Acinetobacter baumannii Resistant to Colistin With Impaired Virulence: A Case Report From France

To the Editor—In an article recently published in the Journal, Lopez-Rojas et al [1] demonstrated that an in vitro mutant of Acinetobacter baumannii resistant to colistin had reduced in vivo fitness and decreased virulence, in terms of both mortality and survival, in a mouse model of peritoneal sepsis. They suggest that the lower in vivo bacterial fitness and decreased virulence of this mutant may explain the low incidence of colistin resistance in the clinical setting. We report herein the clinical case of a French patient colonized with an A. baumannii colistin-resistant isolate after colistin therapy without clinical signs of infection.

A 58-year-old patient presented with an influenzalike illness on 16 December 2010 and was treated at home with ampicillin-clavulanic acid. On day 3, he was admitted at Salon de Provence hospital for dyspnea, fever, and right lobar pneumonia on chest x-ray. On day 7, the patient required mechanical ventilation after endotracheal intubation for acute respiratory failure. Antibiotherapy was switched to piperacillin-tazobactam and spiramycin. A bronchoalveolar lavage (BAL) sampled at that time was sterile, and influenza virus detection was negative. Treatment was switched to imipenem-amikacin on day 15 for acute respiratory distress syndrome and septic shock. On day 19, extracorporeal membrane oxygenation (ECMO) was started for refractory hypoaxemia, and the patient was referred to an intensive care unit (ICU) in Marseille. On day 21, a colistin-susceptible A. baumannii isolate was recovered from BAL, as well as from 3 blood cultures. Treatment was switched to intravenous colistin and rifampin. ECMO was weaned and sedation was stopped on day 27. Colistin and rifampin were stopped on day 35 but a treatment using imipenem-amikacin-colistin was started on day 37 for a new septic shock episode and stopped on day 41, based on negative BAL and blood cultures. While respiratory status improved, tracheal colonization with colistin-resistant A. baumannii was detected from day 50 to day 60 on biweekly endotracheal aspirate cultures. No clinical sign of infection was present during this period. Asymptomatic bacteriuria to colistin-sensitive A. baumannii was also present by day 50 and was treated with bladder instillations of colistin from day 57. Treatment was stopped on day 67 when colistin-resistant A. baumannii was isolated from urine samples. The patient was discharged alive from the ICU on day 70.

Our case report confirms that colistin-resistant A. baumannii strains may be selected in vivo by the use of colistin but that colistin-resistant strains may be less virulent than expected. A strong association between the use of colistin and development of resistance in clinical strains of A. baumannii has already been reported [2, 3]. However, resistance to colistin in A. baumannii has been reported in sporadic cases and only in 1 nosocomial outbreak in an ICU in Spain in 2009 [4]. Colistin acts by modifying the negative charges of the outer membrane of Gram-negative bacteria. We have recently shown that squalamine, a natural aminosterol, has antimicrobial activity similar to that of colistin against multidrug-resistant Gram-negative bacteria [5] and that this activity required interaction with the negatively charged phosphate groups in the bacterial outer membrane, ultimately leading to the disruption of the bacterial membrane [6]. The mechanisms of resistance to colistin in A. baumannii are not well known and there are, so far, only 2 putative mechanisms elucidated: mutations in 2 genes that constitute a 2-component system (PmrAB) involved in the modification of lipid A, the major constituent of lipopolysaccharide membrane [7] and mutations, deletions, or insertions in genes essential for synthesis of lipid A (lpxA, lpxC, and lpxD genes) [3, 8]. Acquisition of resistance is known to be associated with a fitness cost as well as decreased virulence [9]. One may postulate that modifications of the outer membrane protein, especially modifications of the endotoxic potential of lipopolysaccharide [2], may be responsible for this decreased fitness. Although clinical experience is still meager to decipher the fitness cost due to resistance to colistin, our case report further supports the hypothesis by Lopez-Rojas et al from a clinical standpoint. However, resistant bacteria may improve the costs of resistance by acquisition of additional fitness-compensatory mutations that may lead to more virulent strains under certain environmental conditions [9]. Thus, the increasing use of colistin for treating infections with multidrug-resistant bacteria [10] will inevitably increase the recovery rate of colistin-resistant isolates in the future.

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Jean-Marc Rolain,1 Antoine Roch,1,2 Matthias Castanier,1,2 Laurent Papazian,1,2 and Didier Raoult1

1Unité de Recherche sur les Maladies Infectieuses et Tropicales Emergents (URMITE), CNRS-IRD, UMR 6238, Faculté de Médecine et de Pharmacie,
References


Received 14 April 2011; revised 10 June 2011; Potential conflicts of interest: none reported. Correspondence: Jean-Marc Rolain, PharmD, PhD, URMITE CNRS-IRD UMR 6236, Marseille, France 13385 (jean-marc.rolain@univmed.fr).