Serratia marcescens Endocarditis: A Case Report and Literature Review

Endocardite por *Serratia marcescens*: Caso Clínico e Revisão da Literatura

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ABSTRACT

Serratia marcescens is a rarely implicated agent in endocarditis. We describe a case of a patient that underwent aortic and mitral valve replacement for *Streptococcus agalactiae* endocarditis. Four months later, he was readmitted with an ischemic stroke and fever. Physical examination and repetitive transthoracic echocardiogram were unremarkable. The initial blood cultures were negative. Due to sustained fever, vancomycin, gentamicin and piperacillin-tazobactam were initiated. On subsequent blood cultures, *Serratia marcescens* was isolated and antibiotics switched to ertapenem and gentamicin. In addition to cerebral emboli, a splenic embolus was found. The PET/CT revealed an abnormal hypercaptation in the mitral bioprosthesis. The patient was treated for six weeks. There are no current specific recommendations regarding the treatment of *Serratia marcescens* endocarditis. It is widely accepted that treatment should be prolonged and include a combination of antimicrobial agents. Morbidity and mortality are high, particularly when there's the need for surgical replacement. In this case, however, the patient ended-up only requiring medical treatment due to the favourable response.
Keywords: Endocarditis, Bacterial; Fever; Heart Valve Prosthesis; Positron-Emission Tomography; Serratia marcescens

RESUMO

A *Serratia marcescens* é um agente raro de endocardite. Descrevemos o caso de um doente submetido a substituição das válvulas aórtica e mitral por endocardite causada por *Streptococcus agalactiae*. Quatro meses após, é readmitido por evento cerebral isquémico e febre. Ao exame objetivo não evidenciava alterações e os ecocardiogramas transtorácicos eram normais. As hemoculturas colhidas à admissão foram estéreis. O doente manteve-se febril, iniciando-se empiricamente vancomicina, gentamicina e piperacilina-tazobactam. Após isolamento de *Serratia marcescens* em hemoculturas subsequentes, a antibioterapia foi ajustada para ertapenem e gentamicina. Para além de um êmbolo cerebral, foi encontrada embolia esplénica e hipercaptação anormal na prótese mitral biológica em PET. Foi efetuado tratamento durante seis semanas. Não existem recomendações específicas sobre o tratamento de endocardite por *Serratia marcescens*, mas deve ser prolongado e com terapêutica combinada. A morbimortalidade é elevada, sobretudo quando há necessidade de cirurgia. Neste caso, a evolução clínica favorável do doente permitiu o tratamento médico exclusivo.
Palavras-chave: Endocardite Bacteriana; Febre; Próteses Valvulares Cardíacas; Serratia marcescens; Tomografia por Emissão de Positrões

INTRODUCTION

Serratia marcescens is a facultative anaerobic, Gram-negative bacillus, mostly associated with intravenous drug users (IVDU) and hospital-acquired infections.[1] *Serratia marcescens* endocarditis is extremely rare (0.14% of all cases in a prospective cohort).[1] In non-IVDU patients, it can be associated with immunosuppression, chronic disease, indwelling catheterization and presence of cardiac devices/prosthetic valves.[2]

We describe a case of healthcare-associated endocarditis caused by *Serratia marcescens*.

CASE REPORT

A 61-year-old man, smoker, with severe aortic stenosis, was admitted to hospital due to acute pulmonary oedema. He was diagnosed with mitral endocarditis caused by *Streptococcus agalactiae*. He received treatment with gentamicin 5 mg/kg/day for two weeks and ceftriaxone 2 g/day. After four weeks, he underwent mitral valve replacement with a bioprosthesis due to valvular insufficiency and aortic valve replacement. He had sterile valve and control blood cultures (BC), hence completing two more weeks of antibiotics. Two months later, he was diagnosed with non-small cell lung cancer stage IIB and a transthoracic echocardiogram detected a filiform structure in the mitral bioprosthesis and a thrombus in the left atrial posterior wall, for which he was hypocoagulated with warfarin.

