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Rapidly progressive necrotizing fasciitis caused by *Staphylococcus aureus*

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Necrotizing fasciitis (NF) is a rapidly progressive life-threatening infection located in the deep fascia, with secondary necrosis of the subcutaneous tissues. *Staphylococcus aureus* as a single etiologic agent is rare. The pathogenicity of *S. aureus* infections is related to various bacterial surface components and extracellular proteins. A 56-year-old man developed fever, hypotension, impaired renal and hepatic functions, disseminated intravascular coagulation, and rapidly progressive NF affecting the 4 extremities due to methicillin-susceptible *S. aureus* (MSSA). The initial presenting symptoms were general weakness and muscular pain over bilateral thighs and left shoulder, and gradual onset of weakness of the limbs. On the third hospital day, multiple red-purplish discoloration spread across the right lower leg and left forearm. Fasciotomy and debridement was performed on the fifth hospital day, and the diagnosis of NF was confirmed. MSSA was the only pathogen isolated from 4 sets of blood cultures taken on admission and cultures of tissues collected during surgical debridement. The disease progressed rapidly over the 4 extremities despite appropriate antibiotic treatment. He recovered after multiple extensive surgical interventions and 8 weeks of intensive medical care. Early diagnosis, intensive surgical intervention, antibiotic treatment and intensive medical care are crucial for a successful outcome in patients with septic shock and extensive NF caused by *S. aureus*.

Key words: Bloodletting, necrotizing fasciitis, *Staphylococcus aureus*

Necrotizing fasciitis (NF) is a term that was first used to describe rapidly spreading gangrene of the skin and subcutaneous tissues above the fascial layer, in the 1950s [1]. It is a rapidly progressive life-threatening infection located in the deep fascia, with secondary necrosis of the subcutaneous tissues. The diagnosis is often difficult because subcutaneous changes may not be readily apparent. NF usually originates in traumatic musculoskeletal wounds, operative sites, or follows other types of injuries such as minor cuts, scrapes, or insect bites. The abdominal wall, extremities, and perineum appear to be most commonly affected, but NF can occur in any region of the body. Because of the presence of gas-forming organisms, detection of subcutaneous air is a classic finding in NF. This may be seen only on X-ray or not at all. It moves along the deep fascial plane; the speed of spread is directly proportional to the thickness of the subcutaneous layer. Most often NF is caused by polymicrobial pathogens [2,3]. We report a case of septic shock caused by *Staphylococcus aureus*, in which rapidly progressive NF developed over 4 limbs. The patient recovered after aggressive multiple surgical interventions and intensive care.

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Case Report

A previously healthy 56-year-old man visited the emergency department due to dizziness, weakness and deep colored urine. Two weeks earlier, he began to suffer from general weakness and myalgia. He took some medicines for common cold at that time. Nine days later, low back pain developed and he visited the orthopedic outpatient department where X-ray showed degenerative joint disease of the L-spine. However, pain and weakness of bilateral thighs and left shoulder developed gradually. Two days prior to admission, he underwent bloodletting procedure with tip of acupuncture needles over bilateral fingers and toes for symptomatic relief. Pain initially subsided after the bloodletting, but worsened 1 day later.

On admission, he had an acutely ill appearance. Blood pressure in the right brachial artery in the supine

position was 88/62 mm Hg, pulse 110 beats/min, respiratory rate 36/min and body temperature 38.6°C. All peripheral pulses including the carotids were palpable.

Marked swelling, involving bilateral upper arms and left thigh, and difficulty in the moving bilateral legs were noted. Neurologic examination showed that he was conscious, cooperative, and well oriented in time, place and person. Muscle power was reduced at 4/5 in the right upper limb, and 2/5 in the bilateral lower limbs. Other physical examinations were unremarkable. White blood cell counts were 5220/mm^3 (neutrophils 84.5%), platelet count 149,000/mm^3, hemoglobin 16.3 g/dL, and hematocrit 44.4%. Other laboratory values included elevation of serum creatinine (2.5 mg/dL), blood urea nitrogen (61 mg/dL), creatine phosphokinase (4680 U/L), aspartate aminotransferase (175 U/L), alanine aminotransferase (53 U/L), serum total bilirubin (4.6 mg/dL), and C-reactive protein (50.97 mg/dL), and depressed levels of albumin (1.2 mg/dL), sodium (122 mEq/L), and potassium (3.2 mEq/L). Arterial gas analysis showed pH of 7.322, bicarbonate level of 11.5 mEq/L and a base excess of –12.2 mEq/L; his lactic acid level was 3.2 mEq/L. The oxygen saturation was 98% while the patient breathed ambient air.

Partial thromboplastin time was elevated at 42 sec. Urinalysis results was 1+ for protein and bilirubin; the sediment contained 3-5 white cells, 14-16 red cells, and bacteria 2+ per high-power field. Abdominal sonography performed at the emergency department showed fatty liver and mild increased echogenicity of both kidneys. He was admitted for treatment of presumed septic shock with multiple organ dysfunction syndrome. Ceftriaxone, doxycycline and penicillin G were initially administered empirically. On the third hospital day, multiple red-purplish discoloration spread across his right lower leg and left forearm (Fig. 1A, 1B). On the same day, 4 sets of blood cultures obtained on admission revealed Gram-positive cocci. All of them were reported to be methicillin-susceptible *S. aureus* (MSSA) 4 days later. Intravenous oxacillin (8 g/day divided into 4 doses) was administered. Echocardiography revealed no abnormalities. On the fifth hospital day, extensive fasciotomy and debridement of subcutaneous tissues of right lower leg and left forearm were carried out under the impression of NF (Fig. 1C, 1D). Microscopic histopathology of the necrotic tissue is shown in Fig. 2A, 2B. Gross necrosis was observed throughout the fascia of subcutaneous tissue. Acute dermatitis and septal panniculitis with

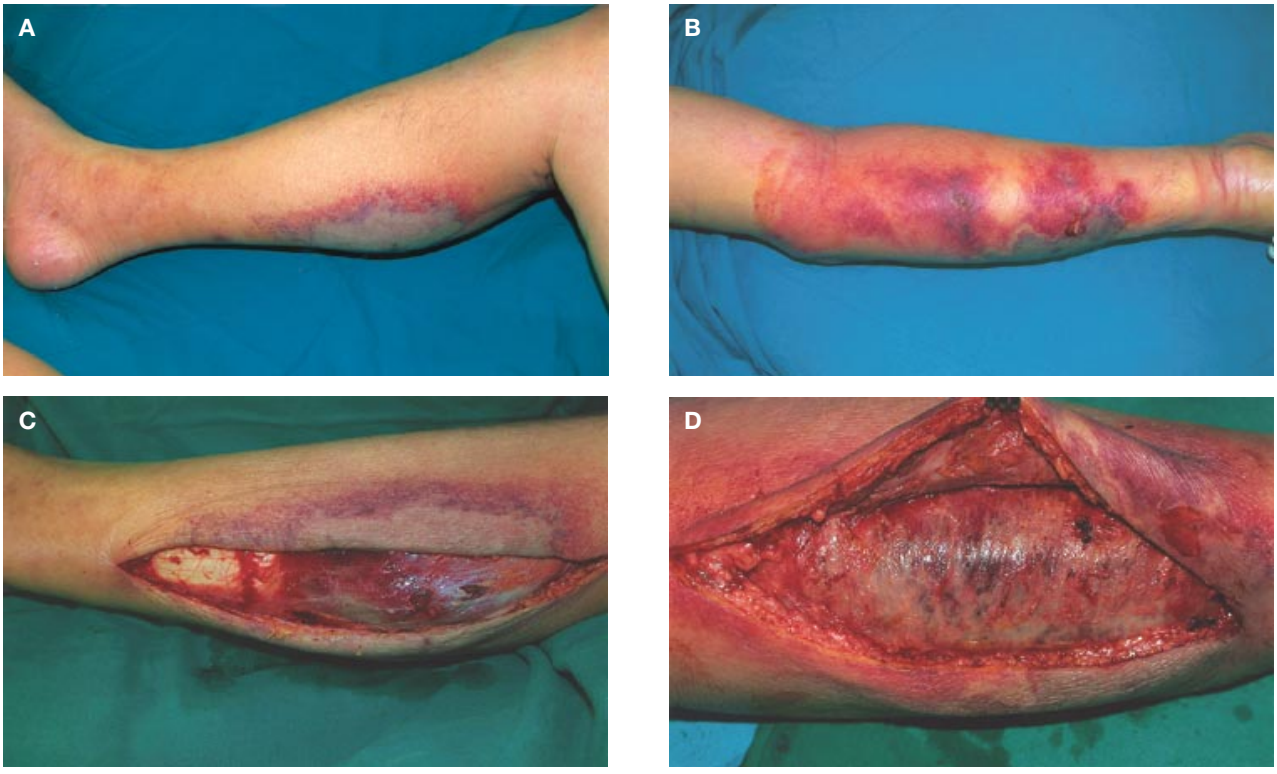

Fig. 1. A, B) Extensive erythema, induration and tenderness of right lower leg and left forearm before operation. C, D) Extensive necrotic fascial tissue of right lower leg and left forearm were revealed intraoperatively after debridement.

