CASE REPORT

INDICATIONS OF CARBAPENEM RESISTANCE EVOLUTION THROUGH HETERORESISTANCE AS AN INTERMEDIATE STAGE IN Acinetobacter baumannii AFTER CARBAPENEM ADMINISTRATION

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SUMMARY

We describe an in vivo evolution of an antimicrobial profile from susceptibility to full-resistance to carbapenems, with heteroresistance as an intermediate stage, in an Acinetobacter baumannii strain. Heteroresistance was characterized by the growth of sub-populations within the susceptibility halo in both disk-diffusion and Etest. PCRs for the main A. baumannii carbapenemases were negative. The exact resistance mechanism, diagnostic methods and clinical relevance of heteroresistance in A. baumannii warrant further investigations. This is the first description of such phenomenon in vivo and the second report of heteroresistance to carbapenems in A. baumannii.

KEYWORDS: Acinetobacter baumannii; Carbapenem-heteroresistance; Meropenem treatment.

INTRODUCTION

Acinetobacter baumannii, which is associated with a wide range of infections, particularly pneumonia among intensive care unit (ICU) patients, has emerged as an important nosocomial pathogen in many parts of the world. The carbapenems, imipenem and meropenem, are among the drugs of choice used to treat nosocomial infections due to multidrug-resistant A. baumannii isolates. As other Gram-negative rods, resistance in these bacteria is known to be homogeneous within a culture although a report has described the spread of hetero-carbapenem-resistant A. baumannii isolates. In the present report, we describe the recovery from blood of an A. baumannii isolate presenting heteroresistance to carbapenems in a patient receiving meropenem due to an intra-abdominal abscess.

CASE REPORT

In March 2006, a first A. baumannii resistant to both imipenem and meropenem was identified in our institution. Two isolates were recovered from an intra-abdominal abscess secretion and from the blood of a 67-year-old female patient at ICU, respectively. Identification of the isolates has been based on biochemical tests, including mobility, oxidase activity, oxidation of glucose on OF-medium; and API 20 NE method (6.0 version, bio-Merieux, Marcy L’Etoile, France). This patient was receiving I.V. meropenem (1g IV every eight hours) for exactly 31 days, for the treatment of the abscess after an esophagectomy for a carcinoma of the esophagus. The therapy was changed for polymyxin B (75 mg IV every 12 hours) when the culture results became available (three days after collection), but the patient ultimately died of septic shock seven days after starting new antimicrobial treatment.

Phenotypic tests for MBL detection using a disk approximation test with imipenem (Oxoid) in the presence of EDTA were negative for both isolates. Additionally, PCR for carbapenemases genes (bla\text{IMP}, bla\text{VIM}, bla\text{SPM}, bla\text{OXA-23}, bla\text{OXA-24}, bla\text{OXA-51} and bla\text{OXA-58}) was carried out using specific primers as described elsewhere, but there was no product of amplification for any primers, except for the bla\text{OXA-51}.

Forty-three days latter, a carbapenem-resistant A. baumannii was
recovered from the tracheal aspirate and blood. This patient had not received carbapenem.

DISCUSSION

We presented a rare case of a carbapenem-heteroresistant *A. baumannii* recovered from blood and abscess secretion of a patient receiving meropenem therapy. A previous report has described heteroresistance to carbapenems in eight *A. baumannii* isolates which were also neither MBL nor oxacillinase producers. As in this previous study, the exact mechanism of resistance in our strain could not be determined. Although the main *A. baumannii* carbapenemases have been ruled out, the isolate carried a gene encoding an OXA-51-like group β-lactamase, a gene present in most *A. baumannii* strains, but with a non-clearly defined role in carbapenem resistance.

Heteroresistance, which may be defined as a phenotypic manifestation of resistance within a genetically homogeneous strain, has only rarely been described in Gram-negative bacteria. Although authors are not certain about the clinical impact of this resistance phenotype in Gram-negative rods, our report suggests that heteroresistance may adversely affect the outcome of patients, since the *A. baumannii* isolate was recovered from the blood of a patient receiving meropenem therapy.

In conclusion, heteroresistance in nonfermentative Gram-negative bacteria is a rare and poorly understood phenomenon, the exact mechanism determining this phenotype, the best diagnostic methods and its clinical relevance warrant further investigations.

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RESUMO

Indicações da evolução da resistência ao carbapenem através da heteroresistência como estágio intermediário no Acinetobacter baumannii após administração de carbapenem

Descrevemos a evolução in vivo, de um perfil de sensibilidade aos antimicrobianos, passando de sensibilidade a resistência total aos antibióticos carbapenêmicos, com um estágio intermediário de heteroresistência em isolado de Acinetobacter baumannii. A heteroresistência foi caracterizada pelo crescimento de sub-população na zona de inibição pelo método de disco-difusão e pelo Etest. PCRs para as principais carbapenemases envolvidas com resistência neste microrganismo foram negativas. O exato mecanismo de resistência envolvido, método diagnóstico e relevância clínica justificam investigação adicional. Esta é a primeira descrição deste fenômeno in vivo e o segundo relato de heteroresistência em *A. baumannii*.

REFERENCES


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