Case Report

Endocarditis caused by *Lactobacillus jensenii* in an immunocompetent patient

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Lactobacilli are Gram-positive rod-shaped bacteria that inhabit the oral cavity, gastrointestinal tract, vagina and nasal cavity. In this report, a rare case of *Lactobacillus jensenii* endocarditis in a 47-year-old immunocompetent patient is described. Blood cultures and a replaced mitral valve were positive for *L. jensenii* as assessed by 16S rRNA gene sequencing. Based on susceptibility tests the patient was successfully treated with a mixture of teicoplanin and meropenem antimicrobial therapy.

Introduction

Lactobacilli are Gram-positive, catalase- and oxidase-negative, non-sporulating, strict or facultative anaerobic rod-shaped bacteria belonging to the lactic acid bacteria group (Collins *et al.*, 1991; Murray *et al.*, 2003). They are part of the normal bacterial flora of human mucosa (vagina, gastrointestinal tract and oropharynx), and are traditionally used in the production of fermented foods and as probiotics (Alvarez-Olmos & Oberhelman, 2001; Salminen *et al.*, 2002).

The isolation of lactobacilli from clinical specimens is usually considered uncommon, although they have been identified in some clinical reports as the causal agents of infection (Antony *et al.*, 1996; Cannon *et al.*, 2005; Chanet *et al.*, 2007; Husni *et al.*, 1997; Salminen *et al.*, 2002; Salvana & Frank, 2006). In particular, endocarditis caused by lactobacilli is a rare but serious event in humans, with a high mortality rate of 30 % (Cannon *et al.*, 2005; Husni *et al.*, 1997). The most frequently isolated species causing infections are *Lactobacillus casei*, *Lactobacillus rhamnosus* and *Lactobacillus plantarum* (Cannon *et al.*, 2005; Salminen *et al.*, 2002; Salvana & Frank, 2006). Commonly, these infections can be correlated with pre-existing illnesses

(recent surgery, transplants, diabetes mellitus, AIDS and cancer), which could facilitate the growth of the micro-organism. Here, we describe a rare case of endocarditis caused by *Lactobacillus jensenii* in an immunocompetent patient.

Case report

A 47-year-old woman was admitted to the Department of Infectious Disease of Sant'Andrea Hospital (Sapienza University of Rome, Rome, Italy) with a 10 days history of asthenia, pharyngalgia and fever to 38 °C. Her medical history was positive for hypertension. Before admission, the patient underwent 5 days of antibiotic therapy with levofloxacin (0.5 g once a day) without relief of the symptoms.

On examination, the patient showed a heart rate of 120 beats min^{-1}, blood pressure of 120/70 mmHg, hepatomegaly, a normal spleen and a negative chest X-ray. An electrocardiogram showed sinus tachycardia and a left atrial enlargement. Laboratory findings were indicative of leukocytosis (14.15×10^3 white blood cells mm^{-3}), thrombocytosis (758×10^3 platelets mm^{-3}) and hypoalbuminae-

mia (3.3 g albumin dl^{-1}). High values of aspartate aminotransferase (705 U l^{-1}), alanine aminotransferase (451 U l^{-1}), lactic acid dehydrogenase (1139 U l^{-1}) and C-reactive protein (7.7 mg l^{-1}), and a high erythrocyte sedimentation rate in the first hour (53 mm h^{-1}) were also detected.

After admission the patient's fever spiked to 39.8 °C, thus three sets of blood cultures were taken at 3 h intervals (overall total of six blood samples) for detection of the growth of aerobic and anaerobic micro-organisms (BACTEC 9120 system; Becton Dickinson). On day 2 of hospitalization, the anaerobic blood cultures revealed the presence of a Gram-positive non-haemolytic, catalase- and oxidase-negative bacillus. Phenotypic identification, performed with an API CH test kit and API CHL medium (bioMérieux) in accordance with manufacturer's instructions, did not result in an acceptable identification, although these phenotypic tests suggested the possibility of *L. plantarum*.

To unambiguously identify the bacterial isolate at the species level, bacterial genomic DNA was extracted using a commercial kit (QIAamp DNA mini kit; Qiagen) and approximately 100 ng DNA was used for PCR amplification of the 16S rRNA gene with 16S rRNA universal primers 27f (5′-GAGAGTTTGATCCTGGCTCAG-3′) and 1495r (5′-CTACGGCTACCTTGTTACGA-3′). The purified PCR product (approximately 1500 bp) was subsequently analysed by automated DNA sequencing (ABI 310; Applied Biosystems). The 16S rRNA gene sequence of the bacterial isolate (GenBank acc. no FN557015) was analyzed using three different web-based alignment tools: (i) BLAST analysis (http://www.ncbi.nlm.nih.gov/BLAST); (ii) RDP II (http://rdp.cme.msu.edu); and (iii) BiBi bio-informatic bacterial identification analysis (http://umr5558-sud-str1.univ-lyon1.fr/lebibi/lebibi.cgi). All three different sequence analysis tools applied in this study showed an optimum alignment (>99 % identity) with the 16S rRNA gene sequence of *L. jensenii* JV-V16 (GenBank accession no. NZ_ACGQ01000014). These results allowed us to unambiguously identify our bacterial isolate as *L. jensenii*.

The *L. jensenii* isolate was susceptible to chloramphenicol, tetracycline, penicillin, ampicillin, piperacillin–tazobactam, imipenem, rifampicin, erythromycin, clindamycin and gentamicin, and resistant to ceftazidime, amikacin, ciprofloxacin and colistin, as assessed using the British Society of Antimicrobial Chemotherapy disc diffusion method guidelines (http://www.bsac.org.uk) on Iso-Sensitest agar plates (Oxoid) containing 5 % horse blood (Andrews, 2001; Zé-Zé et al., 2004; Wilks et al., 2004).

On day 3 of hospitalization, when the heart rate was normalized by the propranolol therapy, a cardiac bruit was detected on the patient's mitral valve, and a transthoracic and transoesophageal echocardiography was performed. These examinations revealed the presence of a mobile round hyperechogenic mass (diameter 10 mm) in the left atrium, and a large floating vegetation on the mitral valve, with severe mitral regurgitation. A diagnosis of endocarditis presumptively caused by lactobacilli was made, and an empiric antibiotic therapy was started with intravenous amoxicillin–clavulanic acid (2.2 g every 8 h) and amikacin (1 g once a day) without remission of the fever. Unfortunately, on day 5, the patient developed a thromboembolic complication (right foot and arm). A revascularization of right iliac and subclavian arteries was needed as emergency surgery and, in agreement with the heart surgeon, removal of the atrial mass and replacement of the mitral valve with a mechanical prosthesis were also performed.

On the basis of the results of the susceptibility test, the previous antibiotic therapy was discontinued and intravenous teicoplanin (0.4 g every 12 h) and meropenem (1 g every 8 h) was administrated to our patient. Remission of fever was achieved on day 7 of hospitalization. Microbiological analysis of the mitral valve was positive for *L. jensenii* as assessed by 16S rRNA gene sequencing. The patient was discharged after 4 weeks of antibiotic therapy with teicoplanin and meropenem. After 1 year the patient remained in good health.

Discussion

Bacterial infections caused by *L. jensenii* are not very common with only five cases described in the literature (Atkins et al., 1990; Cannon et al., 2005; Salminen et al., 2002; Salvana & Frank, 2006). In this report a case of *L. jensenii* endocarditis in an immunocompetent patient admitted to the Department of Infectious Disease of the 'Sant'Andrea Hospital' is described.

The identification achieved by conventional biochemical test (API50 CHL; bioMérieux) failed to determine our bacterial isolate at the species level, while our isolate was unambiguously identified as *L. jensenii* only on the basis of the sequencing of the 16S rRNA gene. These data confirm previous reports indicating that lactobacilli can go unrecognized by microbiology laboratories, mainly because most commercial systems are inadequate for the identification of these bacteria (Murray et al., 2003). Recently, it has been reported that 27 % of 66 strains of *Lactobacillus* isolates presumptively identified by phenotypic test were found to be true lactobacilli (Salminen et al., 2002). In particular, Song and co-workers highlighted that the identification of lactobacilli achieved with API50 CHL was difficult and only 30 % of the studied strains were correctly characterized at species level (Song et al., 1999). Moreover, as the 16S rRNA nucleotide sequences are available in databases for the great majority of bacterial species, we recommend the sequencing of the 16S rRNA gene as a valuable tool in microbiology practice for the rapid and correct identification of fastidious micro-organisms.

With respect to the antimicrobial therapy, it is well known that the majority of the documented cases of endocarditis caused by lactobacilli were treated with massive doses of

benzylpenicillin, combined in some cases with an aminoglycoside (Cannon *et al.*, 2005; Griffiths *et al.*, 1992). At admission, our patient was treated with an empiric antibiotic therapy of a mixture of amoxicillin–clavulanic acid and amikacin, but this therapy was discontinued when the susceptibility test data became available. A change of antimicrobial therapy was needed since our *L. jensenii* isolate was resistant to kanamycin, and the amoxicillin–clavulanic acid treatment was ineffective.

Ineffectiveness of the empiric antibiotic therapy for the treatment of lactobacillus infection was not an unexpected event since Salminen and co-workers reported that clinicians changed empiric antimicrobial treatment according to results of susceptibility tests performed in 47 out of the 85 patients examined (Salminen *et al.*, 2002). Moreover, the discrepancy between the *in vitro* susceptibility of our *L. jensenii* isolate to penicillin and the poor *in vivo* therapeutic response could be explained by the ability of some lactobacilli strains to show tolerance to *β*-lactam antibiotics (Bayer *et al.*, 1978). After the administration of a mixture of teicoplanin and meropenem the patient's fever subsided. Nevertheless, surgical treatment was needed for the mitral valve dysfunction with embolic complications. The microbiological examination of the patient's mitral valve showed the presence of *L. jensenii*. This report of *L. jensenii* endocarditis in an immunocompetent individual should alert both clinicians and microbiologists to the possibility of unusual pathogens causing serious illnesses.

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