

# First Identification of a Patient Colonized With *Klebsiella pneumoniae* Carrying *bla*<sub>NDM-1</sub> in Taiwan

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New Delhi metallo-β-lactamase 1 (NDM-1) is a novel type of metallo-β-lactamase (MBL). *Enterobacteriaceae* carrying this NDM-1 encoding gene, *bla*<sub>NDM-1</sub>, have been identified worldwide. Bacteria carrying *bla*<sub>NDM-1</sub> are not only resistant to carbapenem, but also highly resistant to many classes of antibiotics, which indicate the importance of prompt identification of these bacteria and implementation of strict infection control measures to prevent their transmission. Here, we report the first identification and management of a patient colonized with *Klebsiella pneumoniae* carrying *bla*<sub>NDM-1</sub> in Taiwan, who returned from New Delhi where he had been hospitalized for a gun-shot injury. [*J Chin Med Assoc* 2010; 73(11):596–598]

**Key Words:** antibiotics, drug resistance, *Enterobacteriaceae*, New Delhi metallo-β-lactamase 1, Taiwan

## Introduction

A novel type of metallo-β-lactamase (MBL), New Delhi metallo-β-lactamase 1 (NDM-1), was first identified in a *Klebsiella pneumoniae* isolated from a Swedish patient who had been admitted to an Indian hospital in 2009.<sup>1</sup> Since then, *Enterobacteriaceae* carrying this novel MBL have been identified worldwide,<sup>2,3</sup> especially in patients with a traveling history to or a hospitalization history in India or Pakistan.<sup>2</sup>

*Enterobacteriaceae* carrying the gene encoding NDM-1, *bla*<sub>NDM-1</sub>, are not only resistant to carbapenem, but also highly resistant to many classes of antibiotics due to the coexistence of multiple resistant mechanisms.<sup>2</sup> The *bla*<sub>NDM-1</sub> is located on large plasmids with various sizes.<sup>1</sup> Most of the plasmids carrying *bla*<sub>NDM-1</sub> could readily be transferred to *Escherichia coli*,<sup>2</sup> and may also be transferred to other *Enterobacteriaceae*. To date, *Enterobacteriaceae* that have been found to carry *bla*<sub>NDM-1</sub> include *K. pneumoniae*, *K. oxytoca*, *E. coli*, *Enterobacter cloacae*, *Proteus* spp., *Citrobacter freundii*, *Morganella morganii* and

*Providencia* spp.<sup>3</sup> In addition to the dissemination of *bla*<sub>NDM-1</sub> via plasmid spreading, some *K. pneumoniae* isolates carrying *bla*<sub>NDM-1</sub> were clonal, indicating that these strains have the potential to cause epidemics.<sup>2</sup> A worrisome condition is that *bla*<sub>NDM-1</sub> has also been found in *Acinetobacter baumannii*, which is notorious for its intrinsic multidrug resistance.<sup>4</sup> These conditions indicate the importance of prompt identification of bacteria carrying *bla*<sub>NDM-1</sub> and implementation of strict infection control measures, especially for patients returning from endemic areas,<sup>3</sup> to prevent its transmission in the hospital setting. Here, we report the first identification and management of a patient colonized with *K. pneumoniae* carrying *bla*<sub>NDM-1</sub> in Taiwan.

## Case Report

A 38-year-old Taiwanese man, with irrelevant past history, suffered from gun-shot injury to his right lateral abdominal wall on the 2<sup>nd</sup> day after arriving in New Delhi. He received hepatorrhaphy, right



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hemicolectomy with primary anastomosis and transiently stayed in the intensive care unit at a medical center in Delhi for 8 days. He was then repatriated to Taiwan and was admitted to Taipei Veterans General Hospital. At presentation, he was well in appearance, afebrile, and with stable hemodynamic status. On examination, there were 2 insertion sites for prior drainage tubes with some discharge over the right and left lower quadrants of the abdomen, and a well-healed surgical wound over the central abdomen; otherwise, there were no remarkable abnormalities.

Laboratory investigations showed a white blood cell count of 13,800/mm<sup>3</sup> (with 68.2% neutrophils), hemoglobin of 13.8 mg/dL, platelet count of 468,000/mm<sup>3</sup>, blood urea nitrogen of 12 mg/dL, creatinine of 0.98 mg/dL, and glucose of 95 mg/dL. Due to his traveling and hospitalization history, he was admitted to a single isolated room for close monitoring. The health care providers followed strict contact precaution measures while caring for this patient. Urine, stool and pus cultures were sent to the Centers for Disease Control (CDC) of Taiwan for surveillance of bla<sub>NDM-1</sub>-harboring bacteria. *K. pneumoniae* isolates carrying bla<sub>NDM-1</sub> were isolated from 2 consecutive fecal samples from anal swabs. The bla<sub>NDM-1</sub> was detected by PCR with the use of previously described primers<sup>1</sup> and verified by gene sequencing and analysis.

