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Endocarditis due to vancomycin-resistant Enterococcus raffinosus successfully treated with linezolid: case report and review of literature

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ABSTRACT

Enterococcus raffinosus is scarcely found in clinical samples and even less frequently as etiologic agent of endocarditis. We are herein presenting one case of mitral prosthetic-valve endocarditis in a 77-y-o male due to a vancomycin-resistant Enterococcus raffinosus isolate, successfully treated with 6 weeks of linezolid, and a two-year follow up.

Key words: endocarditis, vancomycin resistance, Enterococcus raffinosus, linezolid

RESUMEN

Endocarditis por Enterococcus raffinosus resistente a vancomicina exitosamente tratada con linezolid: caso clínico y revisión de la literatura. Enterococcus raffinosus es una especie poco frecuente en materiales clínicos y menos aún como agente etiológico de endocarditis. En este trabajo se presenta un caso de endocarditis de válvula mitral protésica en un paciente de 77 años debida a Enterococcus raffinosus resistente a vancomicina y que fue exitosamente tratada con linezolid durante 6 semanas, con un seguimiento de 2 años.

Palabras clave: endocarditis, resistencia a vancomicina, Enterococcus raffinosus, linezolid
Table 1. Characteristics of patients with infective enterococcal endocarditis treated with linezolid.

<table>
<thead>
<tr>
<th>Patient N°, age/sex(1)</th>
<th>Preexisting medical condition</th>
<th>Organism(2)</th>
<th>Site of infection</th>
<th>Dose of linezolid</th>
<th>Duration of treatment (3)</th>
<th>Outcome</th>
<th>Previous antibiotic treatment(4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 34 yr/F [3]</td>
<td>Hemodyalisis Congenital cyanotic heart disease None</td>
<td>VR <em>E. faecium</em></td>
<td>Native tricuspid and aortic valves</td>
<td>600 mg/12 h</td>
<td>3 d, i.v. 6 w, p.o.</td>
<td>Cure</td>
<td>Chloramphenicol and Q&amp;D</td>
</tr>
<tr>
<td>2, ND/ND [5]</td>
<td>None</td>
<td>VS <em>E. faecium</em></td>
<td>Pulmonic valve</td>
<td>600 mg/12 h</td>
<td>21 d ND (5)</td>
<td>Death during multiple therapy (probably therapy failure)</td>
<td>No</td>
</tr>
<tr>
<td>3, ND/ND [5]</td>
<td>Diabetes, hemodyalisis, recent abdominal aortic repair Prematurity, tracheostomy, atrial septal defect, indwelling central venous catheter</td>
<td>VR <em>Enterococcus sp.</em></td>
<td>Not reported</td>
<td>600 mg/12 h</td>
<td>6 w ND</td>
<td>Cure</td>
<td>Alatrofloxacin and VAN</td>
</tr>
<tr>
<td>4, 78 yr/M [12]</td>
<td>Diabetes, coronary artery bypass, aortic valve replacement</td>
<td>VS <em>E. faecalis</em></td>
<td>Prosthetic aortic valve</td>
<td>600 mg/12 h</td>
<td>7 w ND</td>
<td>Cure</td>
<td>AMP + GEN</td>
</tr>
<tr>
<td>5, 4 mo/M [1]</td>
<td>Prematurity, tracheostomy, atrial septal defect, indwelling central venous catheter</td>
<td>VR <em>E. faecium</em></td>
<td>Native tricuspid valve</td>
<td>15 mg/kg every 8 h 15 mg/kg every 8 h</td>
<td>7 w, i.v. 2 w, p.o.</td>
<td>Cure</td>
<td>VAN</td>
</tr>
<tr>
<td>6, 64 yr/M [9]</td>
<td>Coronary artery disease, hypothyroidism, hypertension, chronic renal failure</td>
<td>VR <em>E. faecalis</em></td>
<td>Native pulmonic valve</td>
<td>600 mg/12 h</td>
<td>6 w, i.v.</td>
<td>Non-evaluable (1 w. after completion treatment, the patient died due to another cause)</td>
<td>VAN + GEN</td>
</tr>
<tr>
<td>7, 79 yr/F [15]</td>
<td>Prosthetic mitral valve</td>
<td>VR <em>E. faecalis</em></td>
<td>Prosthetic mitral valve</td>
<td>600 mg/12 h 600 mg/12 h</td>
<td>2 w, i.v + GEN 12 w, p.o.</td>
<td>Cure</td>
<td>VAN + GEN Q&amp;D + GEN DOX</td>
</tr>
<tr>
<td>8, 37 yr/F [14]</td>
<td>Hemodyalisis, four failed allografts. Bilateral subclavian subcutaneous hemodyalisis ports HIV, Hep C, cadaveric renal transplant, perinephric hematoma infected with VR <em>E. faecium</em></td>
<td>VR <em>E. faecalis</em></td>
<td>Native aortic and mitral valves</td>
<td>600 mg/12 h</td>
<td>9 d, i.v.</td>
<td>Failure</td>
<td>No Cure with PEN + STR</td>
</tr>
<tr>
<td>9, 64 yr/M [2]</td>
<td>HIV, Hep C, cadaveric renal transplant, perinephric hematoma infected with VR <em>E. faecium</em></td>
<td>VR <em>E. faecium</em></td>
<td>Native mitral valve</td>
<td>600 mg/12 h</td>
<td>6 w, p.o.</td>
<td>Cure</td>
<td>Q&amp;D + AMS Q&amp;D + DOX</td>
</tr>
<tr>
<td>10, 40 yr/M [16]</td>
<td>Hemodyalisis, previous group B streptococcal endocarditis</td>
<td>VS <em>E. faecalis</em></td>
<td>Native tricuspid, aortic and mitral valves</td>
<td>600 mg/12 h</td>
<td>3 w, i.v.</td>
<td>Failure</td>
<td>AMP + GEN and LEV. Cure with AMP + STR and surgery</td>
</tr>
<tr>
<td>11, 77 yr/M [this study]</td>
<td>Bioprosthetic mitral valve replacement</td>
<td>VR <em>E. raffinosus</em></td>
<td>Prosthetic mitral valve</td>
<td>600 mg/12 h 600 mg/12 h</td>
<td>4 w, i.v. 2 w, p.o.</td>
<td>Cure</td>
<td>No</td>
</tr>
</tbody>
</table>

