SPM-1 metallo-β-lactamase-producing *Pseudomonas aeruginosa* ST277 in the UK

Metallo-β-lactamase (MBL)-producing *Pseudomonas aeruginosa* are increasing in incidence in the UK, largely due to the emergence of several internationally recognized 'high-risk' clones (Wright *et al.*, 2015). These predominantly produce VIM carbapenemases, but isolates with IMP and NDM MBLs have also been identified, as have occasional isolates with other, rarer, MBLs such as DIM-1 [Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit, unpublished data].

An isolate of *P. aeruginosa*, cultured in 2013 from the throat of an inpatient, was submitted for investigation of carbapenem resistance to Public Health England’s AMRHAI Reference Unit. Local laboratory testing detected an MBL using a Rosco Diagnostica KPC/MBL Confirm kit (BioConnections). MICs were determined against the AMRHAI Reference Unit’s standard Gram-negative antibiotic panel, which includes imipenem (±EDTA for MBL detection) and meropenem, using agar dilution and interpreted using British Society for Antimicrobial Chemotherapy criteria. Carbapenemase genes were sought by commercial microarray (Check-MDR CT102; Check-Points) and in-house PCR (Ellington *et al.*, 2007). Whole genome sequencing was performed using a HiSeq sequencing system (Illumina). Data were analysed using in-house bioinformatics pipeline to infer multilocus sequence typing (MLST) profile and resistance genes were identified by mapping reads against a library curated in-house from publicly accessible databases (Dounmth *et al.*, 2015).

The *P. aeruginosa* isolate was of intermediate sensitivity to aztreonam (MIC 8 mg l\(^{-1}\)), and resistant to ceftazidime (MIC >256 mg l\(^{-1}\)), piperacillin/tazobactam (MIC 64 mg l\(^{-1}\)), meropenem (MIC >32 mg l\(^{-1}\)) and imipenem (MIC >128 mg l\(^{-1}\)), the latter with ≥8-fold imipenem/EDTA synergy, which is consistent with an MBL phenotype. Pan-aminoglycoside resistance (amicillin, gentamicin and tobramycin MICs >32 mg l\(^{-1}\)) and resistance to ciprofloxacin (MIC >8 mg l\(^{-1}\)) was observed, with the isolate only susceptible to colistin (MIC 1 mg l\(^{-1}\)).

The isolate was negative for acquired carbapenemase genes following screening by microarray, but *bla*spm\(_{1}\) was detected by in-house PCR and confirmed by Sanger sequencing. According to the referral form submitted with the isolate, the patient had no history of recent foreign travel. However, when further patient details were requested from the referring laboratory, it transpired that the patient had been hospitalized and undergone surgery during a visit to Brazil before subsequently being admitted upon return to the UK with a Hickman line in situ.

The isolate belonged to ST277, which has previously been shown to be an endemic clone in Brazilian hospitals and, like our isolate, is susceptible to colistin only (Fonseca *et al.*, 2010; Silva *et al.*, 2011). Identification of SPM-1-producing *P. aeruginosa* from urban river water in Brazil may indicate that these organisms have spread beyond the hospital environment (Fontes *et al.*, 2011). SPM-1-positive *P. aeruginosa* was first reported in Europe following isolation in 2007 from a Swiss patient who had received medical treatment whilst in Brazil (Salabi *et al.*, 2010). MLST data for isolates belonging to ST277 have also been submitted to the *P. aeruginosa* MLST database (http://pubmlst.org/paeruginosa/) from Austria, Australia, Central Africa, China and Spain, although no information is provided as to whether these isolates harbour *bla*spm\(_{1}\) or whether they have connections with Brazil.

Short-read sequencing data mapped against the *bla*spm\(_{1}\)-related genomic island (KP299160) with >98% coverage and homology, indicating that *bla*spm\(_{1}\) was located within a Tn4371 integrative and conjugative element as described by Fonseca *et al.* (2015). Association of *bla*spm\(_{1}\) with this mobile genetic element could potentially result in dissemination to other bacterial genera and species; *bla*spm\(_{1}\) has also been described in clinical isolates of *Acinetobacter baumannii* in Iran (Shahcheraghi *et al.*, 2011). Whole genome sequencing also identified the 16S rRNA methyltransferase gene *rmtD1*, which confers high-level resistance to all 4,6-disubstituted deoxyxystreptamine aminoglycosides and has been described associated with *bla*spm\(_{1}\) (Doi *et al.*, 2007).

This is the first report of an SPM-1-producing isolate identified amongst more than 800 MBL-producing *Pseudomonas* spp. confirmed by the AMRHAI Reference Unit since screening began in 2001 (AMRHAI Reference Unit, unpublished data), and to our knowledge only the second report of the SPM-1-producing *P. aeruginosa* ST277 colistin-only-susceptible clone outside of Brazil. The opportunity for the global spread of SPM-1-producing *P. aeruginosa* following the 2016 Olympic Games in Rio de Janeiro has already been highlighted (Andrade *et al.*, 2014). Hospital laboratories should be alert to the possibility of SPM-1 in *P. aeruginosa* isolates resistant to all relevant carbapenems (i.e. imipenem, meropenem and doripenem), piperacillin/tazobactam and usually ceftazidime in patients who have returned from Brazil. Laboratories that have implemented molecular testing for confirmation of carbapenemase production should note that the majority of commercial molecular carbapenemase detection assays focus on identification of the more prevalent *bla*vim and *bla*ntm alleles (and some platforms offer limited coverage of *bla*imp alleles); therefore, a high level of suspicion should be kept for isolates demonstrating good imipenem/EDTA synergy but negative in molecular assays, and such isolates should be referred to the national reference laboratory.
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Abbreviations: MBL, metallo-β-lactamase; PHE, Public Health England; AMRHAI, Antimicrobial Resistance and Healthcare Associated Infections Reference Unit.

References


