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Endocarditis from Klebsiella pneumoniae carbapenemase-producing: an emerging infection? Two case reports

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ABSTRACT:

Objective: Endocarditis caused by non-HACEK gram-negative bacteria are very rare. However, it is more and more often reported as a nosocomial problem. This is especially serious because of the spread of multidrug resistant micro-organisms.

Here we report the case of two patients who were admitted in our hospital for non-traumatic reasons and who were not affected by chronic diseases. We aimed at raising attention on an old but new threat: endocarditis caused by Klebsiella pneumoniae carbapenemase-producing and its possible treatment.

Keywords: Klebsiella pneumoniae, Carbapenemase, Carbapenem, Ceftazidime, Ceftazidime-avibactam, KPC, AVI/CAZ, Endocarditis.

BACKGROUND

Endocarditis caused by non-HACEK gram-negative bacteria are very rare and considered, at least in the past, to be limited to injection drug users (IDUs)[1]. However, it is more and more often reported as a nosocomial problem, related to cardiac surgeries and cardiac device implantations[2,3]. This is a compelling problem, especially because of the high burden in terms of mortality: the outcome is death in 1 out of 4 endocarditis caused by gram-negative bacilli[2].

Inconsiderate use of antimicrobial drugs led to a real emergency. Multi-(MDR) and extensively-drug-resistant (XDR) are now more widespread than ever, and the weapons we have to fight them are really limited[4-6].

When MDR or XDR gram-negative species are responsible for serious infections such as endocarditis and sepsis, the unavailability of effective combination therapy leads to an even higher mortality, even in previously healthy patients who accessed the hospital for routinely interventions[2,4,7-11]. This is particularly true for endocarditis, for which treatment options are already limited by localization and characteristics of the infection[12].

Here we report about two patients who were admitted in our hospital for non-traumatic reasons and who were not affected by chronic diseases. The aim of this paper is raising attention on an old but new threat: endocarditis caused by Klebsiella pneumoniae carbapenemase-producing and its possible treatment.

CASE PRESENTATION

Case 1

A 40-year-old woman was referred to our Emergency Room (ER) for loss of conscience, following dysarthria and movement difficulties. Her previous medical history was negative for admissions and chronic diseases. A brain

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computerized tomography (CT) scan and a brain magnetic resonance imaging (MRI) showed large ischemic areas in both occipital regions and the thalamic region.

Therefore, the patient was admitted and underwent a cardiac ultrasound (US), which highlighted the presence of vegetation on the native mitral valve. Blood cultures were then performed and an empiric intravenous antibiotic treatment with vancomycin, rifampin and gentamicin was started, according to current guidelines[12]. Low molecular weight heparin was also started.

After three days from the admission, blood cultures resulted positive for Klebsiella pneumoniae carbapenemase-producing (KPC), which showed only sensitivity to gentamicin and colistin. For the critical general conditions, it was not possible to perform a valve prosthesis implantation.

We decided then to stop the antimicrobial treatment with vancomycin and rifampin and start iv ceftazidime/avibactam (AVI/CAZ) 2 g/500 mg tris in die. Gentamicin was continued at a dosage of 240 mg quondam die (qd) diluted in 250 mL of saline solution (0.9%) and infused over 30 minutes[3,13-15]. The treatment lasted 4 weeks after the first negative blood culture. At that time, the mitral valve endocarditis lesion was almost completely disappeared, and inflammation markers (C reactive protein and procalcitonin) were normal. Unfortunately, the patient died three months after the admission due to brain damage complications.

After the treatment was stopped, a monitoring with weekly blood cultures and inflammation markers was performed, showing that the treatment was successful in eradicating the infection.

Case 2

A 74-year-old man was referred to the ER for acute respiratory failure. His previous clinical history was negative for chronic diseases such as diabetes and chronic heart failure. He arrived in critical conditions and was admitted in the Intensive Care Unit.

During the admission, he underwent trans-thoracic first and trans-esophageal cardiac ultrasound then. Both the examinations showed the presence of a severe aortic insufficiency for the presence of endocarditic vegetation on the valvular flaps. Blood cultures were then performed, and the empiric antimicrobial treatment was started. When blood cultures resulted positive for KPC, a combination of AVI/CAZ 1.5 g/375 mg tid and gentamicin 240 mg qd diluted in 250 mL of saline solution (0.9%) infused over 30 minutes was started in place of the previous regimen. The patient's general condition quickly improved, and he was then moved to the Cardiac Surgery Unit. He underwent an aortic valve replacement surgery, with a prosthetic valve, and continued the antimicrobial treatment for 4 weeks. He was monitored with weekly blood cultures, which resulted negative after the surgery. Up to date, all controls are negative, the patient is in good clinical conditions and has resumed a normal life.

DISCUSSION

Infectious endocarditis is a disease burdened by high mortality and severe complications[12]. Unfortunately, all the bacterial infections have the potential to involve the heart valves, making this disease even more deadly[2]. In particular, in this age characterized by serious nosocomial infections caused by MDR and XDR microorganisms, this ability became especially dangerous, given the limited weapons we have in presence of such bacteria[4,7-11].

Endocarditis related to gram-negative microorganisms not belonging to the HACEK group have been reported for more than 25 years, but their importance has increased during the last few years, when antimicrobial resistance became a world problem[4,7].

We presented two cases of endocarditis caused by KPC, both resolved thanks to the use of a "protected" cephalosporin: ceftazidime/avibactam. AVI/CAZ is one of the few weapons available for carbapenem resistant Enterobacteriaceae. However, as expected, its use led to the appearance of AVI/CAZ resistant strain[16].

Therefore, ECDC issued an alert to prevent the spread of these strains, that suggest implementing measures of contact isolation whenever an AVI/CAZ resistant microorganism is found in a person, and to screen every admitted patient for potentially being an asymptomatic carrier[17].

Moreover, the use of a treatment with AVI/CAZ during endocarditis caused by carbapenem-resistant bacteria has been seldomly reported, and there are concerns about the fact that such a prolonged therapy can determine a more rapid onset and spread of resistance[3,18,19].

CONCLUSIONS

Further studies are needed to determine the association of prolonged therapy and the selection pressure towards the appearance of a resistance that would deprive us of one of the few antibiotics active in the case of carbapenem-resistant microorganisms.

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Conflict of Interest:
The Authors declare that they have no conflict of interests.

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