Acinetobacter baumannii Resistant to Colistin Alters Its Antibiotic Resistance Profile: A Case Report From Spain

To the Editor—Rolain et al [1] report a patient colonized with a colistin-resistant *Acinetobacter baumannii* strain after colistin therapy without clinical signs of infection, pointing out the low virulence of *A. baumannii* with acquired resistance to colistin, as previously hypothesized by our group [2]. Moreover, Rolain et al raise the possibility of compensatory mutations restoring the virulence in colistin-resistant *A. baumannii*. We now describe a patient infected by colistin-susceptible *A. baumannii* whose organism acquired resistance to colistin after colistin therapy without losing its infecting capacity.

A 39-year-old man with previous surgical resection of a craniopharyngioma in 1990 was admitted on 7 October 2009 with symptoms of acute hydrocephalus. He was treated with external ventricular cerebrospinal fluid (CSF) decompression. On day 8 following the procedure, the patient presented CSF leakage at the surgical wound and on day 11 had headache with a turbid and xanthochromic CSF, with 5360 cells/μL (98% neutrophils), and 0.028 g/L glucose; treatment with vancomycin (500 mg/intravenously [iv]/6 hours) and meropenem (1 g/iv/8 hours) was prescribed. *A. baumannii* was isolated from CSF and was susceptible to colistin, tigecycline, amikacin, gentamicin, and tobramycin, and resistant to ceftazidime, cefotaxime, cefepime, imipenem, meropenem, piperacillin, ticarcillin, rifampicin, sulbactam, and ciprofloxacin. On day 14, vancomycin and meropenem were discontinued and colistin (2×10^6U/iv/6 hours) was started. On day 23, CSF characteristics remained similar and *A. baumannii* was again isolated with changes in its susceptibility/resistance profile: susceptible to sulbactam, tigecycline, minocycline, amikacin, gentamicin, and tobramycin, and resistant to colistin, ceftazidime, cefotaxime, cefepime, imipenem, meropenem, piperacillin, ticarcillin, rifampicin, and ciprofloxacin; intrathecal gentamicin (10 mg/12 hours) was added. On day 28, CSF remained turbid and xanthochromic, with 980 cells/μL, 100% neutrophils, and 0.076 g/L glucose, with *A. baumannii* again isolated, susceptible to sulbactam, minocycline, cefepime, amikacin, gentamicin, and tobramycin, and resistant to colistin, ceftazidime, cefotaxime, imipenem, meropenem, piperacillin, ticarcillin, rifampicin, and ciprofloxacin. On day 31, ventricular drainage was discontinued. On day 34, antimicrobial treatment was modified, adding sulbactam (1 g/iv/8 hours) and cefepime (2 g/iv/8 hours), stopping gentamicin. On day 57, CSF had 54 cells/μL (100% neutrophils), and 0.651 g/L glucose. Antimicrobial treatment was stopped and the patient was discharged without clinical signs of infection on day 66. All the *A. baumannii* isolates had the same clonal profile by repetitive extragenic palindromic polymerase chain reaction.

This case report confirms, as Rolain et al have described [1], that colistin-resistant *A. baumannii* strains may be selected in vivo by the use of colistin but that such acquisition of resistance does not always indicate a bacterial fitness cost. Moreover, the acquisition of resistance to colistin in *A. baumannii* in this case led us to change the antibiotic resistance profile, as the isolate became susceptible to cefepime and sulbactam.