After hospitalization for 5 days, the patient's wounds were completely healed. He was discharged in a stable condition and in accordance with the suggestion from the Taiwan CDC. His fecal samples will be screened weekly by the Taiwan CDC for bla<sub>NDM-1</sub>-carrying bacteria until the results come back negative.

## Discussion

It is currently unknown where and how the patient acquired *K. pneumoniae* with bla<sub>NDM-1</sub>. A molecular epidemiological study comparing the strain from this patient with reported strains from India might provide a clue as to its origin. Nevertheless, the results from our case imply that implementation of systematic surveillance and control measures for patients (even asymptomatic ones) from endemic areas may be beneficial in preventing the spread of carbapenem-resistant bacteria. However, this approach may become problematic when the number of endemic areas grows rapidly.<sup>3</sup>

Most bla<sub>NDM-1</sub>-carrying *Enterobacteriaceae* are isolated from patients with urinary tract infection, pneumonia or bloodstream infections.<sup>2</sup> Although detailed information regarding the therapy of such patients has not been reported, to date, only 1 patient was reported

to have succumbed to the infection,<sup>3</sup> indicating that bla<sub>NDM-1</sub>-carrying *Enterobacteriaceae* might not be as virulent as their counterparts. In addition, these bacteria can be isolated from asymptomatic patients.<sup>1</sup> Our patient did not have symptoms and signs of infection during his hospitalization, suggesting that the bacterium is most likely a colonizer.

To date, it remains unresolved as to how long a patient colonized with carbapenem-resistant *Enterobacteriaceae* (CRE) should be managed under contact precautions.<sup>5,6</sup> There is no recommendation to quarantine the asymptomatic patient harboring CRE, either in hospital or in the community setting. Neither is there any suggestion with regard to decolonization of these carbapenem-resistant bacteria due to limited treatment options (polymyxins, tigecycline) and insufficient data to warrant their routine use.<sup>6</sup> However, infection control and prevention measures, such as education of staff and patients, environmental sterilization, surveillance, and contact precautions, should be vigorously reinforced when caring for these patients.<sup>6</sup> Since *K. pneumoniae* is a commensal bacterium, it is currently unknown how long this bacterium carrying bla<sub>NDM-1</sub> will colonize the human gut. A periodic culture of fecal samples may be helpful in answering this question.

The importation and spread of bacteria carrying bla<sub>NDM-1</sub> to Taiwan is foreseeable due to globalization<sup>3</sup> with heavy international travel and the characteristics of the bacteria, which are commensal flora in asymptomatic patients. However, systematic surveillance and infection control measures in patients with high risk of acquisition might thwart their transmission. As the first case colonized with bacteria carrying bla<sub>NDM-1</sub> appeared in Taiwan, the public health department, administrative department, and clinicians should be reminded and be organized to implement a disciplinary protocol to monitor the possibility of an epidemic, and to limit the impact of the emergent medical challenge.

## References

1. Yong D, Toleman MA, Giske CG, Cho HS, Sundman K, Lee K, Walsh TR. Characterization of a new metallo-beta-lactamase gene, bla<sub>NDM-1</sub>, and a novel erythromycin esterase gene carried on a unique genetic structure in *Klebsiella pneumoniae* sequence type 14 from India. *Antimicrob Agents Chemother* 2009;53: 5046–54.
2. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, Chaudhary U, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* 2010;10:597–602.

3. Rolain JM, Parola P, Cornaglia G. New Delhi metallo-beta-lactamase NDM-1: towards a new pandemic? *Clin Microbiol Infect* 2010 [doi:10.1111/j.1469-0691.2010.03385.x]
4. Karthikeyan K, Thirunarayan MA, Krishnan P. Coexistence of *bla*<sub>OXA-23</sub> with *bla*<sub>NDM-1</sub> and *armA* in clinical isolates of *Acinetobacter baumannii* from India. *J Antimicrob Chemother* 2010; 65:2253-4.
5. Centers for Disease Control and Prevention (CDC). Guidance for control of infections with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* in acute care facilities. *MMWR Morb Mortal Wkly Rep* 2009;58:256-60.
6. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Management of multidrug-resistant organisms in health care settings, 2006. *Am J Infect Control* 2007;35:S165-93.