Three cases of necrotising fasciitis caused by *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*: the importance of immunosuppression

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**ABSTRACT**

Necrotizing Fasciitis (NF) is a life-threatening infectious emergency, characterized by rapidly progressive fascia and subcutaneous tissue necrosis. NF carries a high mortality rate in the neutropenic period of immunosuppressive patients, not because of co-morbidity but also because antibiotics frequently administered are typically ineffective. Here, we report three cases of NF caused by multi-drug resistant *Pseudomonas aeruginosa* (only colistin susceptible) and *Stenotrophomonas maltophilia*, which both restrict our treatment options. The cases underline the importance of recognition and early intervention of NF in patients with immunosuppression which may be difficult because of concealed sign and symptoms. *J Microbiol Infect Dis* 2015;5(1): 25-28

**Key words:** Hematologic malignity, Necrotising fasciitis, immunosuppression, Pseudomaonas aeruginosa, Stenotrophomonas maltophilia.

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**INTRODUCTION**

Necrotising fasciitis (NF) is a severe soft-tissue infection associated with rapidly progressing necrosis of the subcutaneous tissue and superficial fascia. The primary cause of this condition is a severe polymicrobial infection caused by mixed aerobic-anaerobic microflora. Major clinical features include early onset of systemic toxicity accompanied by crepitation, oedema, bulla, and necrosis. NF is most commonly seen in immunosuppressed patients, making it an important clinical challenge due to the increasing number of severely immunosuppressed individuals worldwide. Due to the poor host immune status, severe infections within this population are usually fatal, even in patients receiving immediate antibiotic therapy and radical debridement. Here, we describe three unusual cases of limb NF in patients with haematologic malignancies. This report highlights the importance of early diagnosis and clinical intervention in cases of NF in immunosuppressed patients, which is often difficult due to the absence of normal clinical symptoms.

**CASE 1**

A 22-year-old male patient diagnosed with of acute myeloid leukaemia (AML) presented with symptoms of fever and neutropenia. Upon physical examination, his temperature was 39°C, blood pressure
120/70 mm Hg, pulse rate 96/min, and respiratory rate 20/min. The initial blood work revealed leukopenia, with a white blood cell (WBC) count of 36/mm³ (neutrophils 10/mm³), accompanied by anemia and thrombocytopenia, based upon a haemoglobin level of 6.4 g/dL, and platelet count of 18.7 cells/L, respectively. Arterial blood gases, chest radiograph, and electrocardiogram were all within the normal range. Piperacillin-tazobactam (4.5 g/6 h/day, IV) therapy was initiated in accordance with institutional standards for care. On the third day of follow-up, teicoplanin (400 mg/day, IV) was added due to signs of inflammation around the catheter insertion point. Ultrasonography revealed increased subcutaneous tissue thickness and inflammation with fluid accumulation. Treatment was then replaced with doripenem (500 mg/8 h/day, IV) and daptomycin, (4 mg/kg/day, IV) as oedema and erythema quickly spread to the neck region accompanied by bulla and necrosis. A fasciotomy was performed to relieve pressure, however full surgical debridement was postponed since thrombocyte levels did not exceed 18,000 cells/L. Colistin (5 mg/kg/day, IV) was added upon detection of multidrug-resistant Pseudomonas aeruginosa by microbiological cultures of the blood and soft tissues. Following thrombocyte replacement therapy and necrotic tissue debrided the patient’s condition stabilised. During follow-up, the clinical infection regressed as the result of multiple surgical debridements and antimicrobial treatment. A definitive diagnosis of NF was finally confirmed by histologic examination of the surgical specimens. Antibiotic therapy was halted after 21 days. A complete recovery was evident following three months of physical rehabilitation including skin graft operations (Figure 1).

CASE 2
A 52-year-old female patient admitted to the haematology ward with a diagnosis of AML was examined following a diagnosis of neutropenic fever. Upon physical examination, her fever was 39.1°C, blood pressure 110/70 mm Hg, pulse rate 94/min, and respiratory rate 18/min. Blood work revealed a WBC count of 279/mm³, neutrophils 12/mm³, haemoglobin 8.3 g/dL, platelets 39,000 u/L, and C-reactive protein 7.7 mg/dL. The patient was treated with piperacillin-tazobactam (4.5 g/6 h/day, IV), followed by the addition of daptomycin (4 mg/kg/day, IV) on day 4 due to the presence of a marked erythema and oedema on the left hand around the catheter insertion site. During follow-up, the soft tissues were observed to have deteriorated, with evidence of significant bulla and necrosis. By day 11, the patient’s fever had returned, and her blood pressure had fallen to 90/60 mm Hg. Treatment was changed to imipenem (500 mg/6 h/day, IV) plus daptomycin, the catheter removed, and blood cultures performed. Due to suspicion of NF, a fasciotomy and excisional debridement were performed in an attempt to preserve the upper limb. Stenotrophomonas maltophilia was identified from the excised tissue, and histological examination confirmed the diagnosis of NF. Trimethoprim sulfamethoxazole (20 mg/kg/day) was added in response to positive microbial culture, and continued for 21 days, after which antibiotic therapy was discontinued. The clinical infection subsided, and the lesion was almost completely healed after 6 weeks of follow-up with vacuum-assisted closure and skin grafts. Additional follow-up was performed at a physical rehabilitation unit for three months.

Figure 1. Repeated surgical debridement of all necrotic tissue has to be the first line in the management of fasciitis

CASE 3
A 68-year-old male patient with a history of multiple myeloma (MM) and mild renal impairment, presented with fever and erythema on the right arm where a routine blood sample had been obtained the previous day, suggesting the needle insertion site as the site of entry of the bacteria. The skin of his arm was inflamed up to his fingers, with some patchy areas having a dusky appearance. He had neutropenia with WBC count of 1300/mm³ (neutrophils 255/mm³), a haemoglobin level of 7.8 g/dL, a platelet...
level of 7430 u/L, and a C-reactive protein level of 18.4 mg/dL. The patient was diagnosed with infectious myositis, and was placed on piperacillin-tazobactam (4.5 g/6 h/day, IV) therapy supplemented with teicoplanin (400 mg/ day, IV). However, despite treatment, the pain and swelling worsened, and was accompanied by visible cutaneous necrosis. The patient was started on imipenem (500 mg/6 h/day, IV) with daptomycin (4 mg/kg/day, IV) in response to ultrasonographic analysis, which revealed thickening and oedema in the skin and subcutaneous tissues extending into the extensor area of the right forearm. Microbiological culture of the deep soft tissue lesion reveals growth of multidrug resistant P. aeruginosa. The organism was susceptible to carbapenems, however his clinical condition deteriorated rapidly over the next 24 h with refractory hypotension and worsening of metabolic acidosis, requiring inotropic treatment and haemodialysis support. His blood pressure was 95/55 mm Hg, and his pulse rate was 120 beats/min. Pure growth of P. aeruginosa were obtained from two consecutive blood cultures, confirming the initial diagnosis. Magnetic resonance imaging (MRI) revealed an extensive muscular necrosis of the forearm. His thrombocytopenia deepened despite replacement therapy, and he became drowsy and mentally confused. Haematological analyses revealed disseminated intravascular coagulation. Histological examination of the excised tissue confirmed the diagnosis of NF. A planned excisional debridement and limb amputation could not be performed due to the patient’s worsening clinical condition. He succumbed to multi-organ failure, and died 6 days after the onset of sepsis (Figure 2).

### DISCUSSION

Although diagnosis of NF is considered relatively straightforward, such a diagnosis is almost always controversial, with the clinical hallmarks of the disease often uncertain in cases of diabetes, malignancy, or steroid use. Obvious infections may not always develop as expected, particularly in immunosuppressed patients in whom the normal inflammatory responses may be absent. This type of immunosuppression causes the signs and symptoms of radiologic and serologic data to become indistinct, with the disease having progressed too far by the time it is properly diagnosed, resulting in a high mortality rate (20 - 40%) even with early surgical debridement. All three of the infections described here were diagnosed promptly within 24 h of admission. Ultrasonography was crucial to the early diagnosis, with confirmation via computerised tomography or MRI occurring during the following days. Although all three of these radiological methods are utilised in the diagnosis of NF, MRI is known to have the highest specificity and sensitivity (93-100%).

In hosts with an underlying disease, polymicrobial infections containing Staphylococcus aureus, Streptococcus spp., Escherichia coli, and P. aeruginosa are the most common. P. aeruginosa is one of the most frequent causes of necrosis during the neutropenic period of immunosuppression in patients with AML, MM, and non-Hodgkin’s lymphoma. In two of our cases, the causative agent was multidrug-resistant P. aeruginosa. Diagnosis of multidrug resistance is of particular importance in neutropenic patients, as fewer treatment options are available. A combination of colistin and tigecycline is the preferred regimen in cases of multidrug-resistant infections, as more common antibiotics, such as carbapenem, quinolone, and aminoglycoside, are generally ineffective against these infections. A total of 38 cases of monomicrobial P. aeruginosa NF has been published to date, with 50% of infections developing during chemotherapy, resulting in ~30% mortality overall.

Necrotising soft tissue infections caused by the opportunistic pathogen S. maltophilia are rare, but represent an important emerging threat among immunosuppressed populations. Clinical characteristics of these infections include cellulitis and NF, and are most commonly encountered in oncology units. Soft tissue infections caused by S. maltophilia and P. aeruginosa are rarely seen in the limbs, and carry a high mortality risk due to underlying co-morbidities, along with widespread resistance to antibiot-
ics. Trimethoprim sulfamethoxazole is the first-line antibiotic in these infections, however quinolones, tigecycline, and chloramphenicol are also effective.

In patients with NF with immunosuppressive condition several antibiotic regimens including ampicillin/sulbactam or piperacillin-tazobactam with an aminoglycoside or triple combination with linezolid, daptomycin or vancomycin have also been shown to be effective against these infections. More aggressive therapy incorporating carbapenems in combination with other drugs should be saved for patients with systemic toxicity findings indicative of sepsis. In the three cases described here, piperacillin-tazobactam was the preferred antibiotic for first-line therapy, in accordance with institutional standards for care. However, therapeutic regimens were subject to frequent revisions in response to changing clinical symptoms and microbial cultures. No experimental treatments were used in any of the cases described, with changing antibiotic therapies consistent with standard regimens based upon the information available at the time. Overall, our data suggest that effective antibiotic therapy and surgical debridement are the two most important factors affecting patient survival. Surgical intervention is an essential step in cases of NF, and should be carried out as soon as possible. Two of our cases underwent extensive debridement surgery within 24-32 h of positive diagnosis or suspicion of NF, and followed regularly at 4-6-h intervals. The third case in which surgical debridement could not be performed due to deep thrombocytopenia died within a week, highlighting the importance of surgical intervention.

Together, these three cases reinforce the need for a multidisciplinary approach to NF, owing to its high rates of both mortality and morbidity. Since diagnosis represents the most difficult step in the treatment of NF in an immunosuppressed patient, all inflammatory signs should be viewed as possible NF, even in the absence of visible necrosis. Early diagnosis, combined with aggressive surgical debridement and appropriate antibiotic treatment, is the most effective treatment for NF, and provides the highest likelihood of a positive outcome.

REFERENCES