Case Report

Necrotizing fasciitis and Legionnaires’ disease after combined renal and pancreatic transplantation: a penalty of overseas travel

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Introduction

Necrotizing fasciitis is a syndrome of rapidly spreading subcutaneous infection characterized by necrosis of the superficial and deep fascia and by thrombosis of the cutaneous micro-circulation [1]. The condition carries a high mortality because of the speed with which patients develop overwhelming sepsis and multi-system organ failure. During the past decade, it has generated much public concern, after being given undue prominence by the non-medical media.

Necrotizing fasciitis is rare after renal transplantation, with only a handful of cases cited in the literature, and survival is infrequent [2–4]. This is the first time that necrotizing fasciitis has been reported in a patient who previously had undergone combined kidney and pancreatic transplantation. She survived the initial illness but died after developing Legionellosis. Two rare *Legionella* serotypes were isolated, raising the possibility of an unusual mode of transmission of the infection.

Case

One year after successful cadaveric pancreaticorenal transplantation, a 51-year-old woman travelled to India to visit her frail, elderly parents. In the fifth week of her holiday, she developed a blistering eruption over the dorsum of the right foot. This started as an innocuous, slightly raised, bluish-red area measuring <1 cm in diameter. Whether the initial injury was a minor abrasion or an insect bite was not known. Topical application of a broad spectrum antibiotic preparation was unhelpful. By the fifth day, the foot had become swollen and painful, and she suffered several rigors. She elected to return immediately to the UK.

She had been an insulin-requiring diabetic patient for nearly 25 years and for seven of them she had been maintained on peritoneal dialysis. Although she came to have moderately severe peripheral neuropathy, retinopathy and peripheral vascular disease as a consequence of diabetes, she had only minor coronary artery disease. In the first month after transplantation, she was treated with ganciclovir for systemic primary cytomegalovirus infection. Thereafter, apart from an episode of streptococcal pneumonia which responded quickly to antibiotics, she was well rehabilitated. Medication consisted of prednisolone 12.5 mg and azathioprine 50 mg daily, cyclosporin 75 mg twice daily, aspirin and ranitidine. She became independent of exogenous insulin and remained normotensive after transplantation; the serum creatinine prior to travel was 75 µmol/l.

On admission to hospital, she showed features of endotoxaemia. She was febrile at 39°C and had signs of a toxic confusional state. She was dehydrated, pulse was 125 per min and blood pressure was 100/60 mmHg. The right foot was swollen and tender. Cellulitis extended proximally to the mid-tibia, arising from a blistering eruption that measured 4 cm in diameter and was centred over the dorsum of the foot. The foot pulses were barely palpable, and some crepitus could be elicited in the subcutaneous tissues. The haemoglobin was 10.2 g/dl, white blood cell count 24.6 × 10^9/l, urea 9.6 mmol/l, creatinine 78 µmol/l, bicarbonate 24.7 mmol/l, ionized calcium 0.88 mmol/l (normal 1.1–1.25) and the C-reactive protein 310 mg/l (normal <10). The blood glucose was 5.4 mmol/l, serum albumin 17 g/l, bilirubin 32 µmol/l, and serum levels of alanine aminotransferase and alkaline phosphatase were normal. Initial arterial blood gases and coagulation studies showed no abnormality. A Lancefield group A *Streptococcus* was isolated from wound swabs and blood cultures.

The patient was resuscitated with i.v. fluids and blood products and she was given benzylpenicillin 1.2 g 4-hourly and metronidazole 500 mg 8-hourly i.v. Hypocalcaemia was corrected with i.v. calcium
supplements. Eight hours after presentation, she underwent the first of a series of three surgical debridements of the wound performed on consecutive days. Culture of the excised tissue taken on the third day subsequently revealed a profuse growth of Proteus species, Enterococcus, Bacteroides and Escherichia coli. Azathioprine was stopped and she was continued on smaller doses of corticosteroid and cyclosporin. After adding imipenem–cilastatin to the antibiotic regimen, her condition improved and her temperature normalized. However, on the eighth day, she again became unwell with a high-grade fever. Re-exploration of the wound confirmed extensive fascial necrosis extending proximally above knee level. The small muscles of the foot were necrotic and the calf muscles oedematous and ischaemic. An above-knee amputation was performed.

A full recovery had been anticipated, but 4 days later she was admitted to the intensive care unit for ventilatory support after developing respiratory failure due to a right upper lobe pneumonia. Haemophilus influenzae and, later, two distinct serotypes of Legionella species were identified in bronchial washings obtained during bronchoscopy. Legionella pneumophila (serogroup 11) and L. longbeachae were cultured and identified by direct immunofluorescent antibody tests. She failed to respond to erythromycin and rifampicin, and died with adult respiratory distress syndrome, disseminated intravascular coagulation and circulatory collapse.