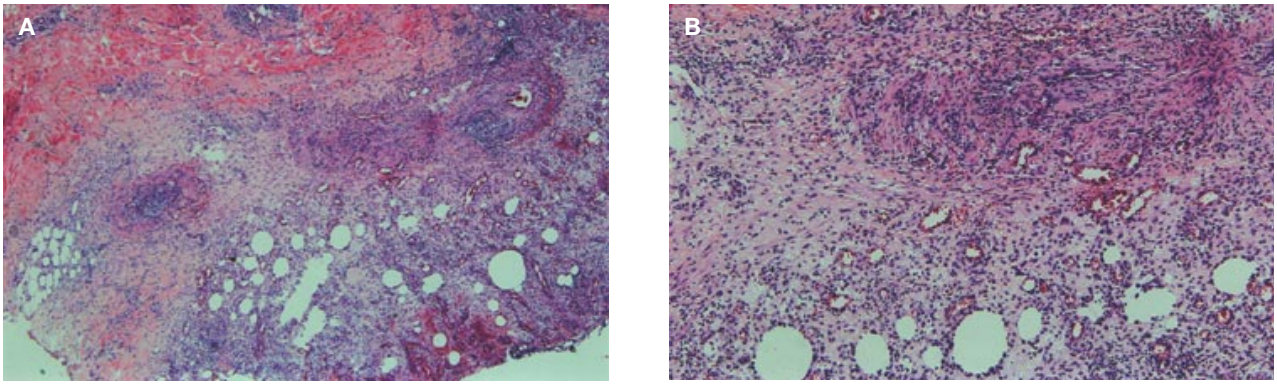

Fig. 2. A, B) Microscopic histopathology of necrotic tissue shows acute dermatitis and septal panniculitis with cellular debris and necrosis.

cellular debris and necrosis were also found. MSSA grew in all aerobic culture plates of the surgical wound tissue. The bacterial isolate was susceptible in vitro to gentamicin, trimethoprim-sulfamethoxazole and ciprofloxacin. On hospital day 9, new ecchymosis was noted over the right forearm and bilateral lower legs. The patient was immediately taken to the operation room, where blisters with necrotic skin and gangrene formation were found. Radical debridement and fasciotomy of the right forearm and bilateral lower legs were performed. On hospital day 16, new redness and ecchymosis was found over the left thigh. Another debridement was performed and NF was noted along the muscle fascia. The necrotic tissues were debrided and removed. All wounds were dressed after the operation. He returned to the operation room on the following day, at which time further debridement, split thickness skin grafts and fascial flap reconstruction were performed (Fig. 3A-3D). The patient received intravenous oxacillin for a total of 26 days, followed by cefepime 1.0 g 12-hourly for 14 days for treatment of a superinfection of wound with *Acinetobacter* spp. Extensive allografting was required to close the wounds, and the patient ultimately had a complete recovery

