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Recurrent necrotizing fasciitis caused by methicillin-resistant *Staphylococcus aureus*

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Abstract Reported here is a rare case of recurrent necrotizing fasciitis due to methicillin-resistant *Staphylococcus aureus* (MRSA). A 46-year-old female with poorly controlled diabetes and chronic ingestion of steroid-containing medications was admitted for treatment of necrotizing fasciitis of the right thigh. Three months following hospital discharge she was readmitted with necrotizing fasciitis of the left hand. On both occasions, MRSA was isolated from tissue cultures obtained during surgical debridement. Patients who develop necrotizing fasciitis are predisposed to severe soft tissue infections due to associated comorbid conditions such as diabetes mellitus. Recurrent soft tissue infection in a patient with previous MRSA-related necrotizing fasciitis should therefore be treated with a high index of suspicion.

Introduction

Necrotizing fasciitis is an infection that primarily involves the superficial fascia and subcutaneous tissue and is associated with systemic toxicity, a fulminant course and high mortality [1]. Bacteriological causes of necrotizing fasciitis encompass two main entities: type I (synergistic aerobic and anaerobic) infections and type II infections. *Staphylococcus aureus* necrotizing fasciitis is usually seen in type II infections, where it is commonly isolated in combination with group A *Streptococcus* [2]. While methicillin-resistant *Staphylococcus aureus* (MRSA) is a

major nosocomial pathogen [3], necrotizing fasciitis due to *Staphylococcus aureus* as a single pathogen is rarely reported [1, 2, 4]. We report a rare case of recurrent necrotizing fasciitis, possibly due to the same MRSA strain carried by the patient. The case highlights the danger of recurrent necrotizing fasciitis occurring in susceptible patients.

Case report

A 46-year-old woman was admitted with progressive swelling of the right thigh and pain of 3 days' duration. She did not recall any antecedent trauma to the affected area. She had poorly controlled diabetes mellitus and was dependent on steroids as a result of chronic ingestion of steroid-containing traditional Chinese medication used to treat osteoarthritis of her knees. She had previously been admitted to hospital on multiple occasions for treatment of diabetes-related foot infections. She also had tuberculous cystitis for which she was on maintenance anti-tuberculosis medications (ethambutol and ofloxacin).

On examination, she was non-toxic and had a low-grade fever. A typical cushingoid appearance was noted and her right thigh was tender, tense and erythematous. No crepitus was felt. Her total leukocyte count was 25.4×10^3 per mm^3 , hemoglobin was 10.7 g/dl, platelet count was 256,000 per mm^3 and electrolyte analysis was normal. A radiograph of the right thigh did not show any free gas in the soft tissue. A provisional diagnosis of cellulitis was made and she was started on parenteral amoxicillin/clavulanate.

A Doppler ultrasound scan was ordered to exclude deep vein thrombosis, but the result of this investigation was suboptimal because of the severe swelling. A magnetic resonance imaging scan was therefore performed. This showed features consistent with necrotizing fasciitis, including thickening of the fascia, and failure of fascia enhancement following the administration of gadolinium contrast medium. Surgical debridement showed extensive necrotizing fasciitis of the right thigh, which was later

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confirmed on histological examination of the resected specimen. Tissue culture taken at operation grew MRSA; however, two blood culture sets performed with the automated BACTEC Fluorescent Series system (Becton Dickinson Microbiology System, Franklin Lakes, NJ, USA) on samples taken at admission failed to yield any organism. Vancomycin was commenced with a 6-week course. Three further surgical debridement procedures were required, followed by a skin graft wound closure. A nasal swab was negative for MRSA. She was discharged after 102 days in the hospital.

Three months later the patient was readmitted with swelling of the left dorsum of the hand and pain that began after a fall that occurred 3 days prior to admission. There was progressive migration of erythema and pain up to the mid-forearm. Her total leukocyte count was 36.2×10^3 per mm^3 with a neutrophil count of 93%, hemoglobin level of 8.1 g/dl, and platelet count of 471,000 per mm^3 . Vancomycin and piperacillin/tazobactam were started for possible cellulitis of the left hand.