Two months later, the patient presented to the emergency department with left homonymous hemianopia and fever. He had a temperature of 38.3ºC, the remaining physical examination was unremarkable. The electrocardiogram showed sinus rhythm. The blood tests showed normal leukocyte count and C-reactive protein (CRP) level of 51 mg/L [< 3.0 mg/L]. A brain computerized-tomography (CT) revealed an ischemic lesion in the left parietal-occipital region and smaller lesions in the left and right parietal regions (Fig. 1). Upon admission, a transesophageal echocardiogram

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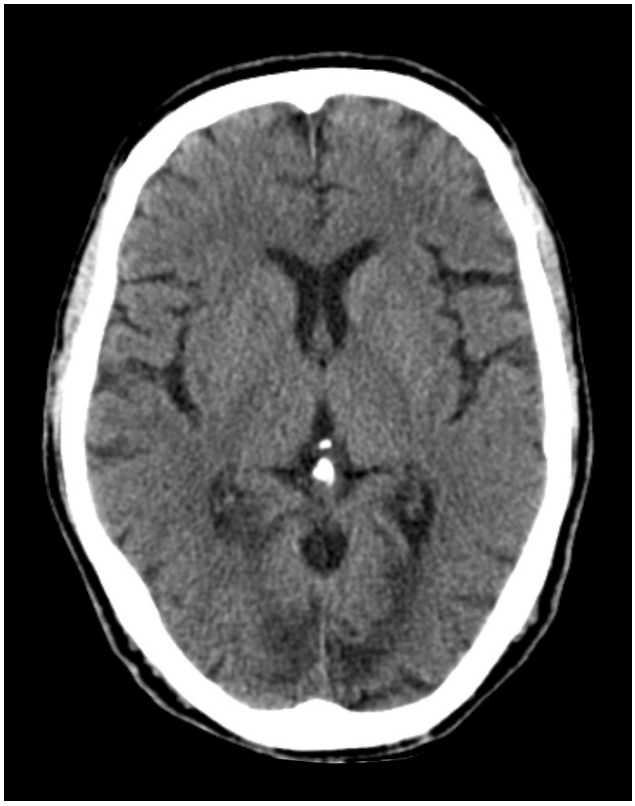

Figure 1 – Brain-CT showing ischemic lesion in the left parietal-occipital region

(TEE) documented a smaller thrombus and absence of valvular vegetations, abscess or ventricular dysfunction. A cardiac-CT did not display signs of inflammation and corroborated these findings. Three sets of BC were negative. The patient remained apyrexial and, in the presence of lung cancer as a possible aetiology, antibiotics were not started.

On the ninth day, the patient had recrudescence of fever and shivering. Blood pressure was 68/43 mmHg, pulse 105 bpm, temperature 39.6ºC and he became disoriented. Neither new extra cardiac sounds or murmurs nor cutaneous changes were noticed. Laboratory data revealed a lactate level of 6.45 mmol/L [< 2.0 mmol/L], increased leukocyte count and CRP (138.9 mg/L). A chest radiography did not show any changes. The blood pressure responded to fluid resuscitation. He received empirical treatment with vancomycin 25 mg/kg/dose and gentamicin 5 mg/kg/day for possible endocarditis and piperacillin-tazobactam 4.5 g each tid for possible nosocomial infection. Two days later, *Serratia marcescens*, without antimicrobial resistance *in vitro*, was isolated in three sets of BC, while urine culture was sterile. Gentamicin was maintained, but the remaining antibiotics were switched to ertapenem 1 g/day. A thoracic-abdominal-pelvic-CT scan revealed a splenic infarct (Fig. 2). Repeated TEE showed overlapping results. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron-emission-tomography (PET-CT) showed an abnormal hypercaptation in the inferior part of the mitral valve.

Because the patient had one major criterion (abnormal activity around the prosthetic valve) and four minor criteria (predisposing heart condition, fever, septic emboli and positive BC), the diagnosis of *Serratia marcescens* endocarditis was established, according to the modified European Society of Cardiology criteria. The patient's favourable clinical evolution and subsequent sterile BC two days after commencing treatment allowed completion of the antibiotic scheme (gentamicin for two weeks due to acute kidney injury and ertapenem for six weeks),and enabled the administration of ertapenem in the outpatient clinic.

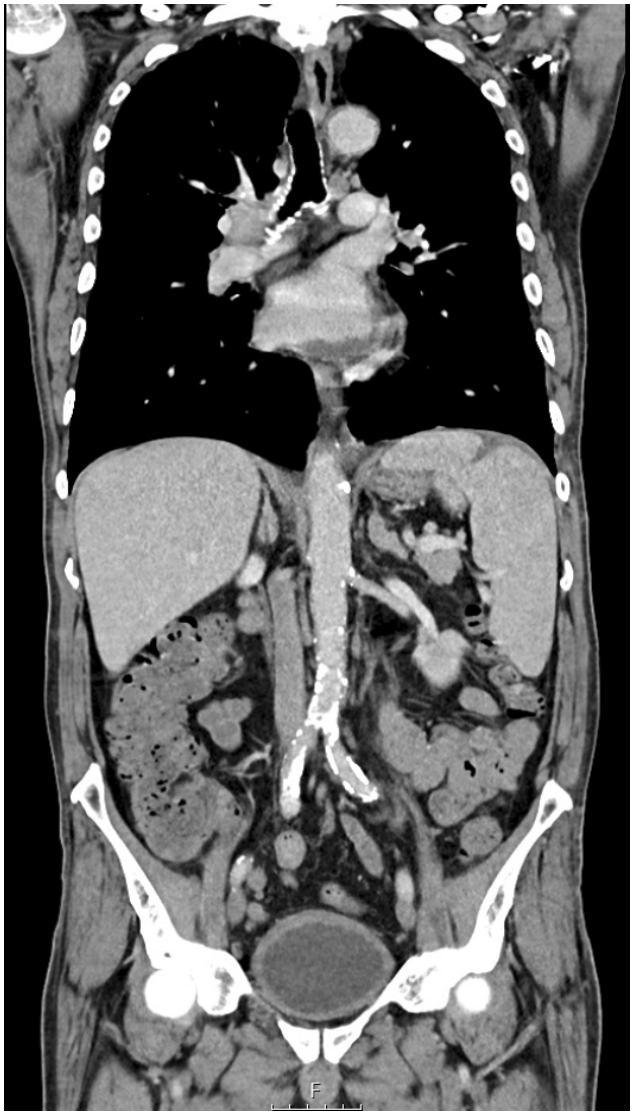

Figure 2 – Abdominal-CT scan revealing an enlarged spleen and an area of infarct in its superior lobe

DISCUSSION

Serratia marcescens endocarditis was first described in 1951.[1] Only 15 cases were reported since 1994 (Table 1).[1-15] In nine cases, the risk factor for infection was IVDU; in the group of health-care-associated endocarditis only one had a prosthetic valve[8] and one pacemaker.[5] Similarly, most of the cases had either immunosuppressive or chronic disease. All patients had positive blood cultures. Three patients died due to systemic and cerebral embolisation; seven patients underwent surgery for foci control. Additionally, this

Table 1 – Published cases of *Serratia marcescens* endocarditis since 1994

Reference	Age / gender	Risk factor	Medical history	Location	Evolution	Treatment	Outcome
J Infect 1994[3]	50yo, female	Health-care associated	Non-Hodgkin lymphoma, central venous catheter	Native AV	Septic emboli to skin	ATB: azlocillin + gentamicin, six weeks	Clinical resolution
Lancet Infect Dis 2007[4]	43yo, female	Not known	Splenectomy	Native MV	CNS embolisation and abscess formation	ATB: cefepime six weeks + gentamicin two weeks	Clinical resolution
BMJ Case Rep 2009[5]	67yo, male	Health-care associated	Pacemaker	Pacing wire	No complication	ATB: meropenem + gentamicin, then ciprofloxacin two weeks + pacemaker explantation	Clinical resolution
Intern Med 2012[6]	85yo, female	Health-care associated	Diabetes mellitus, Hypertension	Native MV	CNS embolisation: multiple infarctions Heart failure	ATB: ceftazidime six weeks + gentamicin one week	Death
J Echocardiogr 2012[7]	82yo, male	Health-care associated	Cirrhosis	Native TV, right ventricle	No complication	ATB: cefmetazole + clindamycin (duration not specified)	Clinical resolution
Scott Med J 2013[8]	65yo, female	Health-care associated	Post-Bentall procedure	Prosthetic AV	Bilateral endogenous endophthalmitis	ATB systemic: meropenem + gentamicin + ciprofloxacin (duration not specified) + local: ceftazidime	Clinical resolution
Infect Dis Clin Pract 2016[1]	46yo, male	IVDU	HIV, HCV, IVDU	Native MV	CNS embolisation: multiple infarctions and haemorrhage	ATB; meropenem (duration not specified)	Death
J Investig Med High Impact Case Rep 2018[9]	42yo, male	IVDU	HCV, IVDU	Native PV	Pulmonary embolism	ATB: ceftriaxone six weeks + valve replacement	Clinical resolution
Case Rep Infect Dis 2018[2]	53yo, male	IVDU	HCV; IVDU, coronary artery disease	Native AV	Multiple site embolisation: CNS, abdomen, testicle, vertebral body	ATB: ertapenem + ciprofloxacin six weeks + valve replacement	Clinical resolution
Case Rep Infect Dis 2019[10]	41yo, male	Health-care associated	Recent knee joint arthrocentesis	Native MV	Localised alveolar haemorrhage	ATB: gentamicin two weeks + meropenem + ciprofloxacin six weeks	Clinical resolution
Aorta 2020[11]	24yo, male	IVDU	Bicuspid AV, chronic Stanford's type-B aortic dissection, IVDU	Native AV	AV root abscess Embolisation: spleen, kidneys	ATB (not stated) + valve replacement	Clinical resolution
IDCases 2020[12]	55yo, male	IVDU	IVDU	Native AV, left ventricle	Embolisation: spleen, kidneys	ATB: cefepime + levofloxacin (duration not specified)	Death
Case Rep Infect Dis 2020[13]	33yo, male	IVDU	Hodgkin lymphoma, AV stenosis, HCV, IVDU	Native AV	Complete AVB, possible AV root abscess	ATB: cefepime six weeks + ciprofloxacin four weeks	Clinical resolution
Heart Lung Circ 2020[14]	50yo, male	IVDU	IVDU	Native AV	AV root abscess, complete AVB, Heart failure	ATB: meropenem + ciprofloxacin 6 weeks + valve replacement + pacemaker implantation	Clinical resolution
Cureus 2020[15]	27yo, female	IVDU	HCV, IVDU	Native TV	Pulmonary septic emboli Blood cultures: *Serratia marcescens* + MSSA	ATB meropenem six weeks (not stated ATB for MSSA) + percutaneous aspiration of emboli	Clinical resolution

