

Necrotizing fasciitis caused by TSST-1 producing penicillin-sensitive *Staphylococcus aureus*—a case report

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A 67-year-old woman was transferred to our Department of Orthopedic Surgery with the diagnosis suspected necrotizing fasciitis (NF). 3 days before hospitalization, she had developed infection in a small ulcer on her left wrist. For many years she had had steroid treatment for rheumatoid arthritis; she had arthrosis in both knees and arthroplasties of both hips. She was not suffering from diabetes mellitus, but had a well-regulated high blood pressure and intermittent angina pectoris.

On admission, she was febrile (39.6°C), normotensive (BP 120/60), slightly tachycardic (103), and confused. Her left leg was red and swollen below the knee (anterior) and far up the femur (posterior). Dorsum pedis was swollen with fluid under subcutis. There was crepitation of the skin and secretion of pus from two small ulcers.

The patient was transferred directly to the operating room. Incisions were made lateral and medial on crus. Subcutis, fascia, and muscles were totally necrotic. An exarticulation at knee level in vital tissue was performed. 5 sterile biopsies were taken for microbiological examination. The operating field was “washed” with saline containing gentamycin. Empirical intravenous antimicrobial treatment was started with high-dose penicillin (5 million IU × 4), metronidazole (0.5 g × 3) and gentamycin (240 mg × 1). Later the same day, intravenous clindamycin (600 mg × 3) and ciprofloxacin (400 mg × 2) were added.

The patient was reoperated 8 h after the first operation, with no signs of new necrosis. Because of emerging redness of the right heel, which was incised exploratively without signs of necrotizing fasciitis, the patient was transferred to another hospital for hyperbaric oxygen treatment. After four days, she had stabilized and was returned to our orthopedic ward. Clinically, the patient was well for 2 weeks. She then deteriorated without any

proven infection and died on day 54 after the toxic shock.

4 sets of blood cultures taken on the day of admission were negative, but all tissue cultures grew *S. aureus* in pure cultures. The isolates were identical to the isolates derived from the wrist ulcer three days before hospitalization. The *S. aureus* isolated, Gram-positive cocci in clusters, catalase-, coagulase- and Staphaurex-positive, was sensitive to all betalactam antibiotics including penicillin and also macrolides, clindamycin and gentamycin. Penicillin sensitivity was confirmed by cloverleaf method (Kjellander and Myrbäck 1964). The isolate was identified as being MecA-negative by PCR and the staphylococcal protein A (SPA) typed as T 1082 by PCR and sequencing. It tested positive for toxic shock syndrome toxin (TSST-1) both by PCR and by a rapid method for toxin F detection (AdvanDx) which is a novel panel of signal amplified, sandwich hybridization assays.

Discussion

Necrotizing fasciitis (NF) is a rare and severe soft tissue infection. It is characterized by rapidly progressing fascial necrosis. Beta-hemolytic *Streptococcus* of Lancefield group A (GAS) remains the most common agent in monomicrobial infection (Seal 2001), but NF is often a polymicrobial infection (Saliba et al. 2003). Besides GAS, many other bacteria can cause NF as a monomicrobial infection, including *Vibrio* species (Seal 2001). *S. aureus* has been implicated as the sole pathogen in only a few case reports (Regev et al. 1998, Saliba et al. 2003, Lee et al. 2005). In one article, 7 patients out of 21 with NF were associated with *S. aureus* infection (Zahar et al. 2005), but no information was given on where the bacteria were isolated

from, and whether the infections were mono- or polymicrobial.

Staphylococcal toxic shock syndrome (STSS) is a potentially lethal multisystem syndrome characterized by fever, rash, desquamation during convalescence, shock, and multiple organ failure. Two forms of STSS exist, menstrual and non-menstrual (Alouf and Muller-Alouf 2003, Jamart et al. 2005). Almost 100% of cases of menstrual STSS are caused by the superantigen exotoxin, TSS toxin-1 (TSST-1), whereas non-menstrual staphylococcal TSS is caused by TSST-1 in 50% of cases and staphylococcal enterotoxin B or C in the remaining 50% of cases (Schlievert 1986).