Despite the antimicrobial therapy, the patient remained febrile with proximal migration of the margins of erythema. Emergency surgical debridement performed 4 days after admission demonstrated necrotizing fasciitis of the left hand. Two sets of blood culture of samples taken at admission and tissue culture of samples obtained during surgical debridement yielded MRSA. The antibiogram of the MRSA isolate was identical to that of the initial organism isolated from her right thigh tissue 3 months previously. Nasal swab was again negative for MRSA. A computed tomography scan of her abdomen and pelvis, a two-dimensional echocardiograph of her heart and a bone scan did not demonstrate any occult septic focus of MRSA. Two further operations were performed for debridement and skin grafting. Vancomycin was given for 7 weeks. She was discharged well after 85 days and was well at 1-month follow-up.

Polymerase chain reaction (PCR) amplification to detect the Panton-Valentine leukocidin (PVL) gene was negative. The oligonucleotides were synthesized commercially. Oligonucleotide primers were designed according to the published sequences of the PVL gene (GenBank accession numbers X72700 and AB006796), and the amplification was performed in accordance with the methods described by Lina et al. [5], with positive and negative controls. This PCR system has been shown to be specific for the PVL gene [5].

Discussion

Recurrent necrotizing fasciitis is rare. To the best of our knowledge, only two cases have been reported previously [6, 7]. In each of these cases, the episodes of necrotizing fasciitis occurred years apart and were attributed to different organisms. In the case reported here genomic fingerprinting of the MRSA isolates was not performed since the specimen from the first episode was no longer available for analysis. However, the close temporal

relationship between the two episodes of necrotizing fasciitis suggests that the infections may have been caused by the same MRSA strain.

Our patient had several predisposing factors that made her susceptible to necrotizing fasciitis; namely, poorly controlled diabetes mellitus and immunosuppression caused by chronic ingestion of steroid-containing compounds [1, 8, 9]. Thus, host susceptibility appeared to be the most significant predisposing factor in this case. The patient also had multiple risk factors for MRSA colonization, including repeated hospitalization, previous administration of multiple antimicrobial agents, diabetes mellitus and immunosuppression. In patients with severe MRSA infection, particularly if the infections are recurrent, carrier states and occult sites of infection, including intra-abdominal abscesses, infective endocarditis and osteomyelitis, should also be investigated and targeted for eradication. The commonest site of colonization is the anterior nares. Other sites of colonization include oropharyngeal sites, the perineum, the skin and sometimes the gastrointestinal tract [2]. From these sites, the carriers transfer the organism to their skin. Minor trauma provides a portal of entry with subsequent local infection. While intranasal mupirocin ointment is often effective for eradicating nasal carriage of MRSA, re-colonization is common and remains a significant problem in susceptible patients [10]. Furthermore, recurrent MRSA infection is possible even in patients without nasal colonization, as occurred in the case reported here. Potential causes include the many other potential sites (such as the perineum and axilla) that may harbor MRSA but are not routinely investigated. Despite the apparently adequate treatment administered during our patient's initial episode of fasciitis, as demonstrated by normalization of her C-reactive protein levels, she was admitted 3 months later with another episode of fasciitis. Patients with severe soft tissue infection such as necrotizing fasciitis could possibly be colonized by virulent MRSA strains.

The danger of necrotizing fasciitis recurring should be borne in mind, particularly if the time interval between soft tissue infections is short. The antimicrobial agent selected should target MRSA as well as other pathogens commonly associated with soft tissue infections. Early establishment of strict contact precautions should be employed upon readmission. A previous episode of necrotizing fasciitis in a susceptible patient demonstrates that conditions conducive to the development of necrotizing fasciitis exist in that particular patient. Early diagnosis is imperative and improves survival [1]. When diagnostic doubt exists, means of detecting necrotizing fasciitis early in its evolution, such as a magnetic resonance imaging scan of the affected area, should be considered.

Panton-Valentine leukocidin is a gene that encodes a virulence factor for severe primary skin infections and necrotizing pneumonia. While PVL has only occasionally been detected in *Staphylococcus aureus* (mainly in community-acquired MRSA infections) [5], the importance of PVL as a potential virulence factor in cases of necrotizing fasciitis led us to search for this gene in the

MRSA strain we isolated. The result, however, was negative. Host susceptibility therefore seems to have been the most significant factor leading to the recurrent MRSA-related necrotizing fasciitis in our patient.

Recurrent MRSA necrotizing fasciitis should be actively excluded in patients with a previous episode of fasciitis. Appropriate antimicrobial selection, early diagnosis and aggressive surgical debridement are the cornerstones of treatment for this rare but deadly disease. Recurrent soft tissue infections in a patient with previous necrotizing fasciitis caused by MRSA should be treated with a high index of suspicion.

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