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CASE REPORT

The growing threat of carbapenem resistant enterobacteriaceae (CRE) within in-patient spinal rehabilitation units

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This case report highlights the present threat and challenges with treatment and transmission of infections caused by carbepenem-resistant enterobacteriaceae (CRE) within in-patient spinal rehabilitation units. The setting is within the Spinal Cord Injury Unit, Royal North Shore Hospital, Sydney, Australia. We report the case of a 45-year-old female with T9 complete paraplegia who developed CRE urinary tract infection (UTI) and sepsis 1 month post injury while in an in-patient spinal rehabilitation unit. We describe the challenges in treatment with colistin, the implications of infection on her rehabilitation and challenges in containing the spread of CRE to other patients in the unit. We present our experience with the management of CRE bactaeraemia in a spinal rehabilitation unit and the enhanced importance of infection control and surveillance strategies required to successfully contain risk of transmission.

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INTRODUCTION

Carbapenem-resistant enterobacteriaceae (CRE), which are resistant to most types of antibiotics, are now a growing threat.[1,2] CRE are more likely to affect patients with poor functional status, prolonged hospital stay, multiple exposures to different antibiotics, prior mechanical ventilation, admission to an intensive care unit, indwelling medical devices such as indwelling catheter (IDC), diabetes mellitus and travel to areas where CRE is endemic.[2,3] Most in-patients in spinal cord injury units have at least six if not more risk factors, placing them at significantly high risk for CRE.

CASE REPORT

We present our challenges with CRE in the Spinal Cord Injury Unit at Royal North Shore Hospital in Sydney, Australia. Our in-patient rehabilitation unit is part of an acute care hospital. The unit consists of 6 single-person occupancy/isolation rooms with *en suite* bathrooms and 13 shared rooms with shared bathrooms. Equipment including wheelchairs and shower commodes are often shared between patients. There is a common gymnasium and occupational therapy and activities of daily living room which is used by patients between one and three times per day. There are common kitchen and laundry facilities for use by patients and their visitors.

CRE was first isolated in our acute spinal in-patient rehabilitation unit from the urine of a patient transferred from a hospital in Greece. In the next 6 months, we encountered a total of six CRE clinical infections and five CRE carrier status patients.

The patient we are presenting is a 45-year-old female. After falling 5 m she sustained a hyper-flexion injury, resulting in T11/T12 fracture and T9 complete paraplegia, Grade A on the American Spinal Injury Association (ASIA) Impairment Scale. Acute T10-L1 posterior decompression and fusion were performed to stabilise the spine.

One month after injury, while undergoing rehabilitation as an in-patient, she was noted to have malodorous urine. A catheter urine specimen (CSU) grew CRE—*Klebsiella pneumoniae* sensitive to nitrofurantoin, amikacin, colistin and fosfomycin —which was successfully treated with oral nitrofurantoin. A subsequent CSU obtained 10 days later on catheter change post treatment revealed no growth, after which she began 4-h intermittent self-catheterisation (ISC). On transitioning to 6-h ISCs she was found to have high post-void residual volumes.

An IDC was inserted to rest the bladder once the post ISC-residue reached 770 ml for 24 h as per the protocol on the unit. On recommencing ISCs, the patient developed fevers, rigors and abdominal and back pain within 10 h. IDC was reinserted and the CSU grew *K. pneumoniae* CRE with preliminary results revealing resistance to meropenem. The initial advice from the Infectious Diseases team was to

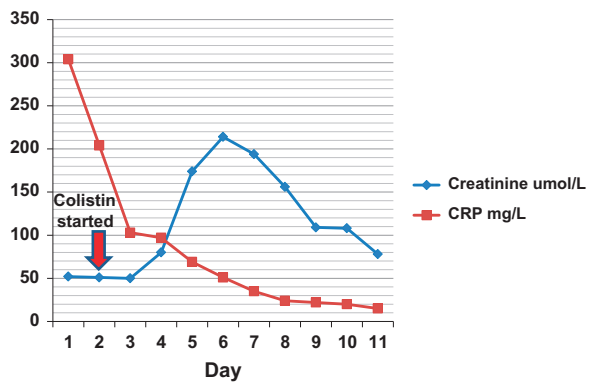

Figure 1. Trend in creatinine and CRP.

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Table 1. Infection prevention and control review and action plan