process involved the valve annulus at the site of attachment with extension to adjacent structures. The valve was removed with extensive debridement and resection of the annular tissue. Replacement with a mechanical prosthetic valve was performed prior to reconstruction of the destroyed annulus. The patient had an uneventful recovery within a two-year follow-up. Cultures of the replaced valve tissue were negative.

Treatment of enterococcal endocarditis simultaneously resistant to vancomycin, penicillin and aminoglycosides is really a major challenge. Despite its already known bacteriostatic effect, LZD was chosen in this case for lack of better options. In fact, LZD also behaved as bacteriostatic agent in this isolate as shown in the corresponding time-killing curve (data not shown).

There has been limited experience in the use of LZD to treat infective endocarditis due to enterococci. Tsigrelis et al. described one case of endocarditis due to vancomycin-resistant (VR) *E. faecalis* in a 37-yr-o female patient that had failed to respond to LZD therapy administered during nine days by intravenous route (case 8, Table 1). She had no predisposing heart condition but had undergone prolonged hemodialysis, four failed allografts, multiple failed arteriovenous grafts and fistulas, and the placement of bilateral subclavian subcutaneous hemodialysis ports. Finally, she was successfully treated with penicillin plus streptomycin (14). These authors had reviewed all VR *E. faecalis* endocarditis that fulfilled the modified Duke criteria for definite or possible infective endocarditis. Only two out of six patients had been treated with LZD. One of them, a 79-yr-o woman was cured after two weeks of intravenous treatment with 600 mg/12 h LZD plus 80 mg/12 h gentamicin (case 7, Table 1) (15). The other, a 64-yr-o man with pulmonic valve endocarditis, died one week after completion of LZD therapy (case 6, Table 1). No pathogen was isolated from blood cultures and no evidence of acute myocardial infarction or gastrointestinal bleeding was recorded. As no autopsy was performed, the outcome could not be evaluated (9).

In Table 1, in addition to the three previously commented cases, we included other seven enterococcal endocarditis episodes that were treated with LZD: four endocarditis due to *E. faecalis*, one of them susceptible to VAN (VS), one case due to an unidentified VR *Enterococcus* sp. and two cases due to VS *E. faecalis*.

Babcock et al. and Archuleta et al. reported the cure with LZD of two patients with endocarditis by VR *E. faecium* and severe preexisting medical conditions: hemodialysis plus congenital heart disease in the first case, and HIV, hepatitis C plus renal transplantation in the second (2, 3).

Chien et al. partially described several patients infected with VRE. Among them, there was one patient who died due to VS *E. faecium* endocarditis after 21 days of therapy with LZD, and another case of endocarditis due to an unidentified VR *Enterococcus* sp. that was cured with a 7-week treatment with the same antibiotic (5).

Ang et al. reported the cure of a pediatric patient with a VR *E. faecium* endocarditis with 15 mg/kg/8 h LZD (1).

One of the two cases of VS *E. faecalis* endocarditis located in a prosthetic aortic valve and treated with LZD, was successfully cured with 7 weeks of antibiotic treatment. The other case, involving native tricuspid, aortic and mitral valves, failed after three weeks of intravenous therapy (12, 16).

The whole experience with these eleven patients (Table 1) is similar to that published by Birmingham et al. related to cases of VR *E. faecium* endocarditis recorded from compassionate treatments with LZD: 10 clinical cures, 2 clinical failures and one indeterminate case; 7 microbiological cures, and 4 microbiological failures (4).

Falagas et al. reviewed the efficacy of LZD in infective endocarditis due to multidrug-resistant gram-positive cocci and found approximately the same results: of 33 evaluable patients (25% of them with prosthetic valve), 21 (63.6%) were cured after LZD administration; in 66.7% of cases it was administered alone. Most cases were staphylococcal endocarditis, but the outcome of the subgroup of 8 patients with VRE was not significantly different from the whole (cure = 75%, improvement = 12.5%, failure = 12.5%) (7).

We described one case of mitral prosthetic-valve endocarditis in a 77-yr-o male cured with 6 weeks of LZD. To the best of our knowledge, this is the first report of a case of prosthetic endocarditis due to a VR *E. raffinosus* isolate successfully treated with LZD, with a two-year follow-up. We will have to wait for other similar reports to define the best therapeutic scheme (dose, intervals, administration route and treatment duration).

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