

Local acquisition and nosocomial transmission of *Klebsiella pneumoniae* harbouring the *bla*_{NDM-1} gene in Australia

The emergence of carbapenem-resistant Enterobacteriaceae constitutes a critical global issue. Isolates harbouring the metallo-β-lactamase gene *bla*_{NDM-1} have few available treatment options. We report a case of an Australian adult with a locally acquired, community-onset *bla*_{NDM-1} *Klebsiella pneumoniae* infection and likely nosocomial transmission to another patient.

Clinical records

Patient A, a 68-year-old Australian-born woman living with her husband and son, had never travelled overseas and had no known contact with overseas visitors. Her past history included chronic bilateral lymphoedema with recurrent lower limb cellulitis, requiring multiple previous hospital admissions and home nursing care. She presented with septic shock and right leg erythema surrounding a 10×10 cm ulcer near the right lateral malleolus. Magnetic resonance imaging showed bony oedema and enhancement in the lateral malleolus, suggestive of osteomyelitis. *Pseudomonas aeruginosa* was isolated from blood cultures. A tissue biopsy from the overlying ulcer cultured *P. aeruginosa*, non-multiresistant methicillin-resistant *Staphylococcus aureus* (NORSA), and carbapenem-resistant *Klebsiella pneumoniae*, resistant to all first-line antimicrobials tested and susceptible to only colistin and fosfomycin.

She was given intravenous ceftazidime and vancomycin for treatment of *P. aeruginosa* and NORSA infection. After 6 weeks of treatment, the ulcer was not healing, and treatment for the carbapenemase-producing *K. pneumoniae* was commenced with intravenous colistin methanosulfonate (120 mg colistin base activity 12-hourly). Colistin was ceased after 3 weeks owing to acute kidney injury, and oral fosfomycin (3 g every 3 days) was administered for a further 6 weeks, in addition to oral ciprofloxacin and rifampicin for ongoing treatment of NORSA and *P. aeruginosa* infection. Since the cessation of her antibiotics, she has not required further antibiotic treatment of her ulcers.

Patient B, a 35-year-old Australian-born man with no history of overseas travel, was admitted with bilateral thigh cellulitis and septic shock. He had bilateral thigh debridement, with no evidence of necrotising fasciitis. Methicillin-susceptible *S. aureus* (MSSA) was isolated from multiple blood cultures. MSSA and *Serratia liquefaciens* were isolated from a thigh wound swab culture. Transthoracic echocardiogram revealed a left ventricular thrombus. He was commenced on intravenous flucloxacillin and ciprofloxacin. Two weeks after admission, further surgical samples from his thigh wounds cultured carbapenem-resistant *K. pneumoniae*, with similar antimicrobial susceptibility phenotype to Patient A. The

isolate was deemed to be colonising the wound only, and no antimicrobials were commenced for treatment.

Both *K. pneumoniae* isolates demonstrated carbapenemase activity using the Carba NP assay.¹ Molecular tests using polymerase chain reaction and sequencing for carbapenemase, extended-spectrum β-lactamase, plasmid-mediated AmpC β-lactamase and 16S ribosomal RNA methylase genes were performed as described elsewhere.² The metallo-β-lactamase gene *bla*_{NDM-1} was detected in both isolates, in addition to *bla*_{CTX-M-15} and 16S ribosomal RNA methylases (*armA* and *rmtB*), which confer resistance to aminoglycosides, including amikacin. The relatedness of isolates was determined by semi-automated repetitive sequence-based polymerase chain reaction using a DiversiLab *Klebsiella* kit (bioMérieux). This analysis showed a >95% genetic similarity between the two isolates. Further, the isolates were genetically distinct from two *bla*_{NDM-1}-harbouring isolates that we isolated previously in patients with a history of overseas travel.

Patients A and B were admitted in December 2013 to a high dependency unit (HDU) — a four-bed area separated by curtains. They were one bed apart for 5 days before being moved adjacent to each other for 1 day, with Patient B occupying the bed cubicle space formerly occupied by Patient A for a further 5 days. The carbapenem-resistant *K. pneumoniae* was first identified in Patient A in the HDU, and 2 weeks later was isolated from Patient B.

After detection of the carbapenem-resistant *K. pneumoniae*, strict contact precautions were implemented. Environmental cleaning of the four-bed HDU and other rooms occupied by Patients A and B was undertaken with microfibre and steam cleaning, which has been shown to be an effective cleaning method.³ An exposure investigation was conducted, with environmental sampling and screening rectal swabs collected from all direct patient contacts of Patients A and B inoculated on chromogenic selective media. No other carbapenem-resistant organisms containing *bla*_{NDM-1} were isolated from clinical, screening or environmental samples.

Discussion

The metallo-β-lactamase gene *bla*_{NDM-1} was first described in a patient hospitalised in Sweden after travel to India in

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2008⁴ and subsequently identified in a series of patients in the United Kingdom, many of whom had travelled to the Indian subcontinent.⁵ There have been documented cases of infection with imported *bla*_{NDM-1}-containing bacteria in Australia.⁶⁻¹⁰ These carbapenem-resistant bacteria are challenging to treat, as available treatment options are often limited to infrequently used drugs such as colistin, fosfomycin and tigecycline.

The case of Patient A has significant public health ramifications as the first detection of carbapenem-resistant *bla*_{NDM-1}-harbouring *K. pneumoniae* infection locally acquired in Australia, independent of international travel or documented contact with a traveller. The case suggests that there may be more cases of *bla*_{NDM-1}-harbouring bacteria in our community than previously suspected. We hypothesise that this carbapenem-resistant Enterobacteriaceae isolate was acquired after transmission from an unidentified carrier of *bla*_{NDM-1} possibly during previous hospital admissions or receipt of home nursing care.

The transmission from Patient A to Patient B may have occurred via a number of mechanisms. First, environmental contamination may have contributed, given that both patients shared the same bed area at different times. We previously reported an outbreak of

carbapenem-resistant Enterobacteriaceae harbouring the metallo- β -lactamase gene *bla*_{IMP-4'} associated with contaminated sinks in an intensive care unit; in that case, no carbapenem-resistant organisms containing *bla*_{NDM-1} were isolated from environmental samples.¹¹ The second possible contributing factor for transmission is lapses in infection control practices by health care staff, which emphasises the importance of adhering to standard precautions such as hand hygiene.¹²

These cases highlight the evolving Australian epidemiology of multidrug-resistant organisms, particularly bacteria harbouring *bla*_{NDM-1}. Such resistance is no longer exclusively associated with obvious international travel. There is an increasing need for effective antimicrobial stewardship and infection control measures to prevent potential future nosocomial spread of these organisms. In addition, further research and surveillance is needed in monitoring these local isolates to identify potential risk factors for local acquisition and any reservoirs within the Australian health system and community.

Competing interests: No relevant disclosures.

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