Little is known about the resistance to colistin in *A. baumannii*. It has been associated with mutations in the PmrAB 2-component system [3], which produce modifications in bacterial lipopolysaccharide that lead to an addition of phosphoetanolamine to lipid A, conferring colistin resistance [4]. Acquisition of polymyxin resistance is associated with differences in protein expression: 35 proteins were downregulated in the colistin-resistant strain, including outer membrane proteins, chaperones, protein biosynthesis factors, and metabolic enzymes [5], which

translated to a loss of biological fitness and virulence [2]. On the other hand, high-level colistin resistance in *A. baumannii* has been linked to a complete loss of lipopolysaccharide due to the inactivation of the *A. baumannii* lipid A biosynthesis, as an effect of mutations in 1 of the first 3 genes of the lipid A biosynthesis pathway (*lpxA*, *lpxC*, and *lpxD*) [6], or as the inactivation of the *lpxA* and *lpxC* genes by the insertion sequence element IS*Aba11* [7]. The acquisition of polymyxin resistance where a complete loss of lipopolysaccharide is involved is associated with a decrease in the outer membrane integrity, and to an increased susceptibility of these strains to other antibiotics, including cefepime, as in the case we reported here, and some that are usually active only against Gram-positive bacteria [6, 8].

In summary, resistance to colistin in clinical strains of *A. baumannii*, although still sporadic, may occur due to the increasing use of colistin. Although colistin resistance may suggest a fitness cost for bacteria, the case we describe here indicates that it does not always occur, as unidentified compensatory mutations may appear to maintain the virulence of *A. baumannii*.

Rafael López-Rojas, Manuel Enrique Jiménez-Mejías, José Antonio Lepe, and Jerónimo Pachón

Unidad Clınica de Enfermedades Infecciosas, Microbiologıa y Medicina Preventiva, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocıo/CSIC/Universidad de Sevilla, Spain

References

1. Rolain JM, Roch A, Castanier M, Papazian L, Raoult D. *Acinetobacter baumannii* resistant to colistin with impaired virulence: a case report from France. J Infect Dis **2011**; 204:1146–7.
2. Lopez-Rojas R, Dominguez-Herrera J, McConnell MJ, et al. Impaired virulence and in vivo fitness of colistin-resistant *Acinetobacter baumannii*. J Infect Dis **2011**; 203:545–8.
3. Adams MD, Nickel GC, Bajaksouzian S, et al. Resistance to colistin in *Acinetobacter baumannii* associated with mutations in the PmrAB two-component system. Antimicrob Agents Chemother **2009**; 53:3628–34.
4. Beceiro A, Llobet E, Aranda J, et al. Phosphoethanolamine modification of lipid A in colistin-resistant variants of *Acinetobacter baumannii* mediated by the pmrAB two-component regulatory system. Antimicrob Agents Chemother **2011**; 55:3370–9.
5. Fernandez-Reyes M, Rodriguez-Falcon M, Chiva C, Pachon J, Andreu D, Rivas L. The cost of resistance to colistin in *Acinetobacter baumannii*: a proteomic perspective. Proteomics **2009**; 9:1632–45.
6. Moffatt JH, Harper M, Harrison P, et al. Colistin resistance in *Acinetobacter baumannii* is mediated by complete loss of lipopolysaccharide production. Antimicrob Agents Chemother **2011**; 54:4971–7.
7. Moffatt JH, Harper M, Adler B, Nation RL, Li J, Boyce JD. Insertion sequence ISAba11 is involved in colistin resistance and loss of lipopolysaccharide in *Acinetobacter baumannii*. Antimicrob Agents Chemother **2011**; 55:3022–4.
8. Li J, Nation RL, Owen RJ, Wong S, Spelman D, Franklin C. Antibiograms of multidrug-resistant clinical *Acinetobacter baumannii*: promising therapeutic options for treatment of infection with colistin-resistant strains. Clin Infect Dis **2007**; 45:594–8.

Received and accepted 10 June 2011.
Potential conflicts of interest: none reported.
Correspondence: Rafael López-Rojas, PhD, Servicio de Enfermedades Infecciosas, Hospitales Universitarios Virgen del Rocıo, Avda Manuel Siurot s/n, 41013, Sevilla, Spain (rlopezrojas@hotmail.com).

The Journal of Infectious Diseases 2011;204:1147–48

0022-1899 (print)/1537-6613 (online)/2011/2047-0025$14.00
DOI: 10.1093/infdis/jir476