Nephrotic syndrome complicated by necrotizing fasciitis is rare. Necrotizing fasciitis is a skin and soft tissue infection with a rapid progression and difficult diagnosis. Moreover, the early presentation of necrotizing fasciitis is similar to that of cellulitis. *Serratia marcescens* is a rare pathogenic cause of necrotizing fasciitis, even in skin and soft tissue infection. We present a patient with nephrotic syndrome complicated by necrotizing fasciitis caused by *Serratia marcescens*. A 49-year-old Chinese woman presented with minimal change disease and nephritic syndrome. She was admitted for pain in her right leg, for which she received cefazolin and clindamycin. However, 3 days later, a sanguineous bulla developed over her left calf, and she developed septic shock. After an emergency fasciectomy and broad-spectrum antibiotic administration, this patient died 12 h after fasciectomy. The blood culture and deep tissue culture collected during surgery both yielded *Serratia marcescens*. This unusual case reminds physicians that gram-negative bacilli can be pathogenic in soft tissue, especially in immunocompromised patients.

Keywords: Necrotizing fasciitis; Minimal change disease

Introduction

Nephrotic syndrome complicated by severe skin and soft tissue infection is unusual. Only a few reports have discussed the pathogenic infection of skin and soft tissue in patients with nephrotic syndrome. In this brief report, we present a patient with nephritic syndrome who developed necrotizing fasciitis caused by an unusual pathogen. Necrotizing fasciitis is a skin and soft tissue infection that features a rapid progression. The diagnosis of necrotizing fasciitis is difficult because its early presentation is similar to that of cellulitis. However, Wong proposed the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score to discriminate between necrotizing fasciitis and nonnecrotizing soft tissue infection, and Wong’s study reported a PPV of 92% and a NPV of 96% for the LRINEC score [1]. Despite improvements in the diagnosis and treatment of necrotizing fasciitis, the mortality rate of necrotizing fasciitis still ranges from 24 to 60% [2]. In a recent case series analysis, approximately two-thirds of cases were polymicrobial, and one-third were monomicrobial; the great majority of monomicrobial cases were caused by gram-positive cocci [3]. However, the pathogenic cause of monomicrobial necrotizing fasciitis in this patient was *Serratia marcescens*.

Case Presentation

The patient was a 49 year old Chinese woman who presented with left calf pain in February 2011. She was diagnosed with minimal change disease and nephrotic syndrome more than 6 years previously. Cyclosporine was prescribed for disease control. She did not take medications regularly for 4 months. She reported edema in her bilateral lower extremities for 2 weeks before returning to our clinic. Upon returning to our clinic, cyclosporine 100 mg once daily was prescribed. Six days later, she developed pain and warmth in her left lower leg, and thus, she again returned to our clinic. She denied the occurrence of both trauma and insect bite during this period.

On physical examination, her body temperature, respiratory rate, and heart rate were 38.3°C, 20 breaths/min and 121 beats/min respectively. Upon physical examination, left calf tenderness and an erythematous change and swelling from the toes to the thigh were observed. Her laboratory data were as follows: white blood cell count, 5600/μl with 86% neutrophils; hemoglobin, 14.8 g/dl; platelets, 3050/μl; and CRP, 1.09 mg/dl. Biochemical evaluation revealed the following data: glucose, 132 mg/dl; blood urea nitrogen, 25 mg/dl; creatinine, 0.89 mg/dl; sodium, 135 mmol/l; and albumin, 1.0 g/dl. Her protein to creatinine ratio in urine was 7.35. According to the LRINEC score, the risk of necrotizing fasciitis in our patient was less than 50%.

Under the diagnosis of progression of nephrotic syndrome and cellulitis, she was admitted to our ward, and she received cefazolin 2 g by intravenous drip (IVD) every 8 h and clindamycin 600 mg IVD every 6 h because of an allergic reaction to oxacillin. However, on the day of hospitalization, the area with an erythematous change spread to the left thigh, and a sanguineous bulla approximately 3 × 3 cm² in size developed on her left calf. She also felt pain with progression to the lower abdomen. After hospitalization for 12 h, the calf bulla increased to 5 × 5 cm² in size, and newly developed bullae were found on her left foot (Figure 1). However, there was no crepitus palpated over the bilateral thighs and abdomen. Emergency abdominal computed tomography revealed infiltration of the bilateral lower extremities from the thighs to the calves and anterior abdomen without obvious necrotizing signs (Figure 2). Her antibiotic regimen was changed to piperacillin/tazobactam 3375 mg IVD every 6 h. Emergent fasciectomy was performed for the bilateral legs and left abdomen because SIRS was suspected (body temperature, 38.8°C; respiratory rate, 28/min; heart rate, 148/min; and white blood cell count, 500/μl with 31% neutrophils and 15% band cells).

