Emergence of KPC-producing *Klebsiella pneumoniae* ST512 isolated from cerebrospinal fluid of a child in Algeria

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Abstract

We report class A carbapenemase (KPC)-3-producing *Klebsiella pneumoniae* meningitis in a 6-month-old child in Algeria. Multilocus sequence typing showed that the sequence type obtained corresponded to ST512, an allelic single-locus variant of the pandemic ST258 widely distributed in KPC producers from Europe. To our knowledge, this is the first report of KPC-3-producing *K. pneumoniae* ST512 in a North African country.

Keywords: Algeria, Carbapenem resistance, *Klebsiella pneumoniae*, KPC, ST512
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Emergence of carbapenemase-producing Enterobacteriaceae is one of the major problems faced in hospitals worldwide [1]. *Klebsiella pneumoniae* that produce class A carbapenemases (KPC) are frequently identified worldwide [2]. Here, we report what to our knowledge is the first case of infection by *K. pneumoniae* carrying the bla_{KPC} gene isolated from a child in the North African country of Algeria.

In June 2013, a 6-month-old child with hydrocephalus was admitted to neurosurgery ward of Sétif University Hospital, Algeria. After analysis of a cerebrospinal fluid sample, a *K. pneumoniae* isolate was isolated and identified using the API 20E identification system (bioMérieux, Marcy l'Etoile, France) and confirmed by matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (Microflex, Bruker Daltonics, Bremen, Germany).

Antibiotic susceptibility testing performed using the disk diffusion on Mueller-Hinton agar and Etest methods described by the Antibiogram Committee of the French Society for Microbiology (http://www.sfm-microbiologie.org/) showed that the isolate was resistant to most antibiotics tested, including β-lactams, aminoglycosides and fluoroquinolones, with minimum inhibitory concentrations against imipenem, ceftazidime, amikacin and ciprofloxacin of 8 μg/mL, >256 μg/mL, 64 μg/mL and >32 μg/mL, respectively. The isolate remained susceptible to tigecycline and colistin with low minimum inhibitory concentrations (1 and 0.094 μg/mL, respectively). In order to identify the mechanism of resistance to carbapenems, the isolate was screened for the production of carbapenemase encoding genes using phenotypic tests, including the modified Hodge test [3] and the Carba NP test [4], which were both positive. Metallo-β-lactamase activity performed with the EDTA synergy method [3] was negative.

The presence of genes encoding for extended-spectrum β-lactamases (bla_{CTX-M}, bla_{TEM}, bla_{SHV}, bla_{PER}, bla_{VEB}) [5], KPCs (bla_{KPC} [6] and bla_{GES} [7]), class D carbapenemases (bla_{OXA-48} [8]), and metallo-β-lactamases (bla_{NDM-1} [5], bla_{IMP}, bla_{VIM} [9], bla_{SIM} [10], bla_{GIM} [11]) was determined by standard PCR and sequencing. Analysis of β-lactamase genes by PCR revealed the presence of bla_{TEM}, bla_{SHV} and bla_{KPC} genes. The nucleotides sequences of bla_{TEM}, bla_{SHV} and bla_{KPC} genes, when compared to those on record in the National Center for Biotechnology Information database, showed a complete match with bla_{TEM-1}, bla_{SHV-11} and bla_{KPC-3} genes, respectively. Screening for genes encoding aminoglycoside modifying enzymes and 16S rRNA methylase genes demonstrated that the isolate contained *aac(6′)-Ib* and *aadA* genes.

Genotyping of the isolate was performed by multilocus sequence typing (MLST) according to the Pasteur schemes available at Institute Pasteur's MLST Web site (http://www.pasteur.fr/mlst). According to MLST analysis, the *K. pneumoniae* isolate was attributed to sequence type (ST) 512 (allelic profile: 54-3-1-1-1-79), an allelic single-locus variant of the ST258.

To our knowledge, and according to data in the literature, this is the first report of a KPC-producing *K. pneumoniae* in Algeria. KPC was first described in North Carolina, USA, by

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Yigit *et al.* [12] in 2001; since then, it has been reported in other region in the world, including Europe, South America, the Middle East [13] and Africa [14].

Carbapenemase-producing *K. pneumoniae* can cause life-threatening infections, including bacteremia and pneumonia in critically ill patients [15]. Currently, many studies described the detection of *K. pneumoniae* isolates resistant to carbapenems in children. These isolates may cause several infections in children, including bloodstream, respiratory and urinary tract infections [16].

In our study, carbapenem-resistant *K. pneumoniae* was also isolated from a child. Our findings demonstrate that *K. pneumoniae* resistant to carbapenems have become a serious concern in pediatric care and has emerged in North Africa, especially Algeria.

K. pneumoniae ST258 was the most frequently clone associated with KPC-2 or KPC-3 enzyme production [16]. In late 2005, a carbapenem-resistant *K. pneumoniae* ST512, a single-locus allelic variant of ST258, was identified in Israel [17]. In the Mediterranean countries, outbreaks of KPC-producing *K. pneumoniae* have been also reported [2]. In Italy, Pulcrano *et al.* [16] reported an outbreak of a carbapenem-resistant *K. pneumoniae* ST512 carrying the bla_{KPC-3}, bla_{TEM} and bla_{SHV} genes occurring between February 2011 and January 2012. In our study, the *K. pneumoniae* isolated showed the same β-lactamases and sequence type ST512.

In African countries, KPC producers were first identified by Brink *et al.* [14] in 2012, who reported the emergence of KPC-2-producing *K. pneumoniae* in South Africa. To date, there is no report describing the detection of KPC-producing *K. pneumoniae* in the North African countries. In addition, to our knowledge, the presence of the KPC enzyme in other microorganisms was not described in Algeria and in other North African countries. In Algeria, a recent study described the detection of VIM metallo-β-lactamase-producing *K. pneumoniae* [18], but none of the *K. pneumoniae* isolates that produced KPC has been identified in this country.

Emergence of carbapenemase-producing *K. pneumoniae* with a broad-spectrum antibiotic resistance profile limits the antimicrobial therapy options and poses difficulties for patient treatment. The most active agents that can treat carbapenem-resistant *K. pneumoniae* infections remain colistin and tigecycline [15]. These two antibiotics may be a good therapeutic option in such cases.

In summary, this report documents the emergence of KPC-3 among *K. pneumoniae* ST512 clinical isolate for the first time in a North African country, Algeria. Their prevalence may be increasing in North African countries. However, more efforts to control the spread of carbapenemase-producing *K. pneumoniae* and surveillance measures are urgently needed in Algeria.

Conflict of interest

None reported.

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