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Case report

Lactobacillus jensenii mitral valve endocarditis: Case report, literature review and new perspectives

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ABSTRACT

Lactobacillus is a facultative anaerobic Gram-positive rod usually found in the normal microbiota of the gastrointestinal and genitourinary tract. Frequently dismissed as a contaminant, it is implicated in several diseases. We describe a rare case of endocarditis caused by *Lactobacillus jensenii* in an immunocompetent 40 year-old male patient, with a history of mitral valve repair. He presented complaining of asthenia and his laboratory results showed a moderate increase in inflammatory markers. A trans-thoracic echocardiography confirmed a vegetation on the posterior leaflet of the mitral valve, with associated severe mitral insufficiency. Blood cultures revealed the significant growth of *L. jensenii*. The patient developed an acute abdomen with intestinal ischemia and occlusion of the superior mesenteric artery, requiring urgent surgical laparotomy. A cerebral MRI showed multiple minor emboli in the frontal and left parietal cortex. The patient consequently underwent surgery to have his mitral valve replaced with a mechanical valve. L. *jensenii* was isolated in culture from the mitral valve and from a mesenteric artery thrombus. After one week of combined amoxicillin and gentamicin therapy, ampicillin alone was continued for a total of six weeks and the patient could be discharged in a good general condition. Only five cases of *L. jensenii* are described in literature, and they mainly affect immunocompromised hosts. In our case, a long delay between the start of symptoms and the full onset of the disease was observed. tolerance of Lactobacilli to penicillin is a key determinant of therapy choice.

Introduction

Lactobacilli are facultative anaerobic non-spore forming Gram-positive rods, usually found in the human gastrointestinal and genitourinary tract [1,2]. They grow better at a low oxygen tension, and *in vitro* at a low pH, requiring a special culture media [3].

Although frequently dismissed as contaminants [3], on rare occasions Lactobacilli can cause invasive infections, including, in particular, bacteraemia and endocarditis [4,5]. Several cases of pleuropneumonia, meningitis and urinary tract infections have also been reported [2]. The most common species implicated in these infections are *L. casei*, *L. rhamnosus* and *L plantarum*, while only a few publications report infections caused by *L. jensenii*, the majority of which in immunocompromised hosts [5–8]. Here we describe a case of *L. jensenii* endocarditis.

Case description

A 40 year-old male presented to our Emergency Department complaining of fatigue, nausea, intermittent vomiting, diarrhoea and a 5 kg weight loss in the month prior. He had already presented similar symptoms in the previous weeks and on one particular occasion was treated with intravenous ceftriaxone for suspected bacterial enteritis, with no clinical improvement. His past medical history was relevant for a mitral valve repair due to a congenital

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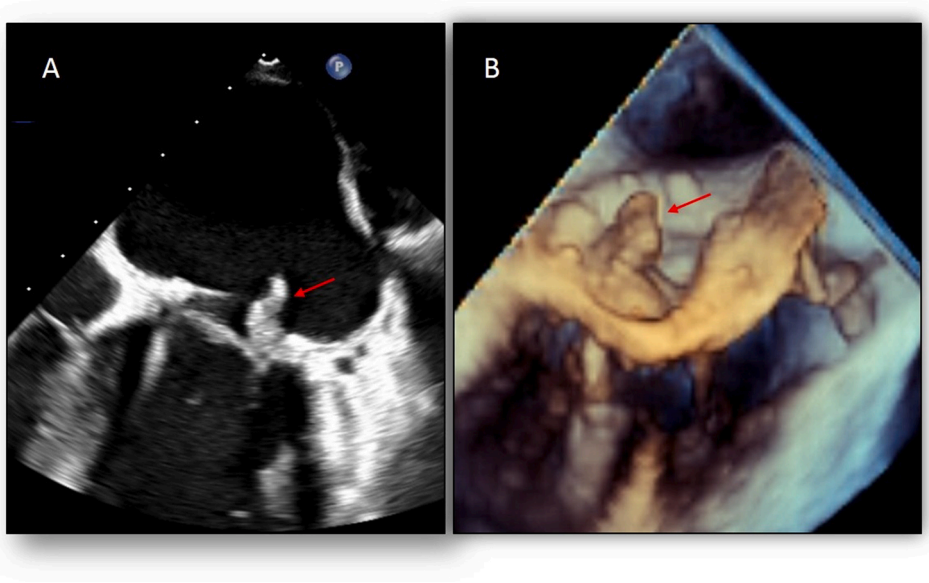

Fig. 1. (A) 2D TOE and (B) 3D TOE images showing endocarditis vegetation (red arrows) on the posterior mitral leaflet in previous mitral valve annuloplasty.

