Abstract 4607

A novel KPC-3 variant associated with CAZ/AVI resistance in an *Klebsiella pneumoniae* ST512 causing bacteraemia

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Background: Ceftazidime-avibactam (CAZ/AVI) is a recent antibiotic which shows *in vitro* activity against many important Gram-negative pathogens including carbapenem-resistant *Enterobacterales* (CRE) producing KPC and OXA-48. Resistance to CAZ/AVI is still rarely reported, but poses a serious threat for the future. We report here the characterization of a CAZ/AVI-resistant *Klebsiella pneumoniae* strain carrying a novel KPC-3 variant.

Materials/methods: Identification was performed by VITEK® MS system (bioMérieux). Minimal inhibitory concentrations (MICs) were determined by a micro-dilution method (Sensititre Diagnostic System, Trek), and interpreted according to EUCASTclinical breakpoints v 9.0. A whole genome sequencing (WGS) approach (Illumina Miseq) was adopted to characterize the resistance mechanism to CAZ/AVI.

Results: A 78-year-old woman was admitted in hospital following a gluteal abscess post-arthroplasty treated with metronidazole and piperacillin/tazobactam, and developed a pneumonia caused by a KPC-producing *K. pneumoniae*, susceptible to CAZ/AVI. For this reason, the treatment was adjusted with CAZ/AVI in combination with tigecycline. However, a breakthrough bacteremia occurred and a KPC-producing *K. pneumoniae* was isolated from blood cultures resulting resistant to CAZ/AVI (MIC >32 mg/L). A severe ischemia due to the occlusion of the iliac-femoral axis led the patient to a fatal outcome. WGS analysis showed that this isolate i) belonged to ST512; ii) had a bla_{KPC} as the only carbapenemase gene; iii) presented a novel amino acid substitution (D179G), inside the omega-loop of KPC-3, previously associated with reduced susceptibility to CAZ/AVI as variant of KPC-2; iv) showed alterations in the outer membrane porins (OmpK35 and OmpK36).

Conclusions: CAZ/AVI resistance mechanisms has largely been attributed to nonsynonymous mutations in KPC-3. In this work, a CAZ/AVI resistant *K. pneumoniae* isolate with a new variant of KPC-3 was described after an initial treatment with this antibiotic, highlighting that a strict antibiotic-stewardship and infection control practices are necessary to preserve the drug efficacy of this recent drug.

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