Case Report

Fatal necrotizing fasciitis due to *Streptococcus pneumoniae* after renal transplantation

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**Keywords:** necrotizing fasciitis; pneumococcal fasciitis; renal transplantation; *Streptococcus pneumoniae*

**Introduction**

Necrotizing fasciitis is an uncommon, devastating soft-tissue infection primarily involving superficial fascia, subcutaneous fat and deep fascia that relatively spares skin and underlying muscle [1]. It most frequently occurs in the abdominal wall, extremities and perineum, where the pathogen may be introduced in the subcutaneous space via disruptions of overlying skin. Besides direct inoculation, haematogenous spread from a distant site may probably occur. The disease predominantly develops in diabetics, alcoholics, immunosuppressed patients, illicit drug users and patients with peripheral atherosclerotic vascular disease. Despite rapid diagnosis and treatment, case fatality rate is high and any delay may correlate with worse outcome [1].

A wide variety of organisms have been implicated in necrotizing fasciitis and are causative for monomicrobial (most often due to β-haemolytic streptococci group A) and polymicrobial (most often due to non-group A streptococci plus anaerobes and facultative anaerobes and often Enterobacteriaceae) infections. Necrotizing fasciitis due to *Streptococcus pneumoniae*, however, is exceedingly rare. Here we report a case of pneumococcal fasciitis in a patient after renal transplantation and present a concise mini-review of the literature.

**Case**

A 64-year-old white male without prior splenectomy underwent living related renal transplantation for autosomal-dominant polycystic kidney disease on 27 November 2001. His initial immunosuppressive treatment (body weight 85 kg) consisted of prednisone (50 mg/day), mycophenolate (1 g twice daily) and cyclosporin (375 mg twice daily); no anti-lymphocyte antibodies were necessary to prevent/treat graft rejection. The patient felt well with stable renal function until 29 December, when he slipped on ice and fell on his left elbow. Six days later, the elbow became exquisitely tender, but on physical examination no abnormal finding was noted and the skin was intact.

On 1 January 2002, the patient was symptomatically treated for coughing and a sore throat; no diagnostic procedure was undertaken. During an outpatient visit on Friday 4 January, conventional radiographies showed a rise in serum creatinine (from 142 to 242 μmol/l; normal range 70–105 μmol/l), a reduction in urine volume and an elevated C-reactive protein (358 mg/l; normal range <5 mg/l) was found. Since an acute transplant rejection was suspected, the patient was scheduled for renal biopsy on the following Monday, but was not hospitalized over the weekend because of the apparently good general clinical condition. On 6 January, the patient noticed exaggerated pain in the left elbow and sudden onset of dyspnoea and anuria for which he presented in the emergency room.

At this time, regular medications included mycophenolate (1 g twice daily), cyclosporin (175 mg twice daily), prednisone (30 mg/day), atenolol (25 mg/day) and dalteparin (5000 IE subcutaneously/day). On physical examination, the patient appeared severely ill with cool and mottled extremities. Blood pressure...
was 70/50 mmHg, his heart rate was 120 beats per
min, respiratory rate was 40 per min and body tem-
perature was 35.7°C. Soon after arrival, the patient
to be intubated because of respiratory failure. On
mechanical ventilation, bronchial breath sounds and
occasional rales were heard over the base of the right
lung. A chest radiograph showed left-sided pleural
effusion and atelectasis as well as an opacification
lung. A chest radiograph showed left-sided pleural
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had to be intubated because of respiratory failure. On
Continuous veno-venous haemodiafiltration was star-
ted for acute anuric renal failure with haemodynamic
instability and maintained during the entire hos-
pitalization. After removal of the splint, a pasty swell-
ing around the elbow with large erythematous changes
of the skin of the upper arm was found. A presumptive
diagnosis of septic shock due to soft-
tissue infection was made and antibiotic therapy
with adjusted doses of clindamycin, piperacillin/
tazobactam and netilmicin was started. Treatment
with cyclosporin and mycophenolate was discon-
tinued. The serum concentration of cyclosporin was
continued. The serum concentration of cyclosporin was
273 μmol/l 12 h after admission. A local aspirate of
the elbow revealed Gram-positive diplocci. Sub-
sequently, repeated blood cultures and local aspirates
yielded S. pneumoniae serogroup 9 with susceptibility
against penicillin. Despite haemodynamic instability
requiring large doses of vasoactive drugs, surgical
exploration and extensive debridement was per-
formed immediately. The intra-operative site showed
vast necrosis of skin, subcutaneous tissue and
muscle fascia. Nonetheless, haemodynamic status
remained unstable, severe lactic acidosis persisted (mini-
mal lactate 8.4 mmol/l) and clinical conditions further
deteriorated with developing neutropenia (nadir 0.64
×10⁹/l), thrombocytopenia (55×10¹²/l), liver failure
(ASAT 23936 U/l, alanine aminotransferase 8593
(< 50) U/l, alkaline phosphatase 302 (30–115) U/l,
ammonia 268 (9–33) μmol/l), rhabdomyolysis (creat-
ine kinase 9137 U/l, myoglobin 41654 (23–72) μg/l,
LDH 24519 (150–420) U/l) and coagulopathy, resul-
ting in severe wound bleeding that could not be
controlled by repeated transfusions of fresh frozen
plasma, platelets and red blood cell units. On 7
January, 35 g of human immunoglobulins were
transfused for uncontrolled septic shock and assumed
β-haemolytic streptococcal fasciitis. Despite a second
surgical debridement and continued antibiotic coverage,
soft-tissue necrosis spread involving the lower
abdominal wall and left leg within one day. The pati-
ent died of multiorgan failure 44 h after admission.
A necropsy was not permitted.

