A case of multiple cutaneous lesions due to *Serratia marcescens* in an immunocompromised patient

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**Introduction:** *Serratia marcescens* is an opportunistic Gram-negative bacillus capable of causing serious nosocomial infection. Skin infections due to *S. marcescens*, although not frequently encountered, can have a variety of manifestations and may progress to become serious debilitating lesions if not diagnosed early and treated promptly. We report here a case of multiple skin lesions due to *S. marcescens* in an immunocompromised patient.

**Case presentation:** A 60-year-old patient on adjuvant chemotherapy for breast carcinoma developed a high fever followed by multiple painful nodular and ulcerated lesions over all four limbs. Multidrug-resistant *S. marcescens* was isolated from the blood as well as from several skin lesions. Removal of the infective source (a chemoport in this case) and administration of tigecycline resulted in resolution of the infection.

**Conclusion:** *S. marcescens* is a nosocomial pathogen capable of causing extensive cutaneous lesions. Multiple samples for culture from the lesions are recommended to identify the aetiological agent and institute appropriate antibiotics. The emergence of multidrug-resistant strains has compromised treatment options for this bacterium, which is intrinsically resistant to several groups of antibiotics.

**Keywords:** bloodstream infection; chemoport; cutaneous nodules and ulcers; multidrug resistant bacteria; *Serratia marcescens*.

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**Introduction**

*Serratia marcescens* is a Gram-negative motile bacillus belonging to the family *Enterobacteriaceae*. *S. marcescens* has been implicated in hospital-acquired infections, particularly catheter-associated bloodstream infections, lower respiratory tract infections, urinary tract infections and wound infections. There are few cases of cutaneous infection caused by *S. marcescens* reported in the literature. These show that *S. marcescens* can cause a variety of dermal lesions in susceptible patients (Carlesimo et al., 2014; Jóao et al., 2008; Langrock et al., 2008). Cutaneous lesions caused by this bacterium are uncommon, and histopathological examination of the skin lesions may mimic other non-infective conditions such as pyoderma gangrenosum. Isolation of the bacteria in culture provides a clue to the underlying aetiology. We report a case of a 60-year-old patient who developed multiple skin ulcers due to *S. marcescens* following bloodstream infection by this organism.

**Case report**

A 60-year-old female patient with invasive lobular carcinoma of the breast on adjuvant chemotherapy presented in the emergency department with a high fever (maximum of 39.4 °C) and painful nodular erythematous rashes over the limbs for the last 4 days. At the time of admission, her total leukocyte count was 4540 mm$^{-3}$ with 84% neutrophils and her platelet count was 85 000 mm$^{-3}$. The patient was started on cefoperazone/sulbactam after collecting blood for culture from both the chemoport and a peripheral vein. Tests for the common causes of fever in tropical countries such as malaria, dengue and typhoid were negative. A chest X-ray and ultrasound of the abdomen done as part of the work-up were within normal limits. The patient continued to be febrile, and the skin lesions increased in size, with a few becoming ulcerated (Fig. 1). A punch biopsy was collected from one of the dermal lesions, and multiple samples from the lesions were collected for culture. Both blood cultures collected...
at the time of admission showed growth of Gram-negative, non-lactose-fermenting bacilli with blood from the central line showing positivity earlier than blood from the peripheral line. The bacillus was identified as non-pigmented (there was no pigment production after 72 h of incubation) \textit{S. marcescens} on the basis of biochemical reactions. The biochemical tests showed negative reactions for indole, methyl red and urease. A citrate utilization test and ornithine decarboxylase test were positive. There was alkaline/acid reaction without \textit{H}_2\textit{S} gas formation in Kligler iron agar suggestive of lactose non-fermentation and glucose fermentation by this bacterium. There was DNase production in DNA agar (Fig. 2). The identity of the bacterium was confirmed using a VITEK 2 GN ID card (bio-Mérieux). Testing of an extended range of antibiotics and applying Clinical and Laboratory Standards Institute guidelines revealed it to be a multidrug-resistant strain showing resistance to carbapenems (MIC for imipenem and meropenem of $\geq 16 \mu g \text{ ml}^{-1}$), aminoglycosides (MIC for amikacin of $\geq 64 \mu g \text{ ml}^{-1}$ and for gentamicin of $\geq 16 \mu g \text{ ml}^{-1}$) and quinolones (MIC for ciprofloxacin of $\geq 4 \mu g \text{ ml}^{-1}$ and for levofloxacin of $\geq 8 \mu g \text{ ml}^{-1}$), and it showed sensitivity only to tigecycline (MIC of $2 \mu g \text{ ml}^{-1}$) (CLSI, 2014). The cefoperazone/sulbactam was replaced with imipenem [1 g intravenously (i.v.) over 2 h every 6 h].

The patient continued to be febrile (maximum of 38.8 °C). The skin biopsy showed acute neutrophilic dermatosis suggestive of Sweet’s syndrome (Fig. 3). However, cultures from the skin lesions (four out of the six samples collected) showed growth of \textit{S. marcescens} with an identical sensitivity pattern to those of the blood culture isolates. Based on the culture and sensitivity results of the skin lesions, a second antibiotic, tigecycline (100 mg i.v. initially, followed by 50 mg i.v. twice daily) was prescribed concurrently with imipenem. Blood cultures from the chemoport and a peripheral line after 5 days of imipenem administration again grew multidrug-resistant \textit{S. marcescens}. A diagnosis of central line-associated bloodstream infection with dissemination to the skin was made. The chemoport was removed and sent for culture. Following removal of the chemoport and institution of tigecycline, the patient started improving and she became afebrile and the skin lesions also started to heal. The central line subsequently showed heavy growth of \textit{S. marcescens} with a sensitivity pattern identical to the previous isolates. The imipenem was stopped after 7 days and tigecycline was continued for 14 days. Repeat blood cultures following the chemoport removal were sterile.

\textbf{Discussion}

\textit{S. marcescens}, a member of the family \textit{Enterobacteriaceae}, was initially thought to be a saprophyte abundantly present in the environment, particularly in damp areas like basins and shower corners. This opportunistic pathogen has been increasingly recognized as a cause of human infections and has been responsible for several nosocomial outbreaks (Gupta et al., 2014). Haddy et al. (1996) showed that the most common underlying disorder for bacteraemia by this
organism is malignancy, followed by renal failure and diabetes mellitus. Most S. marcescens isolates are resistant to several antibiotics because of the presence of plasmids that carry genes encoding resistance factors. Serratia spp. are intrinsically resistant to ampicillin, macrolides, first-generation cephalosporins and the polymyxin group of drugs (Hejazi & Falkiner, 1997). Although both pigmented and non-pigmented biotypes are pathogenic for humans, the non-pigmented biotypes are considered more virulent due to cytotoxin production and presence of plasmid-mediated antibiotic resistance (Carbonell et al., 2000).

Reports of cutaneous infections by S. marcescens are uncommon (Carlesimo et al., 2014; Joao et al., 2008). However, there are several reports of cutaneous infection in patients of chronic granulomatous disease which is a primary immunodeficiency disease that affects phagocytic cells of the innate immune system (Campos et al., 2014; Friend et al., 2009; Herman & Siegel, 2002). The spectrum of skin infections due to Serratia spp. include granulomatous lesions, nodules, abscesses and cellulitis, as well as the more severe and life-threatening necrotizing fasciitis (Carlesimo et al., 2014; Curtis et al., 2014; Friend et al., 2009). Cutaneous infection by this bacterium may be predisposed by an immunocompromised condition, pre-damaged skin, extremes of age or co-morbid conditions such as renal disease or corticosteroid therapy (Bornstein et al., 1992; Garcia et al., 2006; Herman & Siegel, 2002; Langrock et al., 2008; Prelog et al., 2012; Subramani et al., 2013). In our patient with a compromised immune system following chemotherapy, central line-associated bloodstream infection by S. marcescens resulted in metastatic cutaneous lesions. Pollett et al. (2014) reported a similar case wherein necrotizing fasciitis developed following venous access port implantation during induction chemotherapy in a patient with acute lymphatic leukaemia.

