

A Dalbavancin for Successful Treatment of Infective Endocarditis Caused by *Enterococcus faecalis*

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ABSTRACT

Infective endocarditis is a relatively uncommon infection that requires a high index of suspicion, which can sometimes delay its diagnosis. It requires several weeks of intravenous antibiotics, which traditionally requires long hospital stays. Dalbavancin is a novel antibiotic with high activity against several Gram-positive pathogens. Its weekly administration allows the outpatient management of complicated infections requiring parenteral treatment, but only a few cases of *Enterococcus faecalis* endocarditis treated with dalbavancin have been reported in the literature. We here report a case of successful treatment with dalbavancin of an infectious endocarditis caused by *E. faecalis*.

LEARNING POINTS

- Infective endocarditis is a relatively uncommon infection that requires a high index of suspicion and its diagnosis can sometimes be challenging.
- Endovascular infections require long-term parenteral treatment, so outpatient parenteral antibiotic therapy (OPAT) is an option for stable patients in order to avoid prolonged hospital stays.
- Dalbavancin is a novel antibiotic with high activity against Gram-positive pathogens and can be administered weekly.
- There is growing experience in the ambulatory treatment of Gram-positive cocci endovascular infections.

KEYWORDS

Infective endocarditis, dalbavancin, *Enterococcus*, outpatient parenteral antimicrobial therapy, OPAT

INTRODUCTION

Infective endocarditis (IE) is a relatively uncommon infection that requires a high index of suspicion, which can sometimes delay its diagnosis. IE treatment requires several weeks of intravenous antibiotics ^[1], which implies long hospital stays. In recent years, outpatient parenteral antibiotic therapy (OPAT) has been used to minimize hospital stay, with demonstrable benefits for patient healthcare and costs. Dalbavancin is a novel antibiotic with high activity against Gram-positive pathogens ^[2]. Its weekly administration allows the outpatient management of

complicated infections requiring parenteral treatment, but only a few cases of *Enterococcus faecalis* endocarditis treated with dalbavancin have been reported in the literature [3].

CASE DESCRIPTION

A 78-year-old man was admitted to hospital for a 24-hour history of fever, chills and confusion. He had no history of drug allergies but was a former smoker with a diagnosis of chronic obstructive pulmonary disease with severe airflow obstruction. He had dyslipidaemia, tuberculous adrenal insufficiency, mild bilateral sensorineural hearing loss, and metastatic prostate cancer. He had experienced several acute urinary retentions, so he was carrying a bladder catheter. He was able to perform basic daily activities of living and his Eastern Cooperative Oncology Group (ECOG) performance status was 1.

During admission, the patient was diagnosed with bacteraemic urinary sepsis. *E. faecalis* was isolated in both blood and urinary cultures, with demonstrated susceptibility to ampicillin, vancomycin, linezolid and aminoglycosides. A systolic cardiac murmur was detected during physical examination, so transthoracic echocardiography (TTE) was performed. TTE ruled out findings suggestive of endocarditis, and also revealed mild degenerative aortic and mitral valve stenosis and regurgitation. Transoesophageal echocardiography (TEE) was not performed because of low suspicion and the favourable clinical evolution. The patient received a 1-week course of intravenous ampicillin, followed by a 7-day course of oral amoxicillin. After bladder catheter replacement, he was discharged asymptomatic at his baseline status.

Two weeks after discharge and 1 week after the end of the antibiotic treatment, the patient was readmitted for a second episode of fever and confusion. Blood cultures were positive for *E. faecalis* with the same previous susceptibility pattern. Once again, the bladder catheter and underlying urinary anatomical abnormalities were assumed to be the origin of the infection, so he received a second course of intravenous ampicillin followed by oral amoxicillin.

One week after the second discharge, he was readmitted for chills and fever. Blood cultures confirmed for the third time the growth of multi-sensitive *E. faecalis*. TEE was performed and revealed a 13 mm mobile image on the right coronary leaflet of the aortic valve, highly suggestive of endocarditis, associated with a cavitated abscess. A second image of an 8 mm vegetation was seen on the non-coronary leaflet, associated with leaflet perforation and secondary severe aortic regurgitation. A CT scan was also performed, describing already known metastatic bone lesions and a new splenic infarction (Fig. 1).



Figure 1. Splenic infarction

The diagnosis of aortic valve infectious endocarditis by *E. faecalis* was established, and the case was referred to the Cardiac Surgery Service. The aortic valve was replaced with a Trifecta no. 23 biological valve. The postoperative course was complicated by haemopericardium, requiring urgent reintervention, and atrial fibrillation.

After surgery, the patient continued with ampicillin 2 g every 4 hours plus ceftriaxone 2 g every 12 hours. The subsequent evolution was favourable, with no other complications. Blood cultures after surgery were negative, but culture of the removed aortic valve resulted positive for *E. faecalis*, so it was decided to extend the duration of antibiotic treatment to at least 6 weeks after surgery. After 4 weeks of ampicillin plus ceftriaxone, the patient was stable and in good condition. Given the need to maintain parenteral antibiotic therapy for 2 more weeks, treatment was changed to dalbavancin. A first dose of 1000 mg of dalbavancin was administered, and the patient was discharged. One week later the patient attended the day hospital. He was afebrile and asymptomatic.

Blood analysis showed normal renal and hepatic function, so a second dose of 500 mg of dalbavancin was administered. Subsequent follow-up showed no more episodes of fever or other signs of infection. The patient resumed his cancer treatment and maintained a good general condition.

DISCUSSION

The gold standard treatment for *E. faecalis* IE is combination therapy with ampicillin plus gentamicin or plus ceftriaxone [1]. One major concern in its management is the duration of treatment, for which a minimum of 4–6 weeks is recommended. These patients require an initial hospitalized period because of a high risk of complications, normally 2–3 weeks. Thereafter, the only reason to remain in hospital is to receive intravenous antibiotic therapy. There are several alternatives for outpatient continuation treatment [4]. Oral antibiotic therapy is promising, but there is a lack of solid evidence for its efficacy in *E. faecalis* IE. An alternative is OPAT, which has demonstrated benefits for both patients and the healthcare system. Different antimicrobial schedules have been explored in the outpatient treatment of *E. faecalis* IE [4]. Aminoglycoside-based regimens are used less and less. In addition, this patient also had a history of sensorineural hearing loss and risk of renal toxicity. Ampicillin plus ceftriaxone-based therapy is limited by the 12-hour ceftriaxone dosing, which is not suitable for all organizations administering OPAT. Although there is some experience of its use at a dose of 4 g every 24 hours, its efficacy remains unclear. Daptomycin or teicoplanin monotherapy are alternative regimens, but there are some doubts about effectiveness compared with standard treatment.

Dalbavancin is a novel lipoglycopeptide with high activity against several Gram-positive pathogens [2,3]. Its weekly administration allows the outpatient management of complicated infections requiring parenteral treatment, reducing hospital stay and costs [5]. It is currently only approved for the treatment of skin structure infections, although there is growing experience in the off-label treatment of bloodstream infections and endocarditis [2–4]. Its dosage schedule may be especially suitable for patients with barriers to standard care due to social and health system barriers, such as patients who inject drugs, those with repeated hospital discharges against medical advice, and patients with behavioural issues [6]. Despite this, the experience accumulated so far is still scarce, and to date there are only 10 published cases of *E. faecalis* IE treated with dalbavancin, most of them successfully. With this report we would like to add our experience to the available literature.

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