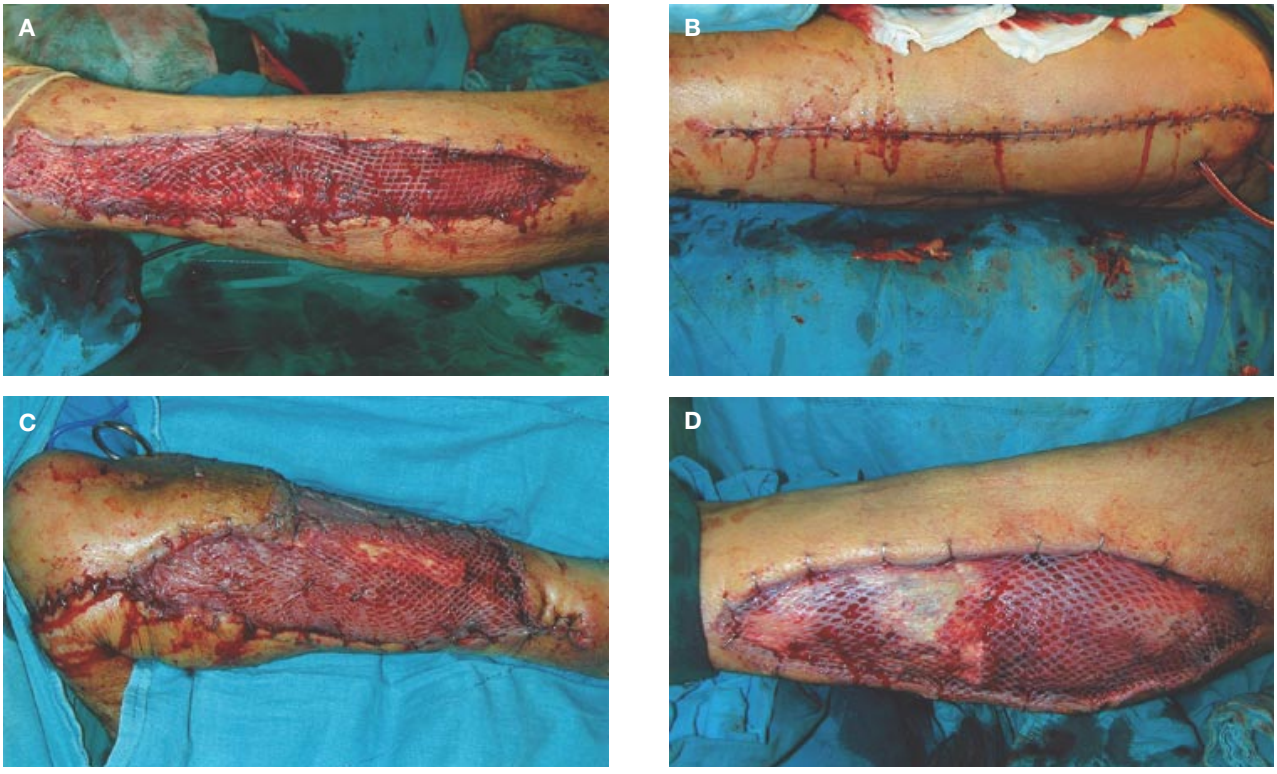

Fig. 3. A, B, C, D) Split thickness skin grafts were applied to reconstruct the area over the left lower leg, left thigh, left upper limb and left forearm.

and was discharged from the hospital 57 days after admission. He remained well at 3 months after discharge.

Discussion

This patient presented with bacteremia and septic shock, followed by a severe, rapidly progressive, and invasive soft tissue infection involving 4 limbs. MSSA was the sole pathogen isolated from blood and wound tissue cultures. In most patients with NF, *S. aureus* has been a part of a mixed flora; *S. aureus* as a single etiologic agent is rare [3,4]. The pathogenicity of *S. aureus* infections is related to various bacterial surface components (e.g., capsular polysaccharide and protein A), including those recognizing adhesive matrix molecules (e.g., clumping factor and fibronectin binding protein), and to extracellular proteins (e.g., enterotoxins, toxic-shock syndrome [TSS] toxin, and Panton-Valentine leukocidin [PVL]) [5,6]. PVL is a gene that encodes a virulence factor for severe primary skin infections. It is a cytotoxin that causes leukocyte destruction and tissue necrosis. It is produced by fewer than 5% of *S. aureus* strains.

In this patient, a constellation of symptoms, signs and laboratory tests led to consideration of but did not completely fulfill the diagnostic criteria for *Staphylococcus* TSS set by the Centers for Disease Control and Prevention in 1980 [7]. He had fever, hypotension, skin rash, and multisystem involvement including muscular, renal and hepatic dysfunctions, and disseminated intravascular coagulation. TSS is an acute febrile, exanthematous illness caused by toxins such as TSS toxin-1 (TSST-1) and other enterotoxins from *S. aureus* with an incidence of 0.5 per 100,000 inhabitants [8]. Patients with non-menstrual TSS have a focus of staphylococcal infection, such as a surgical wound infection or soft tissue abscess. An essential step in the management of such patients is a thorough search for the possible sites of staphylococcal infection to eradicate the source of toxin. After obtaining cultures from all mucous membranes, wounds, blood and urine, antistaphylococcal therapy should be initiated with high-dose beta-lactamase-resistant antibiotics, singly or in combination with other agents. Nafcillin sodium, oxacillin sodium, and first-generation cephalosporins are also used as first-line agents. All surgical wounds require adequate drainage [9-12]. In addition, supportive care including intravenous fluid and vasopressors may be necessary. Despite intensive antimicrobial therapy, our patient experienced progressive and repeated episodes of NF over 4 limbs caused by *S. aureus*. Although circumstantial evidence may implicate the bloodletting procedure on fingers and toes as portals of entry, the correlation between *S. aureus* NF and the bloodletting procedure is not proven. In conclusion, we report a case of *S. aureus* septic shock with rapid and progressive development of NF over 4 limbs despite intensive antibiotic treatment. Multiple extensive fasciotomies, debridements and skin allograft operations led to eventual recovery after 8 weeks of hospitalization. Early diagnosis and intensive surgical intervention in addition to antibiotic treatment and intensive medical care is crucial for a successful outcome in patients with TSS and extensive NF.

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