cost is *c*. 30 euros/test, and this can be reduced further if the test is performed routinely. High plasma concentrations of β-lactams have neurological toxicity [7]. The mental status of patients receiving high doses of β-lactams has not been investigated thoroughly, and the effects of the very high β-lactam concentrations observed in the present study could be insidious and remain unsuspected. For example, lethargy, asthenia, depression and anorexia are common symptoms in elderly patients treated for endocarditis and are investigated rarely.

The main caveat for the systematic monitoring of β-lactam concentrations during treatment of endocarditis is the lack of data on the optimal concentrations required. Although the correlation between very high β-lactam plasma concentrations and toxicity (especially neurological toxicity) is likely, it has not yet been demonstrated formally. Likewise, even though animal models suggest that trough plasma β-lactam concentrations of 4× MIC are sufficient, it is not clear whether these data can be extrapolated to humans. Although there is no reason to increase the trough plasma β-lactam concentrations to >10× MIC for the treatment of endocarditis (R. Tulkens, personal communication), the results of the present study suggest that the use of current guidelines probably leads to even higher concentrations in most patients, and particularly in the elderly. The consequences of these high concentrations remain to be determined. HPLC could offer an opportunity to monitor plasma β-lactam concentrations, and would allow individualised rather than standardised treatment. Prospective, randomised, multicentre studies are required to evaluate the impact of such monitoring on endocarditis therapy.

ACKNOWLEDGEMENTS

This work was presented in part at the 7th International Symposium on Modern Concepts in Endocarditis and Cardiovascular Infections, Chamonix, France, 2003 and the 14th European Congress of Clinical Microbiology and Infectious Diseases, Prague, Czech Republic, 2004.

REFERENCES

1. Cars O. Efficacy of beta-lactam antibiotics: integration of pharmacokinetics and pharmacodynamics. *Diagn Microbiol Infect Dis* 1997; **27**: 29–33.
2. Craig W. Pharmacodynamics of antimicrobial agents as a basis for determining dosage regimens. *Eur J Clin Microbiol Infect Dis* 1993; **12**(suppl 1): S6–S8.
3. Wilson WR, Karchmer AW, Dajani AS *et al*. Antibiotic treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HACEK microorganisms. American Heart Association. *JAMA* 1995; **274**: 1706–1713.
4. Bayer AS, Bolger AF, Taubert KA *et al*. Diagnosis and management of infective endocarditis and its complications. *Circulation* 1998; **98**: 2936–2948.
5. Hoen B, Alla F, Selton-Suty C *et al*. Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA* 2002; **288**: 75–81.
6. Dhawan VK. Infective endocarditis in elderly patients. *Clin Infect Dis* 2002; **34**: 806–812.
7. Bloomer HA, Barton LJ, Maddock RK. Penicillin-induced encephalopathy in uremic patients. *JAMA* 1967; **200**: 121–123.
8. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med* 1994; **96**: 200–209.
9. Pehourcq F, Jarry C. Determination of third-generation cephalosporins by high-performance liquid chromatography in connection with pharmacokinetic studies. *J Chromatogr Anal* 1998; **812**: 159–178.
10. Cockroft DW, Gault MH. Prediction of creatinine clearance from plasma creatinine. *Nephron* 1976; **16**: 31–41.

RESEARCH NOTE

Severe soft tissue infections of the extremities in patients admitted to an intensive care unit

J.-R. Zahar, J. Goveia, P. Lesprit and C. Brun-Buisson

Service de Réanimation Médicale and d'Immunologie Clinique, Hôpital Henri Mondor, Créteil, France

ABSTRACT

This report describes a retrospective analysis of 33 patients admitted to an intensive care unit with suspicion of necrotising fasciitis (NF) of the

Corresponding author and reprint requests: J.-R. Zahar, INSERM U 570, Faculté de Médecine Necker–Enfants Malades, Unité de Pathogénie des Infections Systémiques, 156 Avenue de Vaugirard, 75730 Paris cedex 15, France
E-mail: zahar@necker.fr

extremities. The aim of the study was to clarify the clinical presentation of NF in order to determine when early surgery should be considered. Twenty-one patients with surgically confirmed NF were compared to 12 patients with superficial soft tissue infection. At admission, patients with NF were more likely to have skin areas of ischaemia or necrosis, fluid-filled vesicles, and severe sepsis or septic shock.