These were case reports included in PubMed about *Serratia marcescens* endocarditis, but only the last case in the table reported the isolation of two microorganisms in blood cultures (*Serratia marcescens* and *Staphylococcus aureus* methicillin-susceptible). ATB: antibiotics, AV: aortic valve; AVB: atrioventricular block; CNS: central nervous system; HCV: hepatitis C virus; HIV: human immunodeficiency virus; IVDU: intravenous drug use; MSSA: methicillin-susceptible *Staphylococcus aureus;* MV: mitral valve; PV: pulmonic valve; TV: tricuspid valve

microorganism has an unexplained trend for left-sided valvular involvement[1] with a 68% mortality rate.[12] Right-sided endocarditis was described in three cases: two were IVDU and one had percutaneous transhepatic portal embolization.[7]

In the absence of a clinically evident infection, persistent fever and mild elevation of inflammatory parameters, in a patient with prosthetic cardiac valve, should trigger the suspicion of endocarditis, leading to an exhaustive investigation. In these cases, a negative TEE does not rule out the diagnosis and additional imaging should be performed, particularly PET-CT. The abnormal uptake of FDG in inflammatory tissue around the valve is highlighted in the PET-CT with a sensitivity of 70% - 100%,[1] which increases the likelihood of a positive diagnosis.

After the definitive diagnosis, the choice of antimicrobial therapy posed another challenge as there are no current specific guidelines concerning this issue and existing data comes from case reports. Nevertheless, it is widely accepted that treatment should be prolonged, and that dual antimicrobial therapy should include synergic and bactericidal agents. The suggested treatment is a combination of a beta-lactam and an aminoglycoside for at least six weeks.[2] Another challenge posed by *Serratia marcescens* infections is the presence of strains resistant to multiple antibiotics, namely penicillins, first-, second- and third-generation cephalosporins and, in some cases, carbapenems.[1] These resistances may be induced by prior use of beta-lactams, which may be the reason why a carbapenem is a stronger option in many cases of *Serratia* bacteremia. Therefore, we opted to use carbapenem due to is favourable experience in the literature, with a higher number of successful cases compared with other antibiotics. Resistance is mainly mediated by production of chromosomal AmpC cephalosporinases and synthesis of beta-lactamases, including extended spectrum beta-lactamases and carbapenemases.[1,10] Concurrent administration of aminoglycosides leads to a rapid sterilization of the affected valve.[1]

In most patients, antimicrobial therapy is insufficient and surgical treatment is needed due to poor prognosis[13] and the pathogenicity of the microorganism.[1] This may be recommended within the first seven to 10 days after beginning antimicrobial therapy.[13] In contrast with the majority of cases described, surgery was deemed unnecessary in our patient as he remained asymptomatic with normal valve function after receiving antibiotic therapy. Despite the presence of a prosthetic valve, the causative agent, the patient's comorbidities and the occurrence of cerebral septic emboli, our case may be an example that, in some selected patients and according to clinical evolution, antibiotic treatment may be sufficient.

