First Isolate of KPC-2-Producing Klebsiella pneumoniae Sequence Type 23 from the Americas

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KPC-2-producing Klebsiella pneumoniae isolates mainly correspond to clonal complex 258 (CC258); however, we describe KPC-2-producing K. pneumoniae isolates belonging to invasive sequence type 23 (ST23). KPC-2 has scarcely been reported to occur in ST23, and this report describes the first isolation of this pathogen in the Americas. Acquisition of resistant markers in virulent clones could mark an evolutionary step toward the establishment of these clones as major nosocomial pathogens.

CASE REPORT

A 58-year-old man was admitted at the intensive care unit of a hospital in Buenos Aires, Argentina, on 19 March 2013. He presented with poor general condition, sensory impairment, hypotension, poor peripheral perfusion, crackling rales, and desaturation. He had a history of acute myeloid leukemia in 2012 and was currently undergoing chemotherapy with methotrexate (20 mg/week) and prednisone (150 mg/day). Two days after his admission, a methicillin-susceptible Staphylococcus aureus isolate was obtained from a blood culture and a tracheal aspirate (10^8 CFU/ml), and the patient was treated with cefazolin. A week later, the patient developed catheter-associated bacteremia due to methicillin-resistant Staphylococcus epidermidis, and he presented hypermucoviscous tracheal aspirate (10^7 CFU/ml). The general condition of the patient worsened, and the patient died on 19 April.

Antimicrobial susceptibility tests were conducted on K. pneumoniae 3089 according to CLSI guidelines (1). The isolate was resistant to all beta-lactams, including carbapenems, but remained susceptible to aminoglycosides, fluoroquinolones, trimethoprim-sulfamethoxazole, doxycycline, fosfomycin, colistin, and he received linezolid. He presented the most virulent of K. pneumoniae strains belonging to ST23 was a critical factor resulting in their pandemic expansion (6). In our country, a substantial increase of KPC-2-producing K. pneumoniae was observed in 2010, due to the huge dissemination of the hyperemulcosic sequence type 258 (ST258) clone, which displayed a multidrug-resistant phenotype (5, 7, 8). A multilocus sequence typing (MLST) scheme was conducted on K. pneumoniae 3089 (9). Unexpectedly, this strain displayed the following allelic profile: gapA, 2; infB, 1; mdh, 1; pgi, 1; phoE, 9; rpoB, 4; tonB, 12. This profile corresponded to ST23.

K. pneumoniae strains belonging to ST23 correspond to a hyperemulcosic phenotype. Hyperemulcosic strains are associated with a highly invasive syndrome characterized by bacteraemia, liver abscesses, metastatic infections, and even endophthalmitis, suppurative meningitis, and brain abscess (10, 11). The invasive nature of K. pneumoniae ST23 seems to correlate with the hypermucoviscosity that protects from phagocytosis and serum killing by complement. The plasmid-mediated rmpA (regulator of mucoid phenotype A) and magA (mucoviscosity-associated gene A) genes have been associated with this virulent phenotype (12–14). The latter gene, renamed wzyKPC, is a chromosomal gene that is required for exopolysaccharide biosynthesis and is restricted to K. pneumoniae capsule serotype K1, whose strains are considered the most virulent of K. pneumoniae (13). Most of the isolates from patients with K. pneumoniae liver abscess syndrome (KLAS) belong to the K1 serotype and correspond to ST23 (14, 15). Although KLASs are endemic in Taiwan, they have been reported to occur with increasing frequency in other countries in Southeast Asia. They constitute an emerging infectious disease in the United States and Europe; moreover, they were recently reported to occur in Argentina (11, 13, 16). Hyperemulcosic K. pneumoniae isolates, including ST23 clinical strains, have been found to be susceptible to most antibiotics, including third- and fourth-gen-
eration cephalosporins, monobactams, carbapenems, and ciprofloxacin. As K. pneumoniae 3089 exhibited an extreme colony stickiness and rendered a positive string test result (Fig. 2), the presence of magA and rpmA virulence genes was investigated using the following primers (5’ to 3’): wzy-F, CGCCGCAAATACGAGAA GTT; wzy-R, GCAATCGAAGTAGAAGTGGC; rpmA-F, ACTGG GCTACCTGCTTCA; and rpmA-R, CTTGATGAGCCATCT TTC. Both hypermucoviscosity-associated genes were detected in the studied isolate.

Although K. pneumoniae ST23 isolates can be characterized as susceptible to most antibiotics, here we detected the presence of KPC-2 in an isolate belonging to this invasive sequence type. The presence of KPC carbapenemases in K. pneumoniae ST23 has previously been reported to occur only in isolates from China and Poland, in 2010 and 2011, respectively, displaying the same susceptibility profile as K. pneumoniae 3089 (18, 19, 20). However, no single mention of the virulence factors or hypermucoviscosity phenotype was included in those studies.

In the last few months, three more hypermucoviscous K. pneumoniae ST23 isolates have been referred to our laboratory, displaying phenotypes of susceptibility to all antimicrobials except ampicillin. Considering the virulence factors associated with this phenotype and its highly invasive nature, prompt identification and accurate treatment should be mandatory. These strains can be readily detected by the string test, MLST, and molecular characterization of the hypermucoviscous-phenotype-associated genes.

Antibiotics commonly used in K. pneumoniae infections have been useful for the therapeutic treatment of ST23 clinical isolates; however, the acquisition of resistance genes by these invasive strains could hinder the eradication of these strains, probably making the development of metastatic infections favorable.

A rising number of cases of K. pneumoniae ST23 infection in geographic regions other than Southeast Asia indicate that ST23 is a globally emerging pathogen. According to Brisse et al., K. pneumoniae ST23 constitutes an emerging highly virulent and metabolically versatile clone (14), so the acquisition of an important mechanism of antibiotic resistance such as KPC-2 could mark an evolutionary step toward the establishment of K. pneumoniae ST23 as a major cause of nosocomial infections.

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REFERENCES


