IDCases 24 (2021) e01137

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

Native mitral valve endocarditis associated with KPC producing *Serratia marcescens* bacteremia successfully treated with mitral valve replacement and ceftazidime-avibactam

Alwin Tilanus[a,*], Francisco Mauricio Rincon[b], Aura Maria Rivera[b]

[a] Internist-Infectious Disease Specialist, Department of Infectious Diseases, Clinica Los Nogales, Calle 95 # 23 – 61, Bogotá, Colombia
[b] Cardiovascular Surgeon, Department of Cardiovascular Surgery, Clinica Los Nogales, Calle 95 # 23 – 61, Bogotá, Colombia

ARTICLE INFO

Article history:
Received 8 April 2021
Accepted 22 April 2021

Keywords:
Endocarditis
Serratia marcescens
KPC
Carbapenemase
Ceftazidime-avibactam

ABSTRACT

Consistent with global trends of infections due to multiple-drug resistant Gram-negative bacteria, we report the first official case of native mitral valve endocarditis due to multi-resistant *Klebsiella Pneumonia* Carbapenemase (KPC) producing *Serratia marcescens*. The patient underwent mitral valve replacement and was successfully treated with monotherapy ceftazidime-avibactam.

Introduction

Serratia marcescens is a facultative anaerobic Gram-negative rod which belongs to the *Enterobacterales*. Serratia species are motile and can adhere to cells via fimbria. *Serratia* species are not considered part of the common human fecal flora and acquisition is usually associated with hospital environmental sources which explains why it is typically a nosocomial pathogen and capable of causing outbreaks. However, non-nosocomial infections (for example intravenous drug use) have been reported. *Serratia* infections can cause a great variety of infections such as urinary tract infections, nosocomial pneumonia, bloodstream infections (including endocarditis), skin and soft tissue infections, central nervous system and eye infections [1,2]. Although *Serratia* species typically express low levels AMP-C, expression of ESBL and rarely KPC have been reported [2]. Here we report the first official case of *Serratia marcescens* KPC causing endocarditis treated with monotherapy ceftazidime-avibactam.

Case description

A 70-year-old male was referred to our clinic with symptoms of chest pain, palpitations, shortness of breath and edema of the lower extremities since about one month.

His medical antecedents revealed diabetes, hypertension, dyslipidemia, (benign) prostate hypertrophy, COPD and rheumatoid arthritis for which he was on methotrexate and leflunamide. One month earlier he was hospitalized in our medium care unit for chest pain and uncontrolled hypertension. Cardiac decompensation (NYHA IV) associated with a supra ventricular tachycardia and a urinary retention was diagnosed on admission. A transesophageal echocardiogram (TEE) was performed which showed relevant findings on the mitral valve: a moderate to severe insufficiency, prolapse of the posterior leaflet (due to a tendinous cord rupture) and images of a suspected vegetation (size: 10 × 2 mm) at the posterior on the P2 scallop (Fig. 1a, b, c, d: **Transesophageal ultrasound image**).

The patient was admitted in the medium care unit and started on nitrates, loop diuretics (furosemide), metoprolol, amiodarone and an ACE inhibitor (enalapril) with clinical improvement of the symptoms. His hospitalization was complicated with massive hematuria after the insertion of a urinary catheter and administration of rivaroxaban, reason for which cardiac surgery was postponed. The urologist was consulted who performed endoscopic intervention with transurethral prostate resection and hemostasis was obtained.