**Discussion**

Necrotizing fasciitis may involve any region of the body, especially the limbs, perineum and the abdominal wall [5–7]. Pathogenic bacteria gain entry into the subcutaneous tissues at the site of a minor abrasion, skin ulceration, burns, trauma, previous abdominal or gynaecological surgery or, less frequently, by haematogenous spread from a remote site of infection [7,8]. In 80% of cases of necrotizing fasciitis, infection is polymicrobial, consisting of both Gram-positive and Gram-negative aerobic and anaerobic bacteria [7–9]. In monomicrobial infections, Gram-positive organisms, often Group A Streptococci, predominate.

An apparent increase in the incidence of necrotizing fasciitis probably stems from a greater awareness of this potentially fatal condition and because of an increase in the number of individuals with predisposing factors. Those at special risk include diabetics, alcoholics, intravenous drug abusers, the elderly and those taking immunosuppressive drugs [8,9]. The presence of peripheral vascular disease, malnutrition or obesity are important adverse prognostic factors [7]. In some series, diabetes mellitus or atherosclerotic peripheral vascular disease as co-morbid factors of necrotizing fasciitis have been associated with a mortality rate > 80% [6]. The overall mortality of 34% has changed little since the first descriptions of necrotizing fasciitis in the early part of this century, before antibiotics became available [9,10]. Increasing virulence of certain bacteria [11], particularly Lancefield Group A, and delays in making the diagnosis and initiating treatment are the main reasons for the lack of improvement in the survival statistics [7,9]. Mortality varies directly with the interval between the onset of infection and treatment. It is related to overwhelming sepsis and multi-system organ failure, which may occur within hours of the onset of localized tenderness and pain. Bacterial endotoxins and the release of pro-inflammatory cytokines are responsible for the systemic features of necrotizing fasciitis [12].

Early recognition, expeditious surgical debridement of all non-viable tissue together with appropriate broad spectrum antibiotic therapy and haemodynamic circulatory support are the principal clinical features which influence outcome [7,9]. Hyperbaric oxygen therapy has no established role in treating necrotizing fasciitis and is likely to delay surgical debridement [13]. Early diagnosis of necrotizing fasciitis is made difficult by the relative lack of cutaneous inflammation despite extensive deep fascial necrosis. Anaesthesia of the skin due to infarction of the cutaneous nerves is an additional factor that masks serious infection.

In this patient, the initial pathogen was a Group A Streptococcus and subsequently the wound was colonized by a variety of organisms. The patient was receiving minimal maintenance immunosuppression, but the peripheral vascular disease was a significant risk factor for necrotizing fasciitis. She developed hypocalcaemia, a feature that is observed in 25% of patients and has been attributed to precipitation of calcium in areas of extensive fat necrosis [14]. Secondary nosocomial infections are not uncommon in necrotizing fasciitis [6]. Transplant recipients are particularly susceptible to Legionella infection because of defective cell-mediated immunity induced by immunosuppressant medication [15]. Although most common in the first 3 months after transplantation, Legionella pneumonia may first occur several years later [16]. This patient’s Legionnaires’ disease is unlikely to have been contracted in hospital. Both L. pneumophila (serogroup 11) and L. longbeachae serotypes are extremely rare in the UK. Legionella longbeachae is, however, a common cause of legionellosis in Australia, and infection has been associated with exposure to soil and potting plant mixes [17,18]. The possibility exists that the Legionella infection in our patient was introduced via the foot wound rather than by respiratory droplet infection. Moreover, necrotizing fasciitis involving a limb, caused by Legionella species, has been described in a renal transplant recipient [3]. The tissue excised from our patient was not examined for Legionella infection.

As worldwide travel becomes increasingly practical and affordable, the incidence of infectious diseases in the returning traveller is increasing [19]. For example, currently half of all cases of Legionnaires’ disease reported in the UK are travel-related [20]. Immunosuppressed patients are among the most vulnerable. Transplant recipients must be cautioned over...
the potential risks of infection associated with foreign travel, and appropriate precautions and immunizations should be taken [21].

In conclusion, necrotizing fasciitis is a life-threatening disorder that requires prompt recognition and aggressive treatment, including surgical intervention. It should be suspected in patients with unexplained soft tissue pain, swelling and tenderness, and marked constitutional symptoms. Multiple infections are to be expected in the immunosuppressed, although the reported combination must be very rare.

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References


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