This case highlights the importance of early identification and diagnosis in order for appropriate treatment to be initiated despite the lack of specific guidelines about this subject.

AUTHOR CONTRIBUTIONS

AIF: Follow up of the patient, literature research, draft of the manuscript.

FOS, JR, MH: Follow up of the patient, literature research, critical review of the manuscript.

JA: Follow up of the patient, final approval of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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Campylobacter jejuni Pericarditis: A Case Report

Pericardite por *Campylobacter jejuni*: Um Caso Clínico

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ABSTRACT

Campylobacter jejuni is one of the most common causes of enteritis. In rare cases, extraintestinal infection can occur, with a handful of cases of cardiac involvement, of which the pathophysiological mechanism is unclear. We report a case of pericarditis in a patient with X-linked agammaglobulinemia presenting with chronic diarrhea and chest pain who evolved to cardiac tamponade, requiring a pericardial window and a long course of broad-spectrum antibiotics. To the best of our knowledge, this is the third case of pericarditis caused by *Campylobacter jejuni* reported in the literature, the second in a patient with X-linked agammaglobulinemia. Despite its rarity, this case serves as a reminder of *Campylobacter* as a potential cause of cardiac inflammation for clinicians treating pericarditis/myocarditis, especially in patients with a history of diarrhea or immunosuppression.

Keywords: Agammaglobulinemia; Campylobacter Infections; Campylobacter jejuni; Pericarditis

RESUMO

A *Campylobacter jejuni* é uma das causas mais comuns de enterite. A infeção extraintestinal pode ocorrer raramente, estando reportados alguns casos de atingimento cardíaco, de mecanismo fisiopatológico incerto. Reportamos um caso de pericardite num doente com agamaglobulinemia ligada ao X, que se apresentou como diarreia crónica e dor torácica, evoluindo para tamponamento cardíaco com necessidade de confeção de janela pericárdica e tratamento prolongado com antibióticos de largo espectro. Este é, tanto quanto é do nosso conhecimento, o terceiro caso de pericardite por *Campylobacter jejuni* reportado na literatura, o segundo em doente com agamaglobulinemia ligada ao X. Apesar da sua raridade, este caso serve para reforçar a importância do género *Campylobacter* como causa de inflamação cardíaca para médicos que tratem pericardite/miocardite, especialmente em doentes com história de diarreia ou imunossupressão.

Palavras-chave: Agamaglobulinemia; Campylobacter jejuni; Infecções por Campylobacter; Pericardite

INTRODUCTION

Campylobacter spp. are one of the most common pathogens associated with human enteritis, and represent a zoonosis with a worldwide distribution.[1] Two species account for the majority of infections, with *Campylobacter jejuni* (*C. jejuni*) being the prototype for intestinal infection and *C. fetus* more associated with extraintestinal manifestations, usually as an opportunistic infection. These can be protean, with well documented descriptions of persistent bacteremia, cholangitis/cholecystitis, central nervous system infection, septic arthritis, osteomyelitis, septic abortion, mycotic aneurysms, endocarditis and myopericarditis.[1] The diagnosis requires a high degree of clinical suspicion, due to the relative rarity of these manifestations and frequently absent gastrointestinal symptoms. Compounding this extensive spectrum of clinical expressions, antimicrobial resistance is a growing problem especially in developing countries, with a significant number of isolates being resistant to macrolides and quinolones in particular.[2,3]

Furthermore, *C. jejuni* has been associated with several immunological sequelae, such as reactive arthritis, Guillain-Barré syndrome, hemolytic-uremic syndrome and small intestinal MALT (mucosal associated lymphoid tissue) lymphoma.[1]

CASE REPORT

A 34-year-old male with a history of X-linked agammaglobulinemia treated with monthly subcutaneous immunoglobulin and bronchiectasis presented to the emergency department with a seven-month history of non-bloody diarrhea and intermittent fever, chest pain and orthopnea.

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