About a week after urologic surgery, the patient deteriorated with hypotension and blood cultures became positive with *Serratia marcescens* (KPC) for which the infectious disease specialist was consulted. The patient was started on ceftazidime-avibactam 2.5 g q8 hours. After cardiac compensation, resolution of the hematuria and after the first 14 days of treatment with ceftazidime-

* Corresponding author.
E-mail addresses: alwinrt@clinicanogales.com (A. Tilanus), franciscort@clinicanogales.com (F.M. Rincon), aurisrivera@gmail.com (A.M. Rivera).

http://dx.doi.org/10.1016/j.idcr.2021.e01137

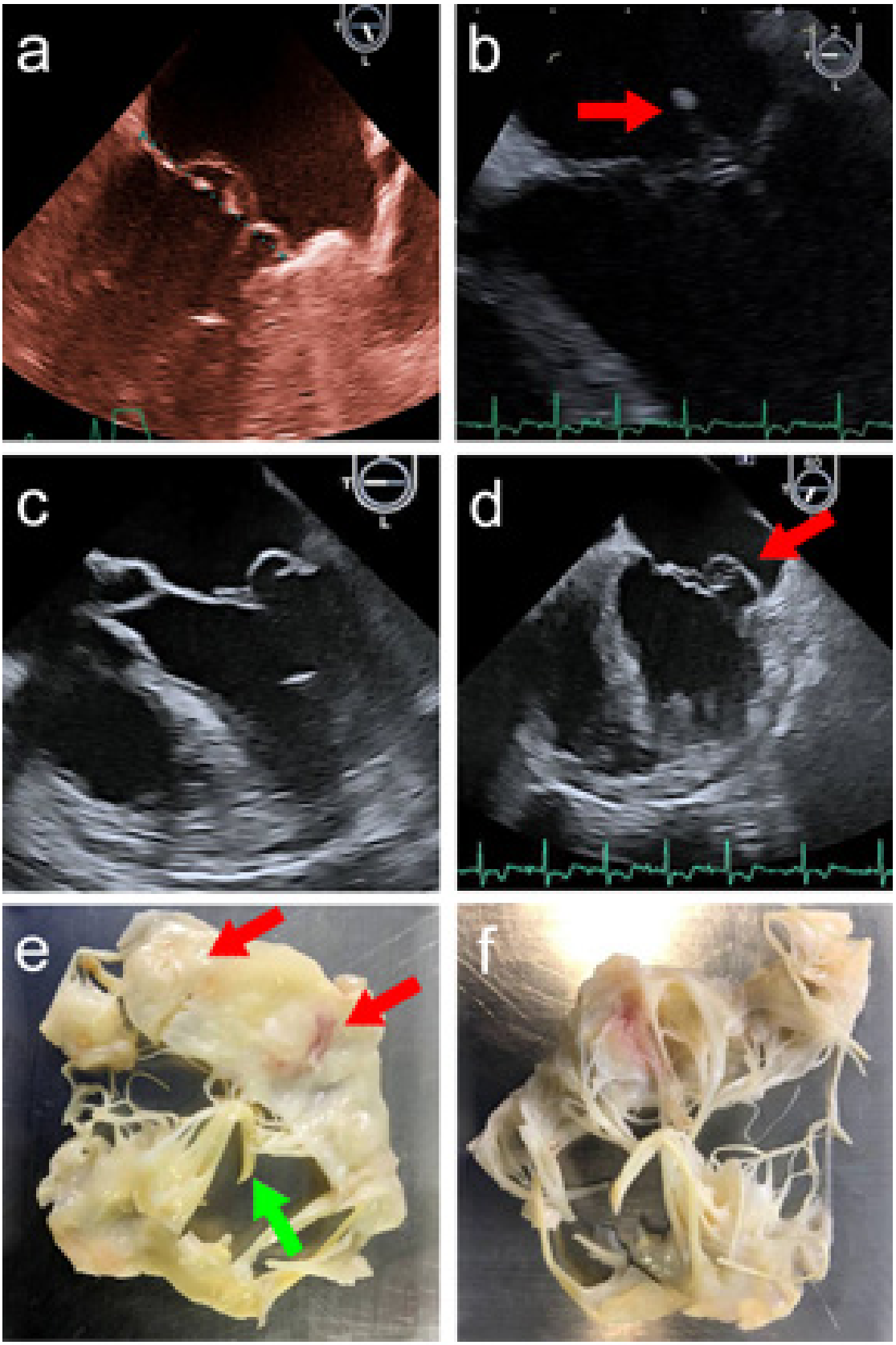

Fig. 1. **a**. Mitral valve annulus dilation (38 mm – dotted line). **b.** Ruptured chordae prolapsing onto the left atrium (red arrow signals the prolapsed chordae). **c.** Posterior leaflet prolapsed. **d.** Posterior leaflet prolapses with suspected vegetations images. **e.** Excised mitral valve showing multiple vegetations on the auricular surface of the leaflets (red arrows). The green arrow shows the first order ruptured tendinous cord corresponding to the P2 prolapse. **f.** Ventricular Surface of the excised mitral valve.

avibactam, the patient was taken to the operating room for mitral valve surgery.

After complete sternotomy, cardiopulmonary bypass was performed. Relevant findings of the mitral valve were a severe regurgitation due to annular dilation, a prolapse of P2 associated with rupture of a first order tendinous cord and the presence of multiple vegetations on the atrial aspect of the anterior leaflet (biggest diameter of approximately 1 cm) causing anatomic structural alteration. The mitral valve was replaced with a biological prosthesis. Cultures of the mitral valve (after 14 days of treatment with ceftazidime-avibactam) remained negative but the surgical specimen showed clear signs of endocarditis (Fig. 1e, f: **Surgical specimen of the mitral valve**).

Based on the surgical findings of endocarditis, we decided to continue ceftazidime-avibactam monotherapy for another 4 weeks. The patient improved rapidly and was discharged in good medical conditions. On postoperative outpatient follow-up visits (8 months) his condition remains uneventful.

Discussion

Endocarditis due to *Serratia marcescens* has rarely been described in the literature. Of note, publications regarding endocarditis due to *Serratia marcescens* bacteremia typically reported blood cultures with Serratia species susceptible to multiple classes of antibiotics. [3–5] To our best knowledge, this is the first official report of endocarditis due to Carbapenemase producing *Serratia marcescens*. We describe a case of a male patient (non-IV drug user) with a *Serratia marcescens* (KPC) bacteremia complicated with native mitral valve endocarditis probably related to his recent prostatectomy and urethral trauma post-insertion of a urinary catheter. Carbapenemase production was suspected due to reported resistance for beta-lactam antibiotics including carbapenems. Positivity of the rapid (colorimetric) test for carbapenemase production (Rapidec Carba NP- biomérieux marcy l'étoile) in addition to a positive synergy test with boronic acid and a negative synergy test with EDTA, confirmed the presence of serine carbapenemase. Although not included in the susceptibility report, in vitro activity of ceftazidime-avibactam was assumed based on the MIC reported for ceftazidime (4 mg/mL). Few studies reported on the susceptibility of ceftazidime-avibactam against *Serratia marcescens* producing *Klebsiella pneumoniae* Carbapenemase (KPC). Sherry et al. tested 50 Australian carbapenemase producing Gram negatives against ceftazidime-avibactam. Some of the carbapenemases included in the study were KPC and OXA-48 group. The authors reported that all the isolates were ceftazidime-avibactam susceptible [6]. Zhang et al. reported in vitro and in vivo (mouse model) bactericidal activity of ceftazidime-avibactam administrated (either alone or in combination with aztreonam) against KPC or New Delhi Metallo-β-lactamase (NDM). All 16 *Klebsiella pneumoniae* strains with blaKPC-2 were susceptible to ceftazidime-avibactam with a MIC range 4–8 mg/L. Interestingly, all strains were resistant to ceftazidime with MIC50 of 32 mg/L and MIC90 of > 256 mg/L, which indicates that avibactam plays an essential role in restoring ceftazidime susceptibility [7]. Ojdana et al. observed that ceftazidime-avibactam when combined with ertapenem or fosfomycin resulted in synergism against KPC producing bacteriae [8]. Ceftazidime-avibactam is thus far approved by the Food Drug Administration (FDA) for the treatment of complicated urinary tract infections, complicated intra-abdominal infections and hospital/ventilator associated pneumonia due to susceptible aerobic Gram negative bacteriae. Iacovelli et al. reported the first case of *Klebsiella pneumoniae* (KPC) thrombophlebitis with right atrial endocarditis treated with a prolonged course of ceftazidime/avibactam plus ertapenem. The patient was initially hospitalized for a chest trauma complicated with a ventilator associated pneumonia with isolation of a *Klebsiella pneumoniae* (KPC) in the bronchial aspirate. The patient was started on combination therapy with Colistin/high dose tigecycline/high dose meropenem (prolonged infusion). The authors reported a breakthrough KPC bacteremia for which initially fosfomycin was added to the therapy. Blood cultures remained positive and a CT scan detected new cavitary lung lesions. A transesophageal echocardiogram (TEE) revealed a 0.8 mm vegetation on the superior wall of the right atrium (no valvular vegetations) and a CT angiography showed jugular and superior cava veins thrombosis, explaining the therapeutic failure. The patient was switched to ceftazidime-avibactam combined with ertapenem based on microbiology susceptibility data. On day 157, the patient was discharged in good clinical conditions. However, despite follow up visits during a 5-month period, the patient eventually had a sudden death 6 months after hospital discharge [9]. Our patient had been treated for 14 days with ceftazidime-avibactam prior to cardiac surgery. Pathology results of the mitral valve showed clear vegetations, although the culture of the valve remained negative. Importantly, follow up blood cultures remained negative indicating the efficacy of monotherapy with ceftazidime-avibactam (without ertapenem or fosfomycin) in this case of *Serratia marcescens* endocarditis. After cardiac surgery we decided to continue with another 4 weeks of monotherapy ceftazidime-avibactam without side-effects indicating it's safety profile when used for a prolonged period of time, although these results require further confirmation.