After surgery, hypotension developed, and laboratory data revealed AKI with metabolic acidosis (Cr: 2.86 mg/dl; pH: 7.274, pCO₂: 16.9 mmHg, and HCO₃⁻: 7.9 mmole/L). Under intensive supportive care, asystole developed, and there was no response to cardiopulmonary resuscitation; the patient died 4 days after presenting with left calf pain. The culture results for tissue obtained during fasciectomy and the initial blood culture both indicated *Serratia marcescens*, which was resistant to cefazolin but sensitive to piperacillin/tazobactam.

*Corresponding author: Chirn-Bin Chang, MD, No135, Nan-Shiao Street, Changhua City, 500, Taiwan, Tel: 886-4-7238595 ext.1031; Fax: 886-4-7285161; E-mail: 129143@cch.org.tw

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Discussion

*Staphylococcus aureus* and *Streptococcus pyogenes* are the most common pathogenic causes of cellulitis; penicillin and first-generation cephalosporins represent the first line of empirical antibiotics if the *Staphylococcus* and *Streptococcus* species do not exhibit significant penicillin or cephalosporin resistance [4]. However, necrotizing fasciitis has a different pathogenic cause than cellulitis. A case series analysis in Taiwan included 46 patients with soft tissue infection caused by a single pathogen that was isolated between 2002 and 2008. Gram-Negative Bacilli (GNBs) accounted for 76% of the isolated pathogens, and the majority of pathogens were Vibrio and Aeromonas species. GNBs rarely cause skin and soft tissue infection with a rapid progression [5]. Otherwise, some less common but emerging organisms include community-acquired methicillin-resistant *Staphylococcus aureus*, group B and C streptococci, certain Enterobacteriaceae and Pseudomonas species [6]. Serratia species are an emerging causative organism of soft tissue infection, and the risk factors of patients are chronic renal failure and diabetes mellitus. However, necrotizing fasciitis related to *Serratia marcescens* was scant. Therefore, the exact mortality rate of necrotizing fasciitis caused by *Serratia marcescens* is limited.

*Serratia marcescens* is a GNB that frequently causes nosocomial infection [7]. Additionally, *Serratia* species possess chromosomal AmpC β-lactamase, and thus, they are resistant to ampicillin and first-generation cephalosporins because of this inducible gene [8]. We reviewed the literature to locate reports of necrotizing fasciitis caused by *Serratia*. In 1989, Dr. Hiroshi reported 118 patients with *Serratia* bacteremia; only 7.9% of the cases were caused by soft tissue infection [9]. In another study in Canberra, the incidence of *Serratia* species-induced bacteremia was 1.03 per 100,000 patients per year, and soft tissue infection was observed in 7.8% of patients with bacteremia. The 7-day and 6-month mortality rates were 5 and 37%, respectively. Additionally, most infections were community-acquired [10]. Case report data for soft tissue infection caused by *Serratia* are scant. Dr. Bachmeyer collected cases of necrotizing fasciitis caused by *Serratia* until 2004, and two of four patients died [11]. In a analytical review covering the period of 1966-1999, 10 cases with *Serratia marcescens* community-acquired soft tissue infection were found, including 2 cases of mortality due to soft tissue infection [12]. From these results, soft tissue infection related to *Serratia* does not carry a significantly high mortality rate.

Regarding host risk factors, our patient did not exhibit the typical risk factors for soft tissue infection caused by *Serratia marcescens*. She did not have a positive LRINEC score. Therefore, early diagnosis and surgical intervention are the primary strategies for reducing the mortality of necrotizing fasciitis, but in immunocompromised patients such as those with nephritic syndrome, broad-spectrum antibiotics may be considered initially to treat GNB infection to reduce the rate of complications. Dr. Cheng analyzed 17 patients with underlying idiopathic nephrotic syndrome who were diagnosed with spontaneous cellulitis. Four patients displayed GNB infection, two patients exhibited *Streptococcus* species infection, and no definite pathogen was isolated from the other patients [13]. Therefore, among patients with nephritic syndrome, gram-negative pathogens should be considered with the presentation of soft tissue infection. In our patient, it was relatively difficult to monitor disease progression because of her edematous status.

Conclusion

*Serratia marcescens* is not a common pathogenic cause of soft tissue infection, but its incidence is increasing, especially among immunocompromised patients. Broad-spectrum antibiotics and timely surgical intervention are the cornerstones for improving the clinical outcome of soft tissue infection caused by *Serratia marcescens*. Therefore, our case findings indicate that GNB infection should be considered in cases of soft tissue infection, especially in immunocompromised patients.

References
