Severe soft tissue infection in a patient with type 2 diabetes mellitus caused by *Serratia marcescens* as single pathogen

ANNA L BISCOE,[1] LUKMAN HAKEEM[2]

Abstract

***Serratia marcescens* is a rare cause of soft tissue infection. However, it has been increasingly recognised as a pathogen causing infection in both immunocompromised patients and in patients in an intensive treatment unit setting. Here we describe an elderly patient with type 2 diabetes mellitus presenting with severe necrotic soft tissue infection due to *S. marcescens* acquired in the community. The literature on *S. marcescens* soft tissue infection is reviewed and management is discussed.**

Key words: *S. marcescens*, soft tissue infection, cellulitis, necrotising fasciitis, diabetes

Case report

An 80-year-old woman with a background of type 2 diabetes mellitus, heart failure, coronary artery bypass graft, atrial fibrillation, chronic renal failure, hypertension and breast cancer was admitted with a one-week history of worsening lower left limb pain, erythema and reduced mobility.

She was initially stable on admission but rapidly deteriorated within an hour. She was febrile at 38°C and her blood pressure dropped to 93/50 mmHg. She was tachycardic at 110 beats/min and tachypnoeic at 26 breaths/min with saturations of 94% on 28% oxygen. Capillary refill time was 4 seconds. Her left leg was erythematous, warm and tender with significant swelling and she had a number of bullae around the mid-thigh.

Arterial blood gases showed hypoxia and a lactate of 5.1 mmol/L. Blood results showed acute on chronic renal failure (urea 14 mmol/L, creatinine 156 μmol/L), white cell count of 11.9 x10^9/L with neutrophilia, platelet count of 77 x10^9/L, C-reactive protein 309 mg/L and deranged coagulation with an International Ratio (INR) of 10 (the patient was on warfarin).

[1] FY2 Doctor, Aberdeen Royal Infirmary, UK
[2] Consultant in Infectious Diseases and Acute Medicine Aberdeen Royal Infirmary, UK

Address for correspondence: Dr Anna Biscoe
Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, UK.
Tel: +44 (0)345 456 6000
E-mail: anna.biscoe@nhs.net

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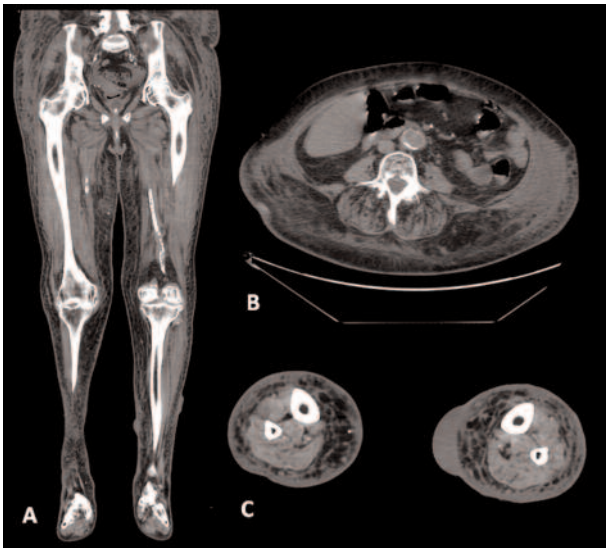
Figure 1. (A) Coronal CT scan demonstrating marked diffuse stranding within the subcutaneous tissues extending along the entire length of both legs. (B) Axial CT scan showing extensive stranding within both flanks and involving the muscle planes of the left abdominal wall. (C) Axial CT scan of the lower legs showing a fluid-filled bulla arising from the medial aspect of the left lower leg.



An emergency CT scan demonstrated marked diffuse stranding within the fat subcutaneously and within muscle planes, particularly affecting the left flank but extending along the entire length of both legs. Multiple fluid-filled bullae were seen in the distal left leg (Figure 1).

Sepsis 6 protocol was initiated and the patient was transferred to the high dependency unit (HDU) after commencing intravenous piperacillin-tazobactam and clindamycin for sepsis secondary to soft tissue infection, but she continued to deteriorate and remained hypotensive despite fluid resuscitation. She also developed haemorrhagic bullae extending to her thighs. Blood cultures were positive for gram-negative bacilli and piperacillin-tazobactam was therefore changed to meropenem.

