LETTER TO THE EDITOR

ROLE OF RARE CARBAPENEMASES IN THE DIFFUSION OF CARBAPENEM RESISTANCE IN *PSEUDOMONAS AERUGINOSA*

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The recent article by Monica Străuț *et al*. published in the latest issue of the *Romanian Archives of Microbiology and Immunology* provided an overview of the β-lactamase genes and the diversity of the surrounding genetic structures associated with resistance to ceftazidime in Romania [1]. In total, the authors have evaluated 93 non-duplicate isolates, most of which (n = 74) were obtained from the respiratory tract.

Even tough not the primary interest of this study, the authors highlight the need for the detection of carbapenem resistance in *P. aeruginosa.*

The main carbapenem-resistance mechanisms in *P. aeruginosa* are:

- Overproduction of chromosomally-encoded cephalosporinase (AMPC) associated to overexpression of efflux pumps and/or porin deficiency

- Quantitative or qualitative alteration of porin D2

- Production of carbapenemases, mostly Ambler's class B metallo-β-lactamases (MBL).

This, however, does not take into account the diversity of carbapenemases encountered in that species. First, a large diversity of MBL has been identified including more than fifteen variants of bla_{VIM}-type or bla_{IMP}-type carbapenemases but also more rarely described MBLs such as bla_{GIM-1}, bla_{SPM-1}, bla_{AIM-1} [2]. Noticeably, class A carbapenemase were also identified in *P. aeruginosa* including bla_{GES}-type and bla_{KPC}-type carbapenemase [3, 4].

In addition to this wide diversity, we have recently characterised four *P. aeruginosa* isolates producing OXA-198, an Ambler class D carbapenemase from Belgian Hospitals from 2010 to 2013 [5,6].

These isolates, including the original index strain, belonged to the Sequence Type 446 (by multilocus sequence typing, MLST) and serotype O11. OXA-198 was carried by an IncP11-type plasmid transferable but not conjugative.

In a previous survey conducted in the Cluj County in Romania, Dortet *et al*. reported a large variety of β-lactamases identified in *Enterobacteriaceae* and *P. aeruginosa* [7]. Among the *P. aeruginosa* isolates, the bla_{VIM-2} and bla_{IMP-13} genes were identified. Overall, epidemiological data concerning Romania remain scarce. In order to limit the spread of these highly drug resistant Enterobacteriaceae and non-fermenters continuous monitoring of the drug resistance levels, but also of the underlying resistance mechanisms is mandatory.

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REFERENCES

1. Străuț M, Dinu S, Oprea M, Drăgulescu E-C, Lixandru B-E, Surdeanu M. Genetic diversity of structures surrounding *bla* genes identified in *Pseudomonas aeruginosa* clinical isolates from Bucharest, Romania. Rom Arch Microbiol Immunol. 2018;77(1):16–27.
2. Cornaglia G, Giamarellou H, Rossolini GM. Metallo-β-lactamases: a last frontier for β-lactams? Lancet Infect Dis. 2011 May;11(5):381-93.
3. Naas T, Bonnin RA, Cuzon G, Villegas MV, Nordmann P. Complete sequence of two KPC-harbouring plasmids from Pseudomonas aeruginosa. J Antimicrob Chemother. 2013 Aug;68(8):1757-62.
4. Bebrone C, Bogaerts P, Delbrück H, Bennink S, Kupper MB, Rezende de Castro R, Glupczynski Y, Hoffmann KM. GES-18, a new carbapenem-hydrolyzing GES-Type β-lactamase from Pseudomonas aeruginosa that contains Ile80 and Ser170 residues. Antimicrob Agents Chemother. 2013 Jan;57(1):396-401.
5. Bonnin RA, Bogaerts P, Girlich D, Huang T-D, Dortet L, Glupczynski Y, Naas T. Molecular Characterization of OXA-198 Carbapenemase-Producing Pseudomonas aeruginosa Clinical Isolates. Antimicrob Agents Chemother. 2018;62(6).
6. El Garch F, Bogaerts P, Bebrone C, Galleni M, Glupczynski Y. OXA-198, an acquired carbapenem-hydrolyzing class D beta-lactamase from Pseudomonas aeruginosa. Antimicrob Agents Chemother. 2011;55(10):4828–33.
7. Dortet L, Flonta M, Boudehen Y-M, Creton E, Bernabeu S, Vogel A, Naas T. Dissemination of carbapenemase-producing Enterobacteriaceae and Pseudomonas aeruginosa in Romania. Antimicrob Agents Chemother. 2015;59(11):7100–3.