Keywords Intensive care unit, necrotising fasciitis, sepsis, soft tissue infection

Original Submission: 13 February 2004; **Revised Submission:** 21 July 2004; **Accepted:** 3 August 2004

Clin Microbiol Infect 2005; 11: 79–82
10.1111/j.1469-0691.2004.01027.x

Severe skin or soft tissue (SST) infections can involve fascia planes, thereby constituting necrotising fasciitis (NF). Such infections are characterised by extensive necrosis and systemic toxicity [1,2]. Early clinical diagnosis of NF, and differentiation between NF and superficial SST infection (erysipela or cellulitis), may be difficult [3,4]. However, early surgical debridement of patients with NF has been associated with improved survival when compared with delayed surgical exploration [5,6]. The present study describes a retrospective analysis of 33 patients admitted to an intensive care unit (ICU) with severe SST infection of the extremities, with the aim of clarifying the clinical presentation of NF and determining when patients should be referred for early surgery.

Data collected included patient demographics, source of infection, predisposing factors, clinical presentation, laboratory parameters, bacteriological findings, management, duration of ICU and hospital stay, and rate of survival. The severity of sepsis at presentation was assessed according to published guidelines and definitions [7], and the severity of acute illness was assessed with the Simplified Acute Physiology Score II (SAPS II) [8]. NF was defined as a soft tissue infection with fascia involvement confirmed at surgery, while superficial SST infection (or 'medical' infection) was defined as either (1) soft tissue infection without fascia involvement, as confirmed by surgical exploration, or (2) soft tissue infection that resolved without surgery. In order to examine features associated with NF cases needing surgical debridement, patients with medical SST infections were compared to patients with confirmed NF. The data were compared by means of the Mann–Whitney *U*-test.

In total, 25 (76%) patients underwent surgical exploration. The mean delay between diagnosis and surgery was 3.4 days (range 0–23 days); 18 patients had surgery within 48 h of diagnosis. At surgery, NF was confirmed in 21 (84%) of these patients, while four patients were diagnosed with superficial SST infection.

Twenty-one patients were referred for primary therapy, including 16 who failed to improve after initial therapy. Four patients presented with severe sepsis and 11 with septic shock. The mean age of the patients was 59 years (range 20–88 years). A medical condition predisposing to soft tissue infection was noted in 21 (64%) patients, namely diabetes mellitus (n = 11), cancer (n = 4; all receiving chemotherapy), corticosteroid therapy (n = 8; all receiving >1 mg/kg/day prednisone equivalent) and liver cirrhosis (n = 4); four patients had received non-steroidal anti-inflammatory drugs. A precipitating factor was recorded for 24 (73%) patients, in that 11 patients had a pre-existing local infection and 13 patients had a recent history of trauma. The latter group included minor or major limb injury (n = 8), intramuscular injections (n = 4) or surgical amputation (n = 1). Seven cases of infection were hospital-acquired after liposuction surgery (n = 1), bedsore infection (n = 2), infected haematoma while receiving anticoagulant therapy (n = 1), leg ischaemia (n = 1) or surgical wound infection (n = 2).

Physical findings are detailed in Table 1. NF was associated significantly with cyanosis, necrotic skin areas, and fluid-filled vesicles. The mean SAPS II on admission was 34.5 (range 10–96). Patients with NF presented frequently with severe sepsis or shock (n = 15; 71%), whereas there were no such cases among patients with medical SST infection (p 0.0003). There was no difference in laboratory test parameters between the two groups (Table 1).

Microbiological findings are detailed in Table 2. *Staphylococcus* and *Streptococus* spp. were the most common isolates (Table 2). No microbial pathogen was isolated from 12 patients. Microorganisms were recovered more frequently from patients with NF (86% vs. 25%; p 0.001). Blood cultures were positive for 15 patients, of whom ten also had positive tissue or fluid culture