An urgent plastic surgical review recommended conservative non-surgical management due to her significant comorbidities.

She continued to be managed on the HDU and her cellulitis

Table 1 Results of a literature review for cases of soft tissue infection caused by Serratia marcescens as a single pathogen in adult patients

Case no (ref)	Year	Age (y)/ sex	Underlying condition and/or risk factor	Site of infection	Presentation	Antibiotic therapy/outcome
1 (4)	1977	51/M	Idiopathic cardiomyopathy, chronic leg oedema	Left lateral thigh	Cellulitis, septic shock	Nafcillin, gentamicin Died
2 (5)	1983	60/M	Peripheral neuropathy, steroid use, left leg trauma	Left calf	Cellulitis, septic shock	Nafcillin, gentamicin Recovered
3 (6)	2005	74/M	NSAID drug use	Leg	Necrotising fasciitis	Not reported Died
4 (7)	1988	71/F	Healthy, left hand injured with a wire	Left hand	Cellulitis	Gentamicin Recovered
5 (7)	1988	23/M	Healthy	Dorsum of right digit	Cellulitis	Gentamicin Recovered
6 (7)	1988	52/M	Diabetes mellitus, diabetic foot ulcer	Right great toe	Cellulitis	Cefotaxime Amputation of great toe, recovered
7 (8)	1991	88/F	Chronic venous dermatitis and lower leg ulceration	Left leg	Cellulitis	Cefazolin, ciprofloxacin Recovered
8 (8)	1991	60/M	Chronic venous dermatitis	Left lateral malleolus	Cellulitis	Ciprofloxacin Recovered
9 (9)	1992	37/F	Chronic renal failure on haemodialysis	Right axilla	Cellulitis, septic shock	Ciprofloxacin, vancomycin Recovered
10 (10)	1996	55/F	Diabetes mellitus	Right leg	Necrotising fasciitis	Ceftizoxime, clindamycin Recovered
11 (11)	1998	69/F	Vascular disease, ingrowing nail removal	Lower leg	Cellulitis	Clindamycin, gentamicin, ciprofloxacin Recovered
12 (12)	1999	66/F	Healthy	Left leg	Necrotising fasciitis	Clindamycin, penicillin G, ceftriaxone, Died
13 (13)	1999	40/M	Lupus, renal failure, steroid use, skin biopsy	Lower leg	Necrotising fasciitis	Penicillin G, ceftazidime Recovered with skin grafting
14 (13)	1999	73/M	Renal failure, steroid use	Lower leg	Necrotising fasciitis	Penicillin, ciprofloxacin Died
15 (14)	2002	81/M	Renal failure, vascular stasis, steroid use	Lower leg	Cellulitis	Ceftaxolin, cefepime, levofloxacin, Died
16 (15)	2004	49/M	Immunocompromise due to chemotherapy for metastatic small cell lung cancer	Right leg	Necrotising fasciitis	Amoxicillin, piperacillin/ tazobactam and amikacin Survived
17 (16)	2005		End stage renal failure, diabetes mellitus, heart failure, scraping his leg on rocks in a river while fishing	Leg	Necrotising fasciitis	Not available Died
18 (17)	2012	97/F	Right-sided heart failure with prolonged hospital treatment, chronic kidney disease, atrial fibrillation	Right leg	Necrotising fasciitis	Flucloxacillin and amoxicillin, Died
19 (18)	2012	57/F	Cml	Right thigh	Necrotising fasciitis	Vancomyocin and tazocin, Died
20 (19)	2013	50/F	Snake bite	Right hand	Cellulitis with tissue necrosis	Ciprofloxacin Recovered
21 (20)	2014	75/M	Prostate carcinoma	Lower left limb	Cellulitis	Vancomyocin and tazocin Amputations and recovery
22	2015	80/F	Diabetes mellitus, chronic renal failure	Lower left and later right limb	Haemorrhagic cellulitis	Tazocin, clindamycin, meropenem Died

gradually resolved. On day 4 blood cultures isolated *S. marcescens*. Her cellulitis improved sufficiently to be stepped down from the HDU. She required tissue viability input for local debridement of necrotic tissue around the calf. Unfortunately on day 50 of her admission she died due to intractable heart failure and pulmonary oedema.