Prior to the present illness, the patient had been
successfully vaccinated for hepatitis B, but he never
received vaccination for pneumococci. Serologies were
negative for HIV-1 and -2, HTLV-1 and -2, and
hepatitis C.

Discussion

**Streptococcus pneumoniae** is an important bacterial
pathogen and major cause of pneumonia, meningitis,
sinusitis and otitis media in humans. It may less
frequently cause endocarditis, arthritis, peritonitis
and, uncommonly, a variety of other infectious dis-

eases. Skin and soft tissue manifestations of invasive
pneumococcal disease are extremely diverse in pre-
sentation and include cellulitis, subcutaneous and
muscle abscesses, wound infections, mastitis and
inguinal adenitis. Nevertheless, necrotizing fasciitis
due to *S. pneumoniae* is rare and only a few cases [3,4]
have been reported to date. In general, primary or
secondary defects in antibody formation and comple-
ment, insufficient or poorly functioning polym-
orphonuclear cells, and defective clearance of
pneumococcal bacteraemia have an important impact
on the immunologic capacity of the host and predispose
to pneumococcal infections. In cases of necrotizing
fasciitis due to *S. pneumoniae*, one patient had
antecedent blunt trauma but was otherwise healthy
[3], whereas risk factors in others included illicit drug
abuse, systemic lupus erythematoses, diabetes mel-
itus, renal insufficiency, tumour necrosis factor
antagonist or other immunosuppressive therapy and
possibly intramuscular injection of nonsteroidal anti-
flammatory drugs. To our knowledge, this is the
first report of a patient who developed rapidly fatal
necrotizing fasciitis due to *S. pneumoniae* shortly after
renal transplantation. Besides immunosuppressive
drugs, no other risk factor could be identified; the
patient was not splenectomized and did not suffer
from frequent infections during his lifetime. Blunt
trauma leading to local haematoma may have
provided a nidus for localization of infection, as
suggested previously [3]. However, the route of
infection in our case remains uncertain, with both
haematogenous spread from an assumed pulmonary
infection or direct inoculation through a small wound
in the skin being valuable possibilities. As evidenced
in this case, the diagnosis may be difficult early in the
course of illness because of the paucity of skin
findings, with cellulitis accompanied by local pain and
fever being commonly the first signs; indeed, pain out
of proportion to physical findings in a patient with
evidence of a systemically toxic condition should raise
the clinical suspicion of necrotizing fasciitis [1]. Treat-
ment modalities comprise early aggressive surgery
with frequent wound debridements, broad-spectrum
antibiotic coverage, hyperbaric oxygen, and supportive
care [1].

The frequency and seriousness of pneumococcal
infections in renal transplant recipients has been recog-
nized for over 20 years and immunization of these
patients has been suggested [5]. Although current guidelines recommend the use of pneumococcal vaccine for all adults aged ≥65 years and for selected people aged <65 years, including those taking immunosuppressive therapy and those who had undergone organ transplantation [6], practices of immunization vary considerably in the latter situation even today. This controversy may be mainly due to studies suggesting suboptimal vaccine coverage since a diminished immune response with loss of protective antibodies has been observed [7]. However, a recent study concluded that polyvalent polysaccharide pneumococcal vaccination is safe and effective in patients with well-functioning renal allografts in the short term [8]. It is of note that the subtype of the S. pneumoniae isolated in our case is covered by the actual polyvalent pneumococcal vaccine. One may only speculate that a prior vaccination would have reduced the severity and ultimately the fatality of pneumococcal disease in this patient. Importantly, further well-designed long-term controlled studies are needed to elucidate the efficiency of a pneumococcal vaccination in the renal transplant population.

References


Received for publication: 11.6.02
Accepted in revised form: 29.8.02