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Case Reports

Arch. Esp. Urol. 2016; 69 (7): 437-440

A NEW CASE REPORT OF URINARY TRACT INFECTION DUE TO KPC-3-PRODUCING KLEBSIELLA PNEUMONIAE (ST258) IN SPAIN

Antonio Sorlózano-Puerto[1], David Esteva-Fernández[2], Jesús Oteo-Iglesias[3], José María Navarro-Marí[4], José Gutiérrez-Fernández[1,4].

[1]Departamento de Microbiología, Facultad de Medicina, Universidad de Granada-ibs. Granada.
[2]UGC de Medicina Interna. Complejo Hospitalario Universitario de Granada-ibs. Granada.
[3]Laboratório de Antibióticos, Servicio de Bacteriología, Centro Nacional de Microbiologia. Majadahonda. Madrid.
[4]Laboratorio de Microbiología, Complejo Hospitalario Universitario de Granada-ibs. Granada. España.

Summary.- *OBJECTIVE: We describe the characterization of a new isolated in Spain of Klebsiella pneumoniae ST258 producing KPC-3, carbapenems non-susceptible, recovered from a sample of urine from a patient with urinary tract infection and no history of carbapenems exposure.*

METHODS: After the isolation, identification of K. pneumoniae was performed by biochemical tests and mass spectrometry. The carbapenems susceptibility testing was performed by microdilution and E-test in cation-adjusted Mueller-Hinton. The study was completed by Rapidec® Carba NP. In order to determine the genetic basis of resistance to carbapenems we used Xpert® Carba-R for carbapenemase type and subtype was subsequently analyzed by amplification by PCR and sequencing.

RESULT: We demonstrated by MLST that the strain belonged to the clone of high-risk ST258.

CONCLUSIONS: This is the first characterization, in our media, of a clinical isolated of K. pneumoniae ST258 producing KPC-3 and no history of carbapenems exposure.

Keywords: *Klebsiella pneumoniae. Carbapenemase. ST258.*

Resumen.- *OBJETIVO: Presentamos la caracterización de un nuevo aislado en España de Klebsiella pneumoniae ST258 productor de KPC-3, no sensible a carbapenémicos, recuperado de una muestra de orina de una paciente con infección del tracto urinario y sin antecedentes de exposición previa a carbapenémicos.*

MÉTODOS: Tras el aislamiento, la identificación de K. pneumoniae fue realizada mediante pruebas bioquímicas y espectrometría de masas y la prueba de sensibilidad a carbapenémicos se realizó mediante microdilución y E-test en Mueller-Hinton ajustado para cationes. El estudio se completó mediante Rapidec® Carba NP. Con el fin de determinar las bases genéticas de la resistencia a carbapenémicos se analizó el tipo de carbapenemasa mediante Xpert® Carba-R, posteriormente se subtipo mediante amplificación por PCR y secuenciación.

RESULTADO: Mediante MLST, se demostró que la cepa pertenecía al clon de alto riesgo ST258.

CONCLUSIONES: Esta es la primera caracterización en nuestro medio de un aislado clínico de K. pneumoniae ST258 productor de KPC-3, sin antecedentes de exposición previa a carbapenémicos.

Palabras clave: *Klebsiella pneumoniae. Carbapenemasa. ST258.*

CORRESPONDENCE

José Gutiérrez-Fernández
Laboratorio de Microbiología
Avenida de las Fuerzas Armadas, 2.
18012 Granada (Spain)

josegf@go.ugr.es

Accepted for publication: May 10th, 2016

INTRODUCTION

Carbapenems are among the most effective treatments for Gram-negative bacterial infections, especially in hospitalized patients (1). However, the presence of carbapenemase-producing bacteria, which frequently possess genes resistant to other antibiotics, beta-lactam or not, limit the therapeutic options and increase morbidity and mortality (2,3). The most clinically relevant carbapenemases are KPCs (Ambler class A), IMP/VIM/NDM (class B), and OXA-48 (class D) (4). KPC

enzymes in *Klebsiella* spp., other *Enterobacteriaceae*, or *Pseudomonas* spp. (4,5), have spread worldwide, including various European countries (1). Although the increased prevalence in Spain is due to the presence of *K. pneumoniae*, producer of OXA-48 or VIM-1, there has been a small increase in KPC-type carbapenemases (6). We report a case of urinary tract infection by KPC-producing *K. pneumoniae* with lethal development.

CASE REPORT

A 90-yr-old female was admitted to the Internal Medicine Department in October 2015 with a diagnosis of community-acquired pneumonia (PCR=183.78mg/L on admission). She presented with atrial fibrillation and moderate heart and kidney failure and had a history of hypertensive heart disease. She had been treated with levofloxacin and prednisone for 48 h prior to admission. At admission, the fluoroquinolone was replaced with intravenous amoxicillin-clavulanic acid and she was catheterized for three days. After a clinical improvement, she was discharged at six days post-admission (PCR=20.13 mg/L). One week later, she was readmitted for respiratory infection of probable nosocomial origin. Treatment was initiated with ceftriaxone, moxifloxacin, and methylprednisolone, and she was again catheterized. Antibiotics were withdrawn at 11 days post-admission

Table I. Antibiotic susceptibility of carbapenemase-producing Klebsiella pneumoniae, according to the MicroScan system and E-test.

Antibiotic	MIC (in µg/ml)	Clinical category
Ampicillin	>16	R
Ticarcillin	>64	R
Amoxicillin/clavulanic acid	>16/8	R
Ampicillin/sulbactam	>16/8	R
Piperacillin/tazobactam	>64/4	R
Cefazolin	>16	R
Cefuroxime	>16	R
Cefoxitin	>16	R
Cefotaxime	>32	R
Ceftazidime	>32	R
Cefepime	>16	R
Imipenem	>8 (>32)*	R
Ertapenem	>1 (>32)*	R
Meropenem	>8 (>32)*	R
Aztreonam	>16	R
Gentamicin	2	S
Tobramycin	>8	R
Amikacin	32	I
Norfloxacin	>8	R
Ciprofloxacin	>2	R
Levofloxacin	>4	R
Nitrofurantoin	>64	R
Fosfomycin	≤16	S
Trimethoprim/sulfamethoxazole	>4/76	R
Colistin	≤2	S
Minocycline	≤4	S
Tigecycline	1	S

** MIC (minimum inhibitory concentration) by the E-test.*

after a favorable progression (PCR=86.87 mg/L at 3 days post-admission and PCR=12.76 mg/L at 10 days) and the disappearance of respiratory infection symptoms. Four days later, however, she developed a high fever with no apparent clinical focus (PCR=59.31 mg/L). Samples were taken for microbiological analysis for the first time (in either hospitalization), and meropenem was prescribed as empirical treatment. As shown in the table, a significant count of multiresistant *K. pneumoniae* was recorded in urine (obtained via catheter), and the patient was isolated and intravesically instilled with colistin. Her condition progressively deteriorated (PCR=231.66 mg/L) due to sepsis, and she died from acute lung edema after a worsening of heart and liver failure.

The MicroScan system (Siemens Healthcare Diagnostics, Madrid, Spain) was used for identification and antibiogram, and mass spectrometry (Biotyper®, Bruker Daltonics, USA) for confirmation. Carbapenemase presence was screened using Rapidec® Carba NP (Biomerieux. Marcy l'Etoile. France) and the E-test. The carbapenemase was identified as KPC with the Xpert® Carba-R test (Cepheid Europe, Maurens-Scopont, France) The genotype was characterized by PCR amplification and sequencing, identifying the bacteria as KPC-3-producing *K. pneumoniae*.

Multilocus Sequence Typing (MLST) was performed as recommended by the Pasteur Institute (http://www.pasteur.fr/recherche/genopole/PF8/mlst/Kpneumoniae.html; access in January 2016) and revealed that the strain belonged to high-risk clone ST258, which has been described as the main cause of KPC carbapenemase dissemination in *K. pneumoniae* worldwide (6) but has only been sporadically reported in Spain (7).

DISCUSSION

The first outbreak in Spain of KPC-3-producing *K. pneumoniae* belonging to the ST512 clone, a single locus variant (SLV) of ST258, was recently reported in Cordoba (2). Infections by KPC-producing *K. pneumoniae* are an emerging problem worldwide, with elevated associated mortality rates. However, they are highly heterogeneous and influenced by patient age, immune status, comorbidities, infection type/severity, and isolate resistance phenotype, among other factors (2,3,8,9). The mortality associated with KPC production is significantly higher than the mortality for infections by *K. pneumoniae* that do not produce this enzyme (10).

In Spain, there have been reports of sporadic cases related to visits to endemic areas in Europe (e.g., Greece or Italy), hospital stays, or previous exposure to antibiotics (3,4,9). Available records for the present patient revealed two hospital admissions and the receipt of antibiotic treatment with fluoroquinolones and non-carabapenem beta-lactams before detection of the bacteria, and she was catheterized in both hospitalizations. However, there was no history of visits beyond her residential area or of previous stays in other hospitals or localizations, and none of these risk factors were reported by relatives, cohabitants, or attending healthcare professionals. Given that no KPC isolates have previously been detected in patients in our hospital, an epidemiological relationship cannot be established.

Key immunosurveillance responsibilities of hospital microbiology departments include the early detection and phenotype (and molecular) characterization of multirresistance bacteria, such as KPC-type carbapenemase-producing bacteria, and the prompt communication of findings to healthcare professionals, due to their clinical repercussions and poor prognosis, thereby minimizing the risk of therapeutic failure.

CONCLUSIONS

This is the first characterization in our setting of a clinical isolate of KPC-3-producing *K. pneumoniae* ST258 in a patient with no history of previous exposure to carbapenems.

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