Vertebral osteomyelitis due to *Lactobacillus paracasei* in a diabetic patient. A case report and literature review

Giuliana Carrega\(^1\), Barbara Ricciardi\(^1\), Valentina Bartolacci\(^1\), Sabrina Brenci\(^2\), Manuela Izzo\(^1\), Patrizia Morelli\(^2\), Stefania Tigano\(^1\), Giovanni Riccio\(^1\)

\(^1\)Infectious Diseases Unit, “Santa Maria di Misericordia” Hospital, Albenga (SV), Italy; \(^2\)Microbiology Unit, “Santa Corona” Hospital, Pietra Ligure (SV), Italy

Article received 14 May 2023, accepted 25 July 2023

**SUMMARY**

Staphylococci are the most frequent cause of vertebral osteomyelitis, but infections due to unusual pathogens are also reported. We describe a rare case of spondylodiscitis due to *Lactobacillus paracasei*. A 74-year-old diabetic male was evaluated for fever and back pain. Blood cultures and vertebral biopsy were positive for *Lactobacillus paracasei*. He often took laxatives and probiotics for chronic constipation. After target treatment the patient improved but he died for a heart attack two months after the end of the treatment. Although *Lactobacillus paracasei* is usually not pathogenic, sepsis is described in immunocompromised patients while vertebral osteomyelitis is rare.

Keywords: Lactobacillus, vertebral osteomyelitis, sepsis, probiotics.

**INTRODUCTION**

Vertebral osteomyelitis, also called spondylodiscitis, is a challenge for physicians [1]. An insidious onset with progressive worsening is usually described. A late diagnosis can have serious consequences in particular neurological damage [2,3]. Vertebral osteomyelitis are grouped into brucellar, tuberculous or pyogenic. The most frequent etiology is *Staphylococcus aureus* but infections due to Gram-negatives and other Gram positive microorganisms are also reported [4]. Infections due to unusual pathogen are rare [5]. We describe a case of vertebral osteomyelitis due to *Lactobacillus paracasei* in a diabetic patient.

**CASE REPORT**

A 74-year-old man was admitted in our center because of fever and back pain. He had type II diabetes and ischemic heart disease. He was not a smoker. He often took laxatives and probiotics for chronic constipation. Other chronic treatments were low-dose salicylate and metformin. One month before, he was admitted in the emergency department for intestinal sub-occlusion. At admission in our center, he was febrile, with severe backache. Blood investigations showed mild anemia, while white cell count and platelets were in the normal range. Erythrocyte sedimentation rate was 91 mm/1st h, C-reactive protein was 33 mg/dl (normal range <5 mg/dl). He had mild renal insufficiency (creatinine 1.43 mg/dl clearance 46 ml/min), glycemia 71 mg/dl, glycosylated hemoglobin 7.1%. Neoplastic markers and HIV test were negatives. Magnetic resonance
imaging (MRI) showed an alteration of the signal affecting the intervertebral disc and the somatic cancellous bone of L1 and L2. Extensive erosions of the opposing somatic plates, more evident on L1, were associated. After administration of contrast medium, peripheral somatic bone and disc impregnation was observed around a central component with a necrotic-colliquative appearance. There were signs of inflammation of the anterolateral paravertebral tissues, with possible initial involvement of the left psoas muscle, and the neural foramina (Figure 1). No sign of endocarditis was observed on trans-thoracic echocardiography. Abdominal computed tomography scan (CT) and colonoscopy were negative. Six blood cultures and a CT-guided needle biopsy on L2 were performed (Figure 2). Histological examination revealed inflammation without neoplastic cells. Blood cultures and biopsy specimen yielded a strain of *Lactobacillus paracasei* (identified using Matrix Assisted Laser Desorption Ionization – Time of Flight -MALDI-TOF- M, Becton Dikinson, USA). The patient was initially treated with ampicillin (3 gr i.v. q 6 h) and levofloxacin (750 mg po q 24 h). Antimicrobial susceptibility of the isolates was determined by Kirby Bauer method and showed sensitivity to clindamycin, levofloxacin, tetracyclines, and resistance to ampicillin. Treatment was switched to clindamycin (600 mg IV q 8 h). Meanwhile ESBL positive *E. coli* was isolated from urine culture and a 10 days course of imipenem/cilastatin (500 mg IV q6 h) was associated. Clinical symptoms evolved favorably with defervescence and progressive reduction of backache. C-reactive protein progressively decreased to normal range.

During hospitalization, the patient had a heart attack and cardiac arrest, which he survived. Antibiotic therapy was discontinued after 6 weeks. One month after the end of treatment, MRI showed reduced but still present the uptake in the L1-L2 vertebral bodies and minimum signal in left psoas muscle. A PET/CT showed minimal F-FDG uptake in L1-L2 level. C-reactive protein was in the normal range. We decided to monitor clinical and laboratory test without other antibiotic treatment. Two months after stopping treatment, patient died for another fatal heart attack.

**DISCUSSION**

The *Lactobacillus* spp. are Gram-positive, non-spor forming rods or cocco-bacilli widely distributed in the environment and humans. They colonize the oral cavity, the gastrointestinal and genital tract and are present in many foods and para pharmaceutical products, including over-the-counter probiotics. Even if their real utility is questionable, these compounds are often prescribed in patients with type 2 diabetes because of reported positive impact on the metabolic control [6, 7]. *Lactobacillus* spp. is considered not pathogenic but sepsis, with or without organ involve-
ment, have been recently and widely reviewed [8-10]. The most severe cases are described in patients with severe underlying conditions and in preterm infant [8-13]. Spondylodiscitis is a rare localization and a challenging diagnosis [4, 5]. Symptoms and imaging allow for clinical suspicion, but microbiological diagnosis is essential for an effective therapy and successful case management. In our case we had 6 positive blood cultures, but in presence of unusual pathogens the Infectious Diseases Society of America Guideline recommends vertebral biopsy [1]. A CT-scan guided vertebral biopsy was performed and resulted positive for the same pathogen confirming *Lactobacillus*-bacteremia as responsible for bone vertebral infection.

*Lactobacillus* spp and *Bifidobacterium* spp are the bacteria most frequently present in probiotics. We performed a MEDLINE search using as keywords *Lactobacillus*, *Bifidobacterium*, probiotics, bacteremia (last search July 7th 2023). Table 1 summarizes cases of probiotic-associated bacteremias included in the reviews and in the MEDLINE search [8-23]. Noteworthy, 5 cases of *Lactobacillus rhamnosus* bacteremia, with associated endocarditis in 2, were reported in patients with diabetes and taking probiotics [8, 14]. Three further cases of *Lactobacillus spp* bacteremia, apparently not associated with probiotics, were described in diabetic patients (in one case diabetes was diagnosed at time of *Lactobacillus* infection) [8, 22, 23]. Two cases of discitis/osteomyelitis, one due to *Lactobacillus* sp and the other to *Lactobacillus casei*/*paracasei* have been described in an intravenous drug abuser and in a patient affected with stroke, diabetes, hypertension, hip prosthesis, cardiac pacemaker and umbilical hernia [5, 23]. Both cases, apparently not related with probiotics assumption, were diagnosed in absence of positive blood cultures.

*Lactobacillus* antimicrobial susceptibilities are poorly defined [25-27]. Different methods are recommended by Clinical Laboratory Standards Institute (CLSI) while the European Committee on Antimicrobial Susceptibility Testing (EUCAST) did not indicate any antibiotic susceptibility threshold for this pathogen [28]. According to the disk diffusion method, our isolate resulted in vitro resistant to ampicillin and susceptible to clindamycin, levofloxacin and tetracyclines. The

<table>
<thead>
<tr>
<th>Reference</th>
<th>Pathogen</th>
<th>Number of cases</th>
<th>Localization</th>
<th>Risk factors/copathologies</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rahman et al. 2023</td>
<td><em>Lactobacillus casei</em></td>
<td>1</td>
<td>Bacteremia + endocarditis</td>
<td>Chronic steroid intake</td>
<td>Recovered</td>
</tr>
<tr>
<td>Hefter et al. 2023 (@)</td>
<td><em>Lactobacillus</em> spp</td>
<td>3</td>
<td>Bacteremia</td>
<td>Impaired intestinal function, Central venous catheter</td>
<td>Recovered: 3</td>
</tr>
<tr>
<td>Mikucka et al. 2022</td>
<td><em>Lactobacillus rhamnosus</em></td>
<td>2</td>
<td>Bacteremia</td>
<td>Intensive care unit admission</td>
<td>Died</td>
</tr>
<tr>
<td>Karime et al. 2022</td>
<td><em>Lactobacillus rhamnosus</em></td>
<td>1</td>
<td>Bacteremia + endocarditis</td>
<td>Ulcerative colitis</td>
<td>Recovered</td>
</tr>
<tr>
<td>Rossi et al. 2022 ($)/$(*)</td>
<td><em>Lactobacillus</em> spp</td>
<td>3</td>
<td>Bacteremia, Bacteremia + meningoencephalitis, Interstitial pneumonia</td>
<td>Extremely low birth weight neonates, Promyelocytic leukemia Cancer, Diabetes</td>
<td>NR</td>
</tr>
<tr>
<td>Rubin et al. 2020</td>
<td><em>Lactobacillus rhamnosus</em></td>
<td>1</td>
<td>Bacteremia</td>
<td>Parenteral feeding</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

Table 1 - Case reports and literature reviews of bacteremias associated with probiotics (some cases were reported simultaneously in different reviews).
A possible role of *Lactobacillus* in the development of invasive infections should be considered in patients who regularly take probiotics [29]. The benefits of using probiotics should be weighed against the potential risks, especially in the most fragile patients.

**Conflicts of interest**

The authors declare that they have no conflicts of interest regarding the publication of this paper.

**Funding**

None to declare

**REFERENCES**