Findings	*Recommendations*
PPE and hand hygiene	Signage on hand hygiene and alcohol-based handrub available throughout the unit. Visitors and staff to perform hand hygiene on entry and exit to ward, rooms and gym. For patients with a MRO, door signs outline the level of precaution required including PPE; visitors are required to wear PPE in patient rooms, as well as in common areas such as the kitchen. All visitors require instruction from staff. All patients, visitors and staff entering the gym are to perform hand hygiene on entry and exit. Staff to assist patients that are unable to perform hand hygiene on their own. All staff and visitors must wear appropriate PPE for patients with MROs. If a patient is to use a specialised piece of communal gym equipment that cannot be easily cleaned and disinfected, the patient is to perform hand hygiene before and after use. All patients with respiratory symptoms are to wear a mask when attending the gym.
Patient equipment	All equipment used between patients including glucometers, blood pressure machines, trolleys and bladder scanner should be cleaned and disinfected between uses. Patient slings should be dedicated to one patient only; no sharing slings between patients.
Kitchen/refrigerator	Patients and visitors using the kitchen and common areas will need to attend hand hygiene. Kitchen area, benches and outside of refrigerator to be cleaned daily. Tables for meals and therapy should be cleaned and disinfected between uses. No material tablecloths to be used and plastic tablemats preferable.
Linen trolley	All stored linen should be kept covered.
Laundry	The domestic washing machine should only be used for personal items. No patient clothing should be left in the laundry and visitors should not use the machine. Patients using the machine should be supervised by staff. Laundry to be cleaned and disinfected daily, including benches and floors.
Patient therapy equipment should be cleaned between patient use	Items which must be cleaned and disinfected between patient use: computer station, keyboard, metal weights on keyboard, chinpad and stereo, dinner trays, shoehorns, metal grabbers, hand mirror strings and beads, plastic pegs, plastic Mocano set, plastic moneybox and money, punch meter, plastic food containers, plastic cones and dishes, metal and plastic spray bottles. Neutral detergent wipe (Tuffie, EBOS Group, Auckland, New Zealand) to be used for cleaning of patient equipment. Disinfectant wipe (Isowipe, Kimberly Clark, Irving, TX, USA) to be used for disinfection of equipment after cleaning, if patient requires additional precautions. Plastic kitchen mixing bowl and cup measures must be cleaned in dishwasher between uses. Nailbrush in the hypersensitivity sensation pack is single use only.
Patient therapy equipment not suitable for cleaning and disinfection between patient use	Items which cannot be cleaned after use, patients to attend hand hygiene before and after use: plastic and nylon cord pulley, wooden easel including colour pencils and art book, fabric Norco hinge lever stick, left hand finger splint orthotics, black splinters (velcro and foam), wooden blocks with screws, hand therapy box (including elastic bands, play dough, finger strengthener and digiflex), games with wooden inserts and metal container, stress foam balls, clothing zips and buttons, paper tape measures, Uno Stocko, paints and brushes, magnetised Sudoku, art set (including crayons, pencils, paints, stapler, sharpener), toolbox with pipe cleaners, wooden pickup sticks, jigsaw puzzle, board games, playing cards, hand grip dynamometer, slings (plastic and metal), modified cutlery for demonstration (metal and foam) and splints (metal and foam). Plastic clipboard with velcro: plastic must be cleaned between uses, velcro unable to be cleaned properly and should be changed between uses. Therabands and wrist braces are for single patient use.
Electric wheelchairs	Electric wheelchairs are shared between patients and have fabric covers (not impermeable); all chairs are to be cleaned thoroughly between patient uses. Covers that can be removed should be sent for laundering. Steam cleaning of chairs is being investigated as an option.
Physiotherapy and occupational therapy store rooms	Shelving and stored equipment require regular high dusting schedule to prevent build-up of dust. Floor to be cleaned regularly. All items should be stored on shelves and no items on the floor. There are written instructions for processing dirty equipment and returning clean equipment to stock room, for example, separating new and used Roho cushions (Belleville, IL, USA). Items with damaged vinyl cover over foam must be discarded and not reused as they cannot be adequately cleaned and disinfected.
Cleaning of gymnasium and associated equipment	Gymnasium to be cleaned daily, disinfected weekly and floor scrubbed monthly. Slings to be sent in blue bag to the laundry if soiled and after patient use. All slings must be labelled with patient name and bagged separately for storage for all patients. The gym equipment/plinths to be cleaned by physiotherapist between all patients with neutral detergent wipes (Tuffie) regardless of MRO status. No patient equipment should be stored on the floor, including weights. If a patient has an MRO, the gym equipment will require both cleaning and disinfection with disinfection wipes (Isowipe, 70% isopropyl alcohol). Specialised physiotherapy equipment such as pressure-relieving cushions require cleaning with a neutral detergent. If specialised equipment is used on a patient with an MRO, it requires both cleaning and disinfection. After cleaning, disinfect the equipment with Diversol (Johnson Diversey, Charlotte, NC, USA) 1000 p.p.m. (make up with cold water; one sachet per 5 l of H20). Covers that require laundering must be sent for laundering in a labelled bag.

Abbreviations: MRO, multi-resistant organism; PPE, personal protective equipment.

commence amikacin, based on previous sensitivities. The bacterium was subsequently found to be resistant to amikacin and the patient's clinical condition started to deteriorate. The white cell count was $15.5 \times 10^9\ l^{-1}$. Flucloxacillin was added given the possibility of surgical hardware infection in the context of back pain.

Blood cultures also grew *K. pneumoniae* CRE and the C-reactive protein (CRP) rose to $336\ mg\ l^{-1}$. High-dose meropenem was started 24 h later. Ongoing testing for mean inhibitory concentration (MIC) of meropenem and daily blood cultures were continued. After three doses of high-dose meropenem and limited clinical response, the final sensitivities were obtained which showed sensitivity to colistin (MIC $0.125\ mg\ l^{-1}$) and meropenem (MIC $0.5\ mg\ l^{-1}$) was consequently ceased.

Colistin was commenced with a loading dose of 300 mg followed by 150 mg twice daily for 2 days ($5\ mg\ kg^{-1}$ per day). Colistin administration is associated with a high risk of nephrotoxicity and a need for haemodialysis,[4,5] and therefore informed consent was obtained from the patient prior to administration of the drug. The patient's clinical condition improved following the first dose of colistin.

Unfortunately, deterioration of renal function occurred in our patient. A slight rise in creatinine on day 3 of colistin administration prompted the cessation of the drug. Creatinine peaked at $214\ \mu mol\ l^{-1}$ 24 h post cessation of colistin then gradually improved and normalised to $78\ \mu mol\ l^{-1}$ 8 days later and returned to baseline a further 3 weeks later. CRