriaxone, cefipime, piperacillin-tazobactam, imipenem, ciprofloxacin, and gentamicin. All patients underwent early surgical debridement; nonetheless, 7 out of 10 patients
(70%) had a fatal outcome. Septic shock with multiorgan failure was the most frequent pathophysiological syndrome leading to death.

In our patient, necrotizing fasciitis of the chest wall might have started with direct seeding of the pectoral fascia through a break in the overlying skin. Alternatively, the chest wall fascia might have become secondarily involved due to hematogenous dissemination. Our patient had several predisposing conditions for invasive soft tissue and bloodstream infections. Chronic hemodialysis and corticosteroid use have previously been shown to be risk factors for gram-negative rod bacteremia (18, 20). Whether prior splenectomy in our patient contributed to infection with *S. marcescens* is not entirely clear. *S. marcescens* is not an encapsulated organism, and splenectomized patients have not been shown to be at increased risk for infections with *Serratia* spp.

In conclusion, we report a case of fulminant necrotizing fasciitis presenting as bilateral breast necrosis. To our knowledge, this is the first reported case of necrotizing pectoral fasciitis due to infection with *S. marcescens*. Despite the unusual presentation, this case illustrates the significant morbidity and mortality that can be associated with *S. marcescens* infections. Moreover, it highlights that in patients with lupus and renal failure presenting with necrotizing fasciitis, the initial antibiotic coverage should be broad enough to cover for multidrug-resistant gram-negative bacilli such as *S. marcescens*.

REFERENCES


Table 1 – Antimicrobial susceptibility profile of *S. marcescens* isolate from blood and breast tissue

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (µg/ml)</th>
<th>Isolate from blood</th>
<th>Isolate from breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>≤4 (S)</td>
<td>≤16 (S)</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin/K Clavulanate</td>
<td>&gt;16/8 (R)</td>
<td>&gt;16/8 (R)</td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>16 (I)</td>
<td>&gt;16 (R)</td>
<td></td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>16/8 (I)</td>
<td>16/8 (I)</td>
<td></td>
</tr>
<tr>
<td>Aztreonam</td>
<td>≤8 (S)</td>
<td>≤8 (S)</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>&gt;32 (R)</td>
<td>≤2 (S)</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime/K Clavulanate</td>
<td>&gt;4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>4 (S)</td>
<td>≤1 (S)</td>
<td></td>
</tr>
<tr>
<td>Ceftazidime/K Clavulanate</td>
<td>&gt;2</td>
<td>≤0.25</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&gt;32 (R)</td>
<td>≤8 (S)</td>
<td></td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>&gt;16 (R)</td>
<td>&gt;16 (R)</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>≤1 (S)</td>
<td>≤1 (S)</td>
<td></td>
</tr>
<tr>
<td>Ertapenem</td>
<td>≤2 (S)</td>
<td>≤2 (S)</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>2 (S)</td>
<td>≤4 (S)</td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td>2 (S)</td>
<td>≤4 (S)</td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>≤2 (S)</td>
<td>≤2 (S)</td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td>≤4 (S)</td>
<td>≤4 (S)</td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>≤2 (S)</td>
<td>≤2 (S)</td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td>8 (I)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticarcillin/K Clavulanate</td>
<td>≤16 (S)</td>
<td>≤16 (S)</td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>4 (S)</td>
<td>≤4 (S)</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>≤2/38 (S)</td>
<td>≤2/38 (S)</td>
<td></td>
</tr>
</tbody>
</table>

MIC = minimal inhibitory concentration; S = susceptible; I = intermediate; R = resistant. MICs were determined with the use of the SIEMENS MicroScan® system using the gram-negative NC44 tray for the isolate from blood and NBPC34 tray for the isolate from breast tissue. Formal testing for extended spectrum beta-lactamase production was not performed.
Table 2 – Reported Cases of *S. marcescens* Necrotizing Fasciitis, 1966 to Present

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Authors Age (y)/Sex</th>
<th>Comorbidities &amp; Risk Factors</th>
<th>Site of Infection</th>
<th>Initial Antibiotic(s)</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| 1        | Rimailho et al. (1987)  
74 / M | NSAID | Right leg | Not reported | Died |
| 2        | Zipper et al. (1996)  
55 / F | Diabetes mellitus | Right leg | Ceftriaxone Clindamycin | Survived |
| 3        | Huang et al. (1999)  
73 / M | Nephrotic syndrome Corticosteroid | Right leg | Ciprofloxacin | Died† |
| 4        | Huang et al. (1999)  
40 / M | ESRD (hemodialysis) Lupus Skin biopsy Corticosteroid | Left leg | Ceftazidime | Survived |
| 5        | Liangpunsakul et al. (2001)  
66 / F | None | Left leg | Penicillin G Clindamycin | Died |
| 6        | Newton et al. (2002)  
2 / F | None | Neck | Vancomycin Cefotaxime Amikacin | Died |
| 7        | Bachmeyer et al. (2004)  
49 / M | Lung cancer s/p chemotherapy Ischemic heart disease Diabetes mellitus | Left leg | Piperacillin/ tazobactam Amikacin | Died† |
| 8        | Curtis et al. (2005)  
51 / M | ESRD (hemodialysis) Diabetes mellitus Heart failure | Left leg | Vancomycin Ciprofloxacin Clindamycin | Died |
| 9        | Statham et al. (2009)  
6 / M | Recurrent otitis media Recurrent pharyngitis | Neck | Vancomycin Cefepime Clindamycin | Survived |
| 10       | Present case (2011)  
43 / F | ESRD (hemodialysis) Lupus SVC syndrome Ligation of arteriovenous fistula Corticosteroid | Chest wall | Vancomycin Piperacillin/ tazobactam Ciprofloxacin | Died |

NSAID = nonsteroidal anti-inflammatory drugs; ESRD = end-stage renal disease; SVC = superior vena cava.
†Death was from aspiration pneumonia and gastrointestinal bleeding (case 3) or metastatic small cell lung cancer (case 7), not necrotizing fasciitis per se.