Funding source

No funding to declare.

Ethical approval

Written and verbal informed consent was obtained from the patient before the publication of this manuscript.

Declaration of Competing Interest

The authors report no declarations of interest.

Acknowledgment

We would like to thank our nurse Raquel Lopez for her kind assistance in explaining the patient about informed consent for this case report.

References

[1] Yu VL. Serratia marcescens: historical perspective and clinical review. N Eng J Med 1979;300:887–93.
[2] Mahlen SD. Serratia infections: from military experiments to current practice. Clin Microbiol Rev 2011;24(4):755–91.
[3] Yeung H, Chavarria B, Shahsavari D. Case report a complicated case of Serratia marcescens infective endocarditis in the era of the current opioid epidemic. Case Rep Infect Dis 20185903589.
[4] Nikolakopoulos A, Koutsogiannis N, Xaplanteri P, et al. Case report a case of Serratia marcescens endocarditis in a nonintravenous drug-using male patient and review of literature. Case Rep Infect Dis 20193715404.
[5] Winkle SM, Gaballa S, Memon A, et al. Serratia marcescens tricuspid valve vegetation and successful use of the AngioVac ® system. Cureus 2020;12(8) e10010.
[6] Sherry NL, Baines SL, Howden BP. Ceftazidime/avibactam susceptibility by three different susceptibility testing methods in carbapenemase-producing Gram-negative bacteria from Australia. Int J Antimicrob Agents 2018;52(1):82–5.

[7] Zhang W, Guo Y, Li J, et al. In vitro and in vivo bactericidal activity of ceftazidime-avibactam against Carbapenemase producing Klebsiella pneumoniae. Antimicrob Resist Infect Control 2018;7:142.
[8] Ojdana D, Gutowska A, Sacha P, et al. Activity of Ceftazidime-Avibactam Alone and in combination with Ertapenem, Fosfomycin, and Tigecycline against Carbapenemase-Producing Klebsiella pneumoniae. Microb Drug Resist 2019;25 (9):1357–64.
[9] Iacovelli A, Spaziante M, Al Moghazi S, et al. Case report: a challenging case of carbapenemase-producing Klebsiella pneumoniae septic thrombophlebitis and right mural endocarditis successfully treated with ceftazidime / avibactam. Infection 2018;46(5):721–4.