Discussion

S. marcescens is a gram-negative Enterobacteriaceae of the genus *Serratia*.[1] It is implicated in a wide range of serious infections most commonly of the lower respiratory tract, urinary tract, bloodstream, wound and meninges.[1,2] It is also a rare cause of endocarditis and soft tissue infections.[1]

In recent years *S. marcescens* has been increasingly recognised as an important opportunistic pathogen. In this vein, it is most commonly recognised as a nosocomial infection especially in immunocompromised hosts and in the intensive treatment unit (ITU) setting.[3] However, it has been estimated that almost half of *S. marcescens* bacteraemias (47%) originate in a community setting.[3]

We conducted a literature search for community acquired soft tissue infections caused by *S. marcescens* using Medline (search criteria: *S. marcescens*, soft tissue infection, cellulitis, necrotising fasciitis, limited to English language) and found 21 other reported cases, as shown in Table 1.[4-20] In all but four cases the hosts were immunocompromised or had an infected wound source, and in three cases the risk factor for contracting *S. marcescens* was diabetes mellitus.

While there are no specific clinical signs which are pathognomonic of *S. marcescens* soft tissue infection, the clinician should be more suspicious of *S. marcescens* in those patients with risk factors such as immunosuppression, diabetes mellitus, renal disease and long-term steroid use. Common empirical management for soft tissue infections is flucloxicillin ± benzylpenicillin. However, if the cellulitis is severe or there is bullous disease, there should be a low threshold to consider gram-negative cover to include *S. marcescens* infection in this group of patients.

S. marcescens is naturally resistant to ampicillin, macrolides and first-generation cephalosporins.[2] Furthermore, extended spectrum beta-lactamases (ESBL) are produced by most *S. marcescens* strains, which make them resistant to third-generation cephalosporins.[1,2] In addition, fluoroquinolones have limited use in severe infection and should only be used in uncomplicated urinary tract infections where sufficient concentrations can be achieved in the urine.[2]

Gentamicin had been used as a single agent during the 1970s but increasing resistance in up to 50%[1] of cases meant that it is no longer used as a single agent.[1,14] With the cessation of its use resistance has fallen to an estimated 6%, but it is still not used as a single agent due to its propensity for resistance.[1]

Third-generation cephalosporins have been used as single agents, but this selects for resistant strains such as Ampicillin class C (AmpC) beta-lactamases and ESBL.[1,14] This approach is therefore no longer favoured. They have been used alongside aminoglycosides, but there are reports of this failing to prevent the emergence of resistant strains.[1]

Fourth-generation cephalosporins or piperacillin-tazobactam are an effective treatment option where resistance to third-generation cephalosporins is evident or likely to develop.[1] They are active against AmpC chromosomal beta-lactamase-producing strains but are still not effective against ESBL-positive isolates.[1]

Most often the antibiotics of choice are carbapenems, which remain active against bacteria expressing high levels of AmpC and ESBL.[1,2,14] However, as has been seen with other coliforms, there is evidence for the emergence of carbapenemase-producing strains against which these will be ineffective.[1] As such definitive therapy should be based on the results of susceptibility testing because multiresistant strains are common.[1,12]

Mortality from *S. marcescens* bacteraemia is high, with approximately one-third of patients dying within 6 months of diagnosis.[3] Early debridement is indicated and appropriate antibiotic and supportive care are the cornerstones of therapy in severe soft tissue infection due to *S. marcescens*. Early surgical review and escalation to ITU/HDU care is vital.

Key messages

- *Serratia marcescens* is a rare but, important cause of severe soft tissue infection in immunocompromised and diabetic patients
- One should have a low threshold for adding gram negative cover if patient is very unwell or develops bullous disease
- Cases should be escalated early to plastics if necrotising fasciitis is suspected
- Consider use of carbepenems in suspected *Serratia marcescens* infection. However, definitive therapy should be based on the results of susceptibility testing because multi-resistant strains are common

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