Enterococcus durans endocarditis in a patient with transposition of the great vessels

S. Stepanović, M. Jovanović, L. Lavadinović, B. Stošović and M. Pelemić

1Department of Bacteriology, Institute of Microbiology and Immunology, School of Medicine, Dr. Subotića 1, 11000 Belgrade, Serbia
2Institute of Infectious and Tropical Diseases ‘Dr Kosta Todorović’, Bulevar JNA 16, 11000 Belgrade, Serbia

A case of native valve endocarditis caused by Enterococcus durans in a patient with transposition of the great vessels is reported. The patient was treated initially with gentamicin and ceftriaxone; after isolation of enterococci, ceftriaxone was switched to ampicillin. The only virulence factors established in the strain were haemolytic activity and biofilm formation.

Introduction

Enterococci have become recognized as significant causes of nosocomial and community-acquired infections. These bacteria cause 7-9–13.1 % of all reported episodes of infective endocarditis (IE) (Olaison & Schadewitz, 2002). Enterococcal IE is caused most frequently by Enterococcus faecalis, followed by Enterococcus faecium (Johnson et al., 1998; Olaison & Schadewitz, 2002). Enterococcus durans is one of several species of enterococci that are reported only sporadically in human clinical infections. It has been estimated that E. durans is responsible for < 1 % of all enterococcal IE episodes (Olaison & Schadewitz, 2002), although only one case was well-documented in available literature (Triopi et al., 1998). The present paper describes in detail a case of community-acquired native valve endocarditis caused by E. durans in a patient with transposition of the great vessels. Virulence markers and the antibiotic susceptibility profile of the strain were also studied.

Case report

A 44-year-old male, a Serb refugee from Kosovo and Metohija, was admitted to the Institute of Infectious and Tropical Diseases in Belgrade with a 3-month history of fever, malaise, chills, night sweats, anorexia and weight loss. He had been living in an overcrowded refugee camp since 1999.

He was born with transposition of the great vessels, but he had not undergone cardiosurgery. Since 1998, he had had insulin-independent diabetes mellitus, which was well-controlled. The patient had slightly elevated blood pressure, which was controlled successfully with diuretics.

On arrival, physical examination revealed a temperature of 38.5 °C, blood pressure of 140/90 mmHg, splenomegaly and regurgitant murmur. Laboratory analyses showed the following values: white blood cell count, 9.9 × 10⁹ cells l⁻¹ (85 % neutrophils, 10 % lymphocytes, 4 % monocytes and 1 % eosinophils); erythrocyte count, 4.76 × 10¹² cells l⁻¹; haemoglobin, 11.5 g dl⁻¹; erythrocyte sedimentation rate, 70 mm h⁻¹; platelet count, 206 × 10⁹ platelets l⁻¹; renal function and hepatic enzyme levels were normal. Transoesophageal and transthoracic echocardiography showed stenosis of the pulmonary artery, significant tricuspid valve insufficiency, high pressure in the right ventricle (164–170 mmHg), a vegetation that measured 7 mm located at the tricuspid valve and moderate mitral valve insufficiency.

On the day of admission, six blood samples were obtained for culture and antibiotic treatment with gentamicin (120 mg day⁻¹) and ceftriaxone (2 g day⁻¹) was introduced. After 72 h treatment, the patient became afebrile and showed improvement in general well-being. However, due to isolation of Enterococcus sp. from all six blood cultures, ceftriaxone was switched to ampicillin (6 g day⁻¹). In total, ceftriaxone was administered for 3 days, gentamicin for 10 days and ampicillin for 6 weeks. Blood cultures performed 2 weeks after initiation of the treatment were negative. The patient was discharged in good condition, 7 weeks after admission. The patient remained clinically well 8 months after completion of the therapy.

Preliminary identification of the isolate as Enterococcus sp. was based on Gram-stain, morphological and cultural characteristics, negative catalase reaction, growth in the presence of 6.5 % NaCl and hydrolysis of aesculin in the presence of bile. Definitive identification of the isolate as E. durans was done by using the API 20 Strep system (bioMérieux) and confirmed by biochemical characterization, as recommended by Facklam & Collins (1989) and Knudtson & Hartman (1992). Susceptibility testing by the disc-diffusion method failed to reveal resistance to penicillin, ampicillin, ceftriaxone, cefotaxime, vancomycin, gentamicin, erythromycin, clindamycin, trimethoprim/sulfamethoxazole and chloramphenicol, as recommended by Facklam & Collins (1989) and Knudtson & Hartman (1992).
method showed that the isolate was susceptible to penicillin, ampicillin, erythromycin, chloramphenicol, gentamicin, tetracycline, ciprofloxacin, rifampicin and vancomycin.

