Case Report

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Multidrug-resistant OXA-48-producing *Klebsiella pneumoniae* mediastinitis treated safely and effectively with imipenem and colistin

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Introduction: Post-operative mediastinitis due to multidrug-resistant Gram-negative bacteria has rarely been described and is associated with increased mortality.

Case presentation: We report a case of mediastinitis caused by a multidrug-resistant OXA-48-producing *Klebsiella pneumoniae* isolate in a patient who underwent coronary artery bypass grafting. Successful treatment consisted of surgical debridement and prolonged administration of imipenem and colistin.

Conclusion: This result shows that a combination of imipenem/colistin could be used to treat serious infections with carbapenemase-producing *Enterobacteriaceae*.

Keywords: *bla*_{OXA-48}; carbapenemase; imipenem; mediastinitis.

Introduction

Carbapenem-resistant *Enterobacteriaceae* have been reported worldwide as a consequence largely of acquisition of carbapenemase genes, which mostly comprise clavulanic acid-inhibited carbapenemase (KPC), metallo- β -lactamases and OXA-48-type carbapenemase (Nordmann *et al.*, 2011).

Carbapenemase-producing *Enterobacteriaceae* (CPE) infections are associated with high mortality rates and are difficult to treat due to multiple mechanisms of resistance (Nordmann *et al.*, 2011). The efficacy of carbapenems for treating infections due to CPE with low-level resistance or susceptibility to carbapenems remains debatable (Daikos & Markogiannakis, 2011). We report a case of mediastinitis caused by a multidrug-resistant (MDR) OXA-48-producing *Klebsiella pneumoniae* isolate that was successfully treated with prolonged administration of imipenem and colistin.

Case report

A 70-year-old morbidly obese and diabetic man developed post-surgical mediastinitis after four-vessel coronary artery bypass grafting. On day 10 after cardiac surgery, the patient presented with fever and purulent discharge from the sternotomy scar. The patient underwent surgical debridement and was given imipenem 1 g three times daily with amikacin (1 g every 24 h). Three sets of blood cultures and cultures of surgical samples yielded a MDR *K. pneumoniae*

isolate. This isolate was resistant to all aminoglycosides, fluoroquinolones, extended-spectrum cephalosporins, ertapenem and trimethoprim-sulfamethoxazole, but it remained susceptible to colistin and imipenem. The MICs of colistin and imipenem were 0.125 and 0.5 mg ml⁻¹, respectively, by both E-testing (bioMérieux) and the standard broth microdilution method according to the updated Clinical and Laboratory Standards Institute guidelines (CLSI, 2009). Molecular testing revealed that the isolate co-produced the *bla*_{OXA-48} and the *bla*_{CTX-M-14} β -lactamase genes. Therapy was then shifted to imipenem (1 g every 8 h) plus colistin (2 Millions every 8 h).

After 1 week of antibiotic therapy, sternum culture results were still positive for the same *K. pneumoniae* isolate and the patient remained febrile; however, blood cultures were sterile. The surgical debridement was repeated twice and the antibiotic therapy was maintained as the MICs of imipenem and colistin were identical to those of the index strain. Moreover, a time-kill study confirmed that this association was synergistic. The patient recovered well after this and cultures of the surgical site were negative on day 35. The patient responded to a 55-day course of imipenem plus colistin therapy and no adverse effects were observed during this therapy. Finally, no relapse was observed after a 1-year follow-up period.

Discussion

Mediastinitis remains the most severe complication of coronary artery bypass grafting. The most commonly

Abbreviations: CPE, carbapenemase producing *Enterobacteriaceae*; MDR, multidrug-resistant.

isolated pathogens in post-sternotomy mediastinitis are staphylococci. *K. pneumoniae* mediastinitis is rare and is frequently associated with a higher risk of mortality. However, the role of carbapenemase-producing *K. pneumoniae* in post-operative mediastinitis is increasing and is complicating the therapy, as these isolates frequently exhibited an MDR phenotype (Risnes *et al.*, 2010).

Here, we report, to the best of our knowledge, the first successful use of imipenem and colistin for treatment of a post-operative carbapenemase-producing *K. pneumoniae* mediastinitis, which required a prolonged course of therapy in addition to appropriate surgical wound care. In fact, many reports have demonstrated that carbapenems are effective against carbapenemase-producing *K. pneumoniae* when the MIC is less than 4 mg l⁻¹ (Daikos & Markogiannakis, 2011). It is also of note that, despite the frequently described evolution of resistance of MDR Gram-negative organisms to colistin, the colistin MIC remained unchanged in all *K. pneumoniae* isolates during the management of our mediastinitis case (Biswas *et al.*, 2012). Moreover, no side effects have been noted. This clinical case shows that certain carbapenem molecules associated with colistin could be used to treat serious infections with *Enterobacteriaceae* that produce OXA-48-type carbapenemases, which may be of interest in a number of countries where OXA-48-type producers are

spreading such as those in the Mediterranean region (Nordmann *et al.*, 2011).

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