Case of aortic endocarditis caused by *Lactobacillus casei*


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A case of *Lactobacillus* aortic valve endocarditis in a 53-year-old immunocompetent patient with past history of rheumatic fever is reported. Clinical symptoms began after a dental extraction and the patient’s diet included several yogurts per day. Blood, bone marrow cultures and the replaced aortic valve were positive for *Lactobacillus*. The clinical isolate was identified as *Lactobacillus casei* by 16S rDNA sequencing.

Introduction

*Lactobacillus* species include a diverse assemblage of Gram-positive, catalase-negative, non-sporulating, aerobic or facultative anaerobic, rod-shaped bacteria (Collins *et al.*, 1991). They inhabit a wide variety of habitats, including the gastrointestinal tracts of animals and phytosphere, and are traditionally used in the manufacture of fermented foods and, in functional foods, as probiotics (Mattila-Sandholm *et al.*, 1999). These micro-organisms are rarely infectious and their presence as commensals in the gastrointestinal tract is associated with protection against pathogens, stimulation of the immune system and positive effects on colonic health and host nutrition (Falk *et al.*, 1998; Hooper *et al.*, 2001; De Champs *et al.*, 2003). Although lactobacilli are usually considered contaminants in blood cultures, they have been identified in some clinical reports as causal agents of dental caries, infectious endocarditis, urinary tract infections, cecalgia, endometritis, meningitis and intra-abdominal, liver and spleen abscesses (Husni *et al.*, 1997). Commonly, these infections can be correlated with previous illnesses (recent surgery, transplants, valvulopathy, diabetes mellitus, AIDS and cancer) with either immunosuppressive therapy or antibiotic treatment, which could promote the development or the selection of the micro-organism. Here, we describe a case of aortic valve endocarditis caused by *Lactobacillus casei* in a 53-year-old immunocompetent patient with a past history of rheumatic fever.

Case Report

A 53-year-old male was admitted to hospital with a history of persistent fever. The patient had a past medical history of rheumatic fever and reported a dental extraction 3 months before admission. Further history was unremarkable, except for his diet, which included several yogurts per day. Two weeks after dental extraction, the patient noted fever associated with muscle and joint pain. He improved markedly on treatment with oral doxycycline (100 mg twice a day) for 2 weeks. However, symptoms reappeared shortly after treatment, and he was admitted to the Department of Infectious Diseases.

On examination, he had a high fever (38.3°C), a heart murmur and splenomegaly, without any other abnormalities. Results from blood tests showed anaemia (Hb 11.2 g dl⁻¹) and a raised erythrocyte sedimentation rate (82 mm h⁻¹). Three aerobic blood and bone marrow cultures yielded a Gram-positive rod, which was sensitive to chloramphenicol and tetracycline, and resistant to penicillin and vancomycin. The patient was treated again with doxycycline for 2 weeks, without changes in the fever pattern. At this point, a change in the existing heart murmur was noted. Although the previous transthoracic cardiac ultrasound had shown no abnormalities, the continued presence of fever, anaemia and a changing heart murmur did not allow us to exclude the
possibility of an endocarditis. A repeated transoesophageal
cardiac ultrasound showed vegetation on the aortic valve. A
diagnosis of endocarditis caused by a Gram-positive rod was
made.

The patient was started on doxycycline and gentamicin,
followed by piperacillin-tazobactam and finally imipenem.
However, on this treatment, he showed no clinical improve-
ment but, rather, continued with progressive weight loss, and
finally became haemodynamically unstable. The patient
underwent valve replacement surgery and was treated with
doxycycline. The same Gram-positive rod isolated from the
blood and bone marrow cultures was isolated from the
culture of the removed valve. Eight months after surgery,
the patient was fully recovered.

**Microbiological Investigation**

Blood cultures were collected into BacT/ALERT FA bottles
and the heart valve was cultured in brain heart infusion
broth. A Gram-positive non-haemolytic bacillus was isolated
from all samples. The isolated bacillus was subcultured onto
Columbia blood agar (bioMérieux) at 37 °C in aerobiosis. Biochemical
tests performed on the isolate showed that reactions for catalase and oxidase were negative. Suscept-
bility tests were performed by the BSAC comparative
method (Andrews, 2001) on DST agar (Oxoid) supplemen-
ted with 5 % blood. The isolate was susceptible to chloram-
phenicol, tetracycline, piperacillin-tazobactam, imipenem,
rifampicin, erythromycin, clindamycin and gentamicin, and
resistant to penicillin, ampicillin, cephradine, cefuroxime,
cefotaxime, ceftazidime, vancomycin, amikacin, colistin,
ciprofloxacin and fusidic acid. Phenotypic tests performed
with API Coryne and API 32A systems (bioMérieux) did not
result in an acceptable identification, although API 32A
suggested the possibility of *Lactobacillus acidophilus*.