In order to determine possible sources of the infection, swab samples were taken from the patient’s nose, pharynx and skin, as well as urine and faeces samples. However, *E. durans* was not isolated from any sample that was submitted for microbiological analysis.

To examine possible virulence factors of the isolated strain, biofilm formation, proteinase activity (gelatinase and casein hydrolysis), lipase activity (splitting of Tween 40 and 80, lipase reaction on Spirit blue agar and splitting of tributyrin), lecithinase activity, DNase activity, fibrinolysin activity, urease activity and haemolytic activity (on sheep blood, human blood and horse blood) were determined as described elsewhere (Stepanović et al., 2001 and references therein). The only difference was the use of Tryptcase–soy agar (bioMérieux) instead of tryptose blood agar base (Difco). Bacteriocin production was determined as described by Padilla et al. (2001), with *Micrococcus luteus*, *E. faecalis*, *Staphylococcus aureus*, *Bacillus subtilis* and *Listeria monocytogenes* as test organisms.

**Discussion**

Transposition of the great vessels is a rare cardiac malformation that accounts for approximately 1% of congenital heart disease (Connelly et al., 1996). Endocarditis occurs in 10–15% of these patients (Connelly et al., 1996). Optimal therapy for IE caused by enterococci requires a synergistic bactericidal combination of a cell-wall-active antimicrobial agent to which the organism is susceptible (penicillin or ampicillin) and an aminoglycoside (usually gentamicin) (Working Party of the British Society for Antimicrobial Chemotherapy, 1998; Mylonakis & Calderwood, 2001; Le & Bayer, 2003). This combination is essential, as penicillin or ampicillin alone produces only a bacteriostatic effect (Le & Bayer, 2003). However, in combination with gentamicin, these β-lactam antibiotics favour intracellular uptake of the aminoglycoside, which results in subsequent bactericidal activity against enterococci (Le & Bayer, 2003). In the absence of penicillin or ampicillin, intracellular uptake of the aminoglycoside is limited (Le & Bayer, 2003). However, treatment of IE should be started before the results of blood cultures are known (Working Party of the British Society for Antimicrobial Chemotherapy, 1998) and after the start of appropriate antimicrobial treatment, fever associated with IE often resolves within 2–3 days (Mylonakis & Calderwood, 2001). Initial therapy for our patient included a combination of gentamicin and ceftriaxone and after 3 days treatment, the patient became afebrile. It is well-known that enterococci are inherently resistant to third-generation cephalosporins, including ceftriaxone (Fuchs et al., 1996). Even if cephalosporins appear to be active in vitro, they are not clinically effective in vivo (National Committee for Clinical Laboratory Stan-

dards, 2002). Therefore, we assume that clinical improvement was probably not due to ceftriaxone and gentamicin, but to other factors.

According to a 5-year nationwide prospective study in Sweden, the mean duration of symptoms in patients with IE caused by enterococci was 21 days (Olaison & Schadewitz, 2002). In five episodes (out of 93), the duration of symptoms was >3 months (Olaison & Schadewitz, 2002). Symptoms in our patient lasted for 3 months. One possible explanation for such a prolonged clinical course is limited virulence of the bacterial strain and, thus, different virulence factors of the *E. durans* isolate were investigated. The isolated strain did not show proteinase, lipase, lecithinase, DNase, fibrinolysin or urease activities. Agglutination of erythrocytes and bacteriocin production were also absent. The only virulence factors that were established in the strain were haemolytic activity and biofilm formation. It should be noted that significance of haemolysin as a virulence factor of enterococci has not been proved, as it has been shown that only 0–16% of blood culture enterococcal isolates display haemolytic activity (Elsner et al., 2000). Moreover, haemolytic activity was more common in non-endocarditis clinical isolates and in hospital faecal isolates than among endocarditis isolates (Coque et al., 1995) and there was no significant association between 14-day mortality and the presence of haemolysin in enterococci (Vergis et al., 2002). On the other hand, formation of biofilms on native heart valves (vegetations) is a well-documented process of considerable significance for the pathogenesis of endocarditis (Donlan & Costerton, 2002).

In conclusion, whilst rarely recovered from clinical specimens, *E. durans* can obviously cause serious invasive infections. Despite the fact that the strain displayed a limited number of virulence factors, this report demonstrates the significance of *E. durans* as a cause of native valve endocarditis.

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