Histopathological examination of the skin lesions may be misleading, and culture of pus, tissue biopsy samples or debrided materials from the ulcers ensure correct diagnosis. In this patient, histopathological examination of the skin lesions was suggestive of Sweet’s syndrome, which is a non-infectious condition for which steroids are indicated. However, the isolation of S. marcescens from multiple skin lesions prompted institution of appropriate antibiotics guided by the antibiogram, and the removal of the infective foci terminated the infection. In this case, administration of steroids on the basis of histopathological examination would have been counterproductive. The resolution of the skin lesions with antibiotics and without steroids re-enforced our diagnosis of infective skin lesions over Sweet’s syndrome. Carlesimo et al. (2014) similarly reported a case of ulcer due to S. marcescens that clinically and histopathologically mimicked pyoderma gangrenosum, but where cultures established the infective aetiology. The treatment of infections due to Serratia spp. is a therapeutic challenge. The occurrence of carbapenemase-producing Enterobacteriaceae in the healthcare setting has led to the widespread use of colistin. This has led to the emergence of bacteria naturally resistant to colistin such as those belonging to the genera Serratia and Proteus (Merkier et al., 2013). S. marcescens frequently exhibits resistance to extended-spectrum β-lactams due to its ability to overproduce the chromosomal AmpC enzyme and to acquire plasmid-borne extended-spectrum β-lactamas. Carbapenems remain the last resort against infections caused by Gram-negative strains resistant to oxyimino-cephalosporins (Suh et al., 2010). However, this has been compromised by the emergence of carbapenem-resistant strains worldwide in diverse geographical locations (Merkier et al., 2013; Pollett et al., 2014; Suh et al., 2010). The occurrence of carbapenem resistance in S. marcescens has serious therapeutic implications (Gruber et al., 2015). Colistin, the antibiotic recommended for treatment of systemic infection by carbapenemase-resistant Enterobacteriaceae has no role in the case of infections caused by S. marcescens. In this case, tigecycline was effective both in vitro and in vivo. However, the role of tigecycline is limited to skin, soft-tissue and intra-abdominal infections, as it achieves a therapeutic concentration at these sites only. It has been recommended that carbapenems administered as prolonged infusion (over 2 h instead of the usual 0.5 h) are effective against Gram-negative bacteria exhibiting high MICs to carbapenems. Jaruratanasirikul & Sudsai (2009) showed that a 2 h infusion of 1 mg imipenem every 6 h produced a favourable response against infections caused by pathogens with a MIC of 4 μg ml⁻¹. In the absence of any suitable antibiotic, imipenem infusion was tried but failed, possibly because the MIC of imipenem (≥16 μg ml⁻¹) was very high in this case. The treatment of systemic infection by multidrug-resistant S. marcescens is extremely difficult and presently there are no antibiotics to treat this type of infection. Fortunately, in this case, with the removal of the infective nidus (chemoport), the systemic infection subsided and the skin lesions subsequently healed with tigecycline treatment.

Conclusion

S. marcescens is an opportunistic pathogen often causing nosocomial infection in susceptible patients. Patients with an underlying malignancy are particularly vulnerable. Skin lesions due to S. marcescens are uncommon occurrences, and a high degree of suspicion can establish the aetioloical diagnosis. The antibiotic therapy for S. marcescens is difficult as it exhibits intrinsic resistance to several antibiotics and the emergence of multidrug-resistant S. marcescens has further compromised treatment options. The current report suggests that a treatment protocol using a 2 h infusion of 1 g imipenem, as described by Jaruratanasirikul & Sudsai (2009), is not effective for strains with a MIC for imipenem of ≥16 μg ml⁻¹. In these cases, tigecycline may be an alternative choice. Every effort should be made to determine the source of infection, as removal of the infective source is of major importance in eradicating the infection.
References


