Emergence of *Klebsiella pneumoniae* ST258 with KPC-2 in Hong Kong

Ho PL,*[1] Cindy WS Tse,[2] Eileen L. Lai,[1] W.U. Lo,[1] KH Chow[1]

[1]Department of Microbiology, The University of Hong Kong, and [2]Department of Clinical Pathology, Kwong Wah Hospital, Hong Kong SAR, CHINA

Correspondance to

Pak-Leung Ho, MD, FRCPath

plho@hkucc.hku.hk

Sir,

The emergence of carbapenemase-mediated resistance to all the β-lactam, including the carbapenem is a major public health threat. In *Enterobacteriaceae*, one of the most frequent carbapenemases is the *Klebsiella pneumoniae* carbapenemase (KPC) enzymes [1-3]. Since the first KPC-producing isolate was identified from North Carolina, United States in 1996, occurrence of KPC-producing bacteria have been reported in other parts of the United States, Europe, South America, the Middle East and Asia [1,2]. In September 2010, Hong Kong set up an enhanced surveillance system for detection of carbapenem-resistant Enterobacteriaceae; following recent concerns that the transmission of these extensively resistant organisms may be associated with medical tourism or surgery abroad in areas where they are endemic [1-3]. In all the public hospitals, all newly admitted patients with potential risk factors for carbapenem-resistant Enterobacteriaceae (e.g. overseas hospitalization) will be actively screened for colonization. In clinical microbiology laboratories, all carbapenem-resistant Enterobacteriaceae isolates will be assessed for carbapenemase activity using inhibition tests with boronic acid and ethylene diamine tetra-acetic acid (EDTA) [1]. Isolates with positive carbapenemase screen test will be sent to the public health laboratory for molecular characterization. Additionally, strains of carbapenem-resistant Enterobacteriaceae previously stored in MicroBank (Pro-Lab Diagnostics Inc., Canada) at -80 ^{o}C in a regional hospital in Hong Kong were retrieved for testing. This lead to the retrospective identification of the first case of KPC-producing *K. pneumoniae* in Hong Kong and the findings were reported here.

In August 2006, a multidrug-resistant *Klebsiella pneumoniae* isolate was recovered from the mid-stream urine sample of a 75 year old lady who attended an outpatient clinic for follow-up. She has history of diabetes mellitus, hypertension and atrial fibrillation. Patient travelled to the United States frequently and sometimes had medical follow up there. Past

health was relevant for a history of cholecystectomy in New York, United States in July 2005. She was totally asymptomatic with no fever or any urinary symptom. Her WBC count was normal. No antibiotic was given. Personal hygiene was advised. The isolate was identified as *K. pneumoniae* using a Vitek system (GNI, bioMerieux, Hazelwood, USA). Disc diffusion test showed that the isolate was resistant to cephalosporins (ceftriaxone, ceftazidime, cefepime), beta-lactam-β-lactamase inhibitor combinations (amoxicillin-calvulanate, piperacillin-tazobactam), imipenem, ciprofloxacin, chloramphenicol, aminoglycosides (amikacin, gentamicin, and netilmicin), nitrofurantoin, and cotrimoxazole at the CLSI breakpoints [4]. For these drugs, there was no inhibition zone or very small inhibition zone around the discs. The MIC for the following drugs was determined by Etest (AB Biodisk, Solna, Sweden): meropenem (32 μg/ml, resistant), imipenem (32 μg/ml, resistant), fosfomycin (24 μg/ml, sensitive) and colistin (0.38 μg/ml, sensitive).

The isolate was retrieved and tested for primers specific for the KPC genes. A positive PCR result was obtained. Subsequent sequencing showed that a KPC-2 gene was carried by the isolate. In order to identify the genetic background of this strain, the organism was characterized by multilocus sequencing (MLST) [2,3]. This strain has an allelic profile 3-3-1-1-1-1-79 (gapA-infB-mdh-pgi-phoE-rpoB-tonB), corresponding to ST258. In the United States, this clone has disseminated widely and accounted for 70% of the national collection from 1996 to 2008 [2]. In contrast, the dominant KPC clone in mainland China is an ST11 variant with the allelic profile 3-3-1-1-1-1-4 [3]. The finding suggests that our patient has likely acquired the organism from the United States during her previous travel visits.

This case raises several important issues. Firstly, the importation of multidrug-resistant bacteria, such as carbapenem-resistant Enterobacteriaceae among patients with history of medical treatment abroad may be underestimated. Kennedy et al reported that colonization with *E. coli* resistant to gentamicin, ciprofloxacin and/or third generation cephalosporins

increased from 7.8% at baseline to 49% after international travel [5]. In 18% of the individuals, prolonged colonization for over 6 months occurred [5]. These individuals may act as reservoirs for infection within the community or sources of outbreak when they are hospitalized [2,3,5]. In many countries, there are no national guidelines for admission screening of individuals who have history of medical treatment abroad. Secondly, the optimal treatment for invasive carbapenem-resistant Enterobacteriaceae infections is uncertain and is complicated by the frequent occurrence of co-resistance to many other antibiotics. The agents that are potentially active against carbapenem-resistant Enterobacteriaceae are colistin, tigecycline, fosfomycin and isepamicin. In solid organ and bone marrow transplant recipient, infections by these organisms represent tremendous threat. In response to these challenges, hospitals in Hong Kong have recently introduced active screening for carbapenem-resistant Enterobacteriaceae carriage at hospital admission. Under the arrangement, all newly admitted patients with history of hospitalization, surgery or dialysis in an overseas institution in the previous 12 months would be screened.

Declarations

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