The need for a reliable diagnosis confirmation prompted
sequencing of the 16S rDNA of the organism. Cells used for
DNA extraction were grown for approximately 16 h at 30 °C
in 20 ml MRS broth (Merck). Genomic DNA was isolated by
the guanidium thiocyanate method (Pitche et al., 1989). 16S
rDNA was amplified with universal primers pA and pH
(Edwards et al., 1999). The PCR amplification protocol was
35 cycles of 1 min denaturation at 94 °C, 1 min annealing at
50 °C and 2 min extension at 72 °C, after an initial
denaturation step of 94 °C for 4 min, with a final extension
step (72 °C for 5 min). The amplified fragment was purified
with Concert rapid PCR purification system (Gibco-BRL)
and cloned into pGEM-T Easy cloning vector (Promega),
according to the manufacturer's instructions. Recombinant
plasmids were obtained by blue-white selection of *Escherichia
coli* MRF’ clones. Plasmid DNA was extracted with Concert
high purity plasmid miniprep system (Gibco-BRL). Selected
clones were sequenced in an automated DNA capillary
sequencer CEQ 2000-XL (Beckman Coulter) by a dye-
labelled dideoxy termination method (DTCS, dye terminator
cycle sequencer start kit; Beckman Coulter). Five sequencing
reactions were performed using vector primers T7 and SP6
and the internal primers 519R (5’-GWATTACC
GGCGGKCTG-3’), 907R (5’-CGCTATTACMTTTRA
GTTT-3’) and 926F (5’-AACCTYAAKGAATTG
ACGG-3’). The sequence was compared with GenBank
entrries using BLAST (Altschul et al., 1997), which indicated
99 % similarity to *L. casei*; the strain was therefore identified
as *L. casei* HSM57872. The 1562 bp sequence of the 16S
rDNA determined in this study was deposited in the
GenBank database under accession number AF526388.

**Discussion**

Although infections are dependent on the aetiological agent,
the degree of illness may be related to the clinical history of
the patient (Husni et al., 1997; Wallet et al., 2002), namely
underlying diseases or immunocompromised states. So,
infections caused by micro-organisms usually regarded as
non-invasive tend to be underestimated and, in some
conditions, become true severe illness. Reports of human
infections caused by micro-organisms that are usually not
pathogenic have become more frequent in recent years (Ha
et al., 1999; Olano et al., 2001; Frebourg et al., 2002; Flaherty
et al., 2003). Usually, immunocompromised children and
elderly individuals are more susceptible to this kind of
infection. Bacteraemia caused by probiotic organisms is rare
but underestimated, since they are normally regarded as
contaminants and their role as primary invaders is also not
always easy to establish. Other drawbacks in the identifica-
tion of unusual disease agents by conventional methods are
(i) that they are fastidious, (ii) that many involve some degree
of subjective evaluation and (iii) that the regular procedures
used in hospitals are, obviously, not designed for them
(Wallet et al., 2002). As the 16S rRNA nucleotide sequence is
available in databases for most bacterial species, 16S rDNA
sequencing becomes a valuable identification strategy for
such micro-organisms.

Since no other micro-organism was isolated from all clinical
samples (blood, bone marrow and aortic valve), patient
bacteraemia was caused primarily by *Lactobacillus* with no
association to polymicrobial infections, contrary to other
reports (Antony et al., 1996; Husni et al., 1997). A correlation
was also found between the consumption of several yogurts
per day and the bacteraemia after dental extraction, caused
by bacteria usually related to probiotics. Although no direct
link for the development of endocarditis by *L. casei* and
yogurt ingestion could be established, the past history of
rheumatic fever could be responsible for a locus of minor
resistance in the aortic valve, allowing the establishment of
the bacteria and the development of the endocarditis. Although *Lactobacillus sp*. bacteraemia is rarely considered
life-threatening, the further development of serious and fatal
illness can be promoted by several underlying clinical
conditions, in which immunosuppressive therapy and use
of sub-optimal antimicrobials or antibiotics without activity
against lactobacilli are usually associated (Bayer et al., 1978;
Husni et al., 1997; Wallet et al., 2002). Since the patient was
immunocompetent and the *Lactobacillus* isolate was susceptible *in vitro* to the antibiotics used in clinical treatment, the hypothesis of sub-optimal dosages cannot be ruled out.

Although the increased consumption of dairy products does not appear to promote an increase in *Lactobacillus* sp. bacteraemia (Salminen *et al.*, 2002), it is noteworthy that a probiotic strain of *Lactobacillus rhamnosus* has been involved in several bacteraemia cases (Salminen *et al.*, 2002) and *Lactobacillus* populations can survive in gastrointestinal tracts of humans after oral administration (De Champs *et al.*, 2003). Regarding the association of *Lactobacillus* endocarditis with ingestion of dairy products and dental extraction procedures, conflicting results have been reported (Presterl *et al.*, 2001; Wallet *et al.*, 2002).

Even though the consumption of probiotics and dental manipulations cannot be considered risk factors in the development of diseases caused by bacteria usually considered non-pathogenic, specific individual clinical histories (namely, underlying diseases and the usage of specific treatments) should be taken into account.

This report of a *L. casei* aortic valve endocarditis in an immunocompetent individual should alert both clinicians and microbiologists to the possibility of unusual pathogens causing serious illnesses. 16S rDNA molecular identification represents a powerful tool in diagnosis confirmation of infrequent pathogens.

**References**