There is no diagnostic test for TSS. In 1994, Ejlersen et al. investigated 436 *S. aureus* bacteremia strains, isolated from 1959 through 1990, for TSST-1 production by means of a latex agglutination kit (Oxoid). They found that already in 1959, 57% of *S. aureus* strains belonging to phage group I and 25% of the non-typable strains produced toxic shock toxin. The present isolate was non-typable (NT). They found no correlation to clinical parameters, and anti-TSST-1 antibodies could not be investigated. TSST-1 is a superantigen, which means that it is capable of stimulating as many as 20% of all T-cells. TSST-1 superantigen activity has been associated with expansion of lymphocyte populations bearing the V β 2 chain, that bind the antigen (MacIsaac et al. 2005). A broad definition of toxic shock syndrome has been suggested based on patient presentation and on the presence of *S. aureus* producing TSST-1, enterotoxin B or enterotoxin C (Schlievert 2005).

Immunosuppression is a predisposing factor for NF (Tung-Yiu et al. 2000, Wong et al. 2004). Our patient was immunosuppressed because of long-term treatment with methyl prednisolone (10 mg daily), but the dose-response relationship remains unclear (Hashimoto et al. 2002). Clinicians should be aware of toxic shock syndrome as a complicating factor in cases of NF, even when the isolate is penicillin-sensitive.

- Alouf J E, Muller-Alouf H. Staphylococcal and streptococcal superantigens: molecular, biological and clinical aspects. *Int J Med Microbiol* 2003; 292 (7-8): 429-40.
- Ejlertsen T, Jensen A, Lester A, Rosdahl V T. Epidemiology of toxic shock syndrome toxin-1 production in *Staphylococcus aureus* strains isolated in Denmark between 1959 and 1990. *Scand J Infect Dis* 1994; 26 (5): 599-604.
- Hashimoto N, Sugiyama H, Asagoe K, Hara K, Yamasaki O, Yamasaki Y, Makino H. Fulminant necrotizing fasciitis developing during long term corticosteroid treatment of systemic lupus erythematosus. *Ann Rheum Dis* 2002; 61 (9): 848-9.
- Jamart S, Denis O, Deplano A, Tragas G, Vandergheynst A, De Bels D, Devriendt J. Methicillin-resistant *Staphylococcus aureus* toxic shock syndrome. *Emerg Infect Dis* 2005; 11 (4): 636-7.
- Kjellander J, Myrbäck K E. A simple test for penicillinase production. *Acta Pathol Microbiol Scand* 1964; 61: 494-??.
- Lee Y T, Chou T D, Peng M Y, Chang F Y. Rapidly progressive necrotizing fasciitis caused by *Staphylococcus aureus*. *J Microbiol Immunol Infect* 2005; 38 (5): 361-4.
- MacIsaac C M, Page M A, Biggs B A, Visvanathan K. Staphylococcal toxic shock syndrome: still a problem. *Med J Aust* 2005; 182 (12): 651.
- Regev A, Weinberger M, Fishman M, Samra Z, Pitlik S D. Necrotizing fasciitis caused by *Staphylococcus aureus*. *Eur J Clin Microbiol Infect Dis* 1998; 17 (2): 101-3.
- Saliba W R, Goldstein L H, Raz R, Mader R, Colodner R, Elias M S. Subacute necrotizing fasciitis caused by gas-producing *Staphylococcus aureus*. *Eur J Clin Microbiol Infect Dis* 2003; 22 (10): 612-4.
- Schlievert P M. Staphylococcal enterotoxin B and toxic shock syndrome toxin-1 are significantly associated with non-menstrual TSS. *Lancet* 1986; 1 (8490): 1149-50.
- Schlievert P M. Staphylococcal toxic shock syndrome: still a problem. *Med J Aust* 2005; 182 (12): 651-2.
- Seal D V. Necrotizing fasciitis. *Curr Opin Infect Dis* 2001; 14 (2): 127-32.
- Tung-Yiu W, Jehn-Shyun H, Ching-Hung C, Hung-An C. Cervical necrotizing fasciitis of odontogenic origin: a report of 11 cases. *J Oral Maxillofac Surg* 2000; 58 (12): 1347-52.
- Wong C H, Tan S H, Kurup A, Tan A B. Recurrent necrotizing fasciitis caused by methicillin-resistant *Staphylococcus aureus*. *Eur J Clin Microbiol Infect Dis* 2004; 23 (12): 909-11.
- Zahar J R, Goveia J, Lesprit P, Brun-Buisson C. Severe soft tissue infections of the extremities in patients admitted to an intensive care unit. *Clin Microbiol Infect* 2005; 11 (1): 79-82.