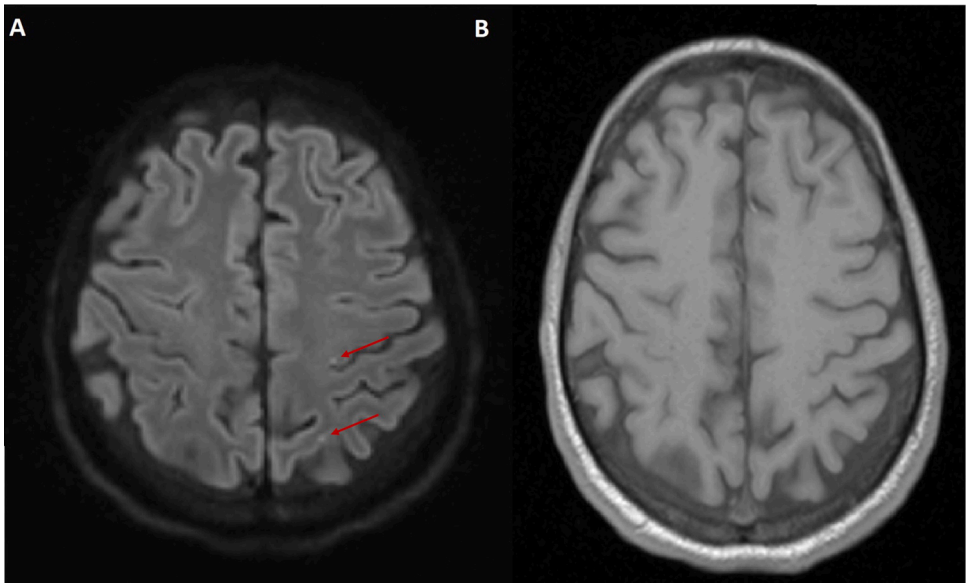

Fig. 2. (A) DWI axial cerebral MRI showing punctiform emboli in the left post-central gyrus and parietal cortex (red arrows). (B) The T2-FLAIR axial sequence does not show the emboli due to very early presentation.

anterior leaflet prolapse 4 years earlier, and epilepsy probably favoured by cannabinoid consumption.

On clinical examination, his temperature was 37.6 °C, blood pressure 110/60 mmHg, heart rate 80/min, oxygen saturation on room air 96%, BMI 20 kg/m2 and GCS 15/15. A cardiac physical examination revealed a holo-systolic murmur of 4/6 at the apex. The rest of his clinical examination was unremarkable.

Laboratory examination documented a C-reactive protein of 131 mg/L and a white blood cell count of 12.2 G/L. An ECG showed a sinus rhythm with left axial deviation, pointed P wave, narrow QRS and diffuse non-specific atypia of ventricular repolarization. A transoesophageal echocardiography showed an echo-dense 18 × 7 mm mass, suggestive of vegetation, on the posterior leaflet of the mitral valve, with severe mitral insufficiency (Fig. 1A). Three sets of blood cultures yielded *L. jensenii,* susceptible to penicillin (MIC: 0.064 mg/l). The patient was started on intravenous amoxicillin at a dose of 2 g six times daily. Several hours after admission he developed an acute abdomen, an abdominal CT showed acute intestinal ischemia with embolic occlusion of the superior mesenteric artery and hence an urgent open embolectomy was performed. Intravenous gentamycin (4 mg/kg body weight every 24 h) was added to the antibiotic regimen. Thrombus culture showed the growth of *L. jensenii*, confirming a septic thromboembolism.

L. jensenii was isolated from both aerobic and anaerobic blood culture bottles incubated at 35 °C in an automatic BACT/ALERT blood culture detection system (bioMerieux SA Mary l'Ètoile, France) after an incubation period of 2–4 days. Aliquots from the positive bottles were sub-cultured on solid agar plates and incubated at 35 °C under aerobic and anaerobic conditions. Growth was observed on Columbia Blood Agar supplemented with 5% sheep Blood (Becton Dickinson, Heidelberg, Germany) under aerobic and anaerobic growth conditions and on Chocolate Poly ViteX Agar (bioMerieux,Mary l'Ètoile, France) incubated aerobically. Bacterial growth was identified using mass spectrometry (MALDI-TOF,

Biomerieux). *Lactobacillus jensenii* was identified at a level of 99.9% from colonies isolated from all the culture plates; no additional species were detected. Bacterial DNA was extracted from a portion of the biopsy using a DNeasy Blood and Tissue Kit (Qiagen, US) and amplified using bacterial broad range PCR, as described previously [9]. Bacterial DNA was amplified and the sequence of the DNA confirmed *L. jensenii.*

In view of the planned valvular surgery, a cerebral MRI was performed, which showed multiple minor emboli in the frontal and left parietal cortex (Fig. 2). The following week the patient underwent an open mechanical mitral valve replacement (Fig. 1B). A biopsy sample was taken from the mitral valve, which exhibited no bacterial growth after an incubation period of 14 days.

The clinical course was complicated by gentamycin-induced nephrotoxicity and, after one week of combined-antibiotic treatment, a six-week course of antibiotic therapy was completed with amoxicillin monotherapy. The patient could then be discharged.

At his follow-up visit seven months after hospital discharge, the patient was asymptomatic and appeared to have a good functional recovery: NYHA class II, VO2 max 23 ml / O2 / Kg / min (63%). A follow-up echocardiography showed a slightly reduced ejection fraction (EF) and a normally-positioned mechanical mitral prosthesis with no signs of valvular leaks.

Discussion

In this paper we describe a rare case of endocarditis caused by *Lactobacillus jensenii* in an immunocompetent patient with an underlying repaired mitral valve defect.

Lactobacilli are estimated to be responsible for approximately 0.05–0.4% of all cases of infectious endocarditis, with *Lactobacillus rhamnosus* being most frequently isolated (24%), followed by *L. acidophilus* (18%), *L. paracasei* (12%) and *L. casei* (12%) [10].

Fifty cases of *Lactobacillus* endocarditis (LE) have been reported in literature [11–16] and only six cases of *L. jensenii*, including our case, have been described thus far (MEDLINE 01.2020). *Lactobacilli* produce lactic acid as a major end-product of carbohydrate fermentation and have been used for centuries in the food industry [2]. They have also been postulated to be an effective treatment for diarrhoea [4] and to enhance vaginal host defences [3]. The pathogenicity of this organism is related to the production of enzymes that break down human glycoproteins and the carriage of proteins that bind extracellular matrix, factors that favour early colonisation, adherence and biofilm formation [2].

In Lactobacillus endocarditis, predisposing factors are present in up to 80% of cases, *i.e.* congenital valve diseases (like in our case), prosthetic valves, immunosuppression, poor dental hygiene or recent dental infection and poorly controlled diabetes mellitus [10,21]. The main portal of entry has been associated with dental (up to 75% of cases) and gastrointestinal procedures [11,21].

A potential problem in the treatment of invasive *Lactobacillus* infections is their ability to develop antibiotic tolerance, a phenomenon first observed in the early 1970 s, and their resistance to glycopeptides [17]. This enables a bacterial population to survive a transient exposure to antibiotics at concentrations that would otherwise be bactericidal. This phenomenon can occur due to slow growth or during the phase between a growth arrest and the restart of the exponential growth phase (*e.g.* lag time) [18,19]. Another postulated mechanism favouring tolerance is the ability of lactobacilli to produce lactic acid and generate an acid environment, hence reducing antibiotic activity (particularly β-lactam and aminoglycosides) [11]. In addition, there have been reports of a discrepancy between *in vivo* and *in vitro* susceptibility, particularly to ß-lactam antibiotics[13–15].

Taking these hypotheses into account, a combination therapy with β-lactam and aminoglycosides has been suggested as a preferred treatment option for invasive lactobacilli-associated infections (especially endocarditis), based mainly on *in vitro* data showing a synergistic bactericidal effect [6,19]. There is increasing literature questioning the benefit of aminoglycosides combination therapy in endocarditis because of the increased risk of adverse events, and in particular, renal failure, ototoxicity and cochlear toxicity [20,21]. Our patient developed transient renal failure under aminoglycosides treatment and had a favourable outcome on β-lactam monotherapy, most probably favoured by the reduction in bacterial inoculum after valvular replacement surgery and a thrombectomy. In fact, valvular surgery is often necessary in the treatment of Lactobacillus endocarditis and is described in about half of the cases reported in literature [1,8,12]. The use of a MBC/MIC ratio has also been suggested to guide antibiotic treatment. Cannon et al. have reported over 200 cases of Lactobacillus infection [13–17]. In this retrospective analysis, in most cases the therapy had been a combination of penicillin antibiotics and aminoglycosides, although in several cases penicillin was given as monotherapy; there is no specific treatment data for *L. jensenii* because only a few cases have been reported [8,21].

Conclusions

In summary, *Lactobacillus* species, often dismissed as contaminants, have the potential to cause a broad range of infectious complications, including infective endocarditis. Infections due to L. *jensenii* are extremely uncommon: we found only six cases of endocarditis (including our patient), mainly affecting immunocompromised hosts. In our case, there was a long delay between the start of symptoms and the full clinical manifestation of the disease, which contributed to a delayed diagnosis and treatment. The recommended treatment for *Lactobacillus sp.* endocarditis includes a combination of penicillin with an aminoglycoside. However, tolerance of *Lactobacillus sp.* to penicillin may jeopardise the treatment outcome. Therefore, alongside a measurement of minimal inhibitory concentration, an additional measurement of minimal bactericidal concentration of penicillin is of paramount importance in order to decide on the most effective treatment for infective endocarditis caused by *Lactobacillus sp*.

Authors' contributions

Study conception and design: LGG and EB. Drafting of the manuscript: LGG and ER. Acquisition and interpretation of data: LGG, ER, LAL. Critical revision of the manuscript: GML, ELP and EB.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Patient Consent Statement

The written patient consent was obtained.

Ethical approval

None.

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