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Letter to the Editor

First reported case of an OXA-48-producing isolate from a Colombian patient

Sir,

OXA-48 is a class D β-lactamase that strongly hydrolyses penicillins but has a low level of hydrolytic activity against carbapenems, with much greater activity against imipenem than meropenem [1]. This enzyme was first identified in a carbapenem-resistant *Klebsiella pneumoniae* isolate from Turkey in 2004, and subsequently has been mainly reported in Enterobacteriaceae, particularly in countries surrounding the Mediterranean area. In South America, this enzyme has been only reported in Argentina and Brazil [2].

We describe the first reported case of an OXA-48-producing *Klebsiella oxytoca* isolate from Colombia. In January 2015, a 75-year-old woman was admitted to a tertiary care centre in Medellín, Colombia, with abundant secretion of faecal matter through the infraumbilical skin for a week and a history of diabetes mellitus type 2.

Her medical record included previous hospitalisation in two different institutions but no travel history to other countries in the last year. Two years previously the patient had surgery for an umbilical hernia and since then she has had secretion through an enterocutaneous fistula and multiple abdominal surgeries.

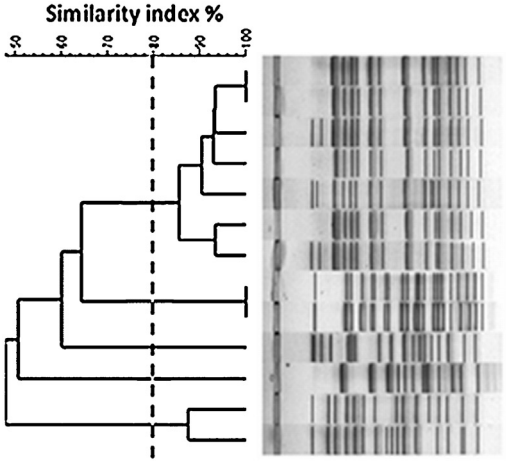
Examination revealed an enterocutaneous fistula with faecal material and surrounding erythema. A central venous catheter (CVC) was placed to initiate parenteral nutrition. C-reactive protein was 12.9 mg/L, thus ampicillin/sulbactam was administered empirically and abdominal computed tomography (CT) was performed to evaluate abscesses that could be drained, which were not observed.

After 2 weeks of hospitalisation, chest radiography showed basal infiltrates tending to consolidation, and cefepime and vancomycin were administered due to nosocomial pneumonia.

In the 20 days of hospitalisation, the CVC was withdrawn because of signs of local infection and the patient presented glycaemia (37 mg/dL) of unknown duration. Metabolic encephalopathy was suspected and cefepime was changed to meropenem for torpid evolution of respiratory symptoms. The patient was transferred to the intensive care unit (ICU), where rectal screening for carbapenem-resistant Enterobacteriaceae was performed at admission as a part of a surveillance programme in this service. Although the result was negative, after 5 days of hospitalisation in the ICU a new rectal screening was performed and *K. oxytoca* was isolated. Identification of the isolate, antimicrobial drug susceptibility testing and extended-spectrum β-lactamase (ESBL) detection were assessed in accordance with Clinical and Laboratory Standards Institute (CLSI) 2014 guidelines using a VITEK®2 system (bioMérieux, Marcy l'Étoile, France) and disk diffusion. The presence of carbapenemases was evaluated by the modified Hodge test (MHT) performed according to the CLSI protocol. The isolate was resistant to imipenem, ertapenem, ceftazidime, ceftriaxone, ampicillin/sulbactam and gentamicin, was intermediate to piperacillin/tazobactam and doripenem, and was susceptible to meropenem, amikacin, ciprofloxacin, cefoxitin, cefepime and tigecycline. The MHT and ESBL test were positive.

The patient remained in hospital with signs of metabolic encephalopathy and hypoactivity and died after 39 days of hospitalisation.

The *K. oxytoca* isolate was sent to Universidad de Antioquia (Medellín, Colombia) for molecular confirmation of carbapenemases using multiplex PCR as previously described [3]. Sequence



ISOLATE	CARBAPENEMASE	DATE (MM/DD/YY)	WARD
CAR106	KPC	02/21/15	9 south
CAR110	KPC	02/20/15	3 south
CAR111	KPC	02/20/15	3 south
CAR112	KPC	03/04/15	3 south
CAR109	KPC	02/18/15	3 south
CAR113	KPC	02/20/15	3 south
CAR114	KPC	03/02/15	3 south
CAR102	KPC	02/28/15	9 south
CAR103	KPC	03/02/15	9 south
CAR108	KPC	03/11/15	9 south
CAR105	OXA-48	02/11/15	2 north
CAR104	KPC	02/17/15	9 south
CAR107	KPC	02/22/15	9 south

Fig. 1. Genetic relatedness of *Klebsiella oxytoca* isolates by pulsed-field gel electrophoresis (PFGE) using the restriction enzyme *Xba*I. The broken line corresponds to the cut-off level (80%) used to define clones as related.

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analysis was performed using BLAST (http://www.ncbi.nlm.nih.gov/BLAST/) and presence of the bla_{OXA-48} gene was confirmed.

At the time of isolation (11 February 2015), a cluster of carbapenem-resistant *K. oxytoca* had just been reported, consisting of 12 strains isolated in other wards of the hospital during February and early March 2015. Pulsed-field gel electrophoresis (PFGE) analysis with *Xba*I digestion (20 U) revealed that the OXA-48-producing strain exhibited a unique PFGE pattern, unrelated to those exhibited by the other 12 isolated strains, which were classified into four distinct patterns and were found to produce KPC-type carbapenemases (Fig. 1).

Infection and colonisation by OXA-48-producing isolates has been associated with travel to endemic countries, but the patient described here had no history of travel to another country and the source of the isolate was unknown [4]. In addition to circulation in hospitals and colonisation in the community, OXA-48-producing isolates have been found in dogs and wastewater treatment plants, representing potential infection sources [2].

The emergence of OXA-48-producing isolates is important because the carbapenem resistance may spread among other Enterobacteriaceae [4]. Moreover, the simultaneous presence of OXA-48 and other resistance mechanisms such as ESBL leads to a significant reduction of effective antimicrobial options, poor prognosis and the need to use colistin-based combined therapy to achieve a better outcome [2].

Detection in the laboratory of OXA-48 may be difficult because this enzyme hydrolyses penicillins at a high level but hydrolyses carbapenems only at a low level. In addition, it shows very weak activity against expanded-spectrum cephalosporins [2]. Another problem is the absence of a phenotypic test for identification. The MHT has shown good sensitivity, but molecular techniques such as PCR are necessary for its confirmation [2].

In Colombia, KPC carbapenemases are endemic among Enterobacteriaceae and other Gram-negative bacilli such as *Pseudomonas aeruginosa*. Likewise, other carbapenemases such as VIM, OXA-23 and NDM have also been reported [5]. Suspicion from the resistance profile and early detection of OXA-48-producing isolates are necessary for adequate epidemiological surveillance of carbapenem resistance in countries such as Colombia, where there is a high consumption of carbapenems and resistance rates are >30%.

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Competing interests

None declared.

Ethical approval

The main project protocol was approved by the Bioethics Committee for Human Research at Universidad de Antioquia (CBEIH-SIU) (Medellín, Colombia) [approval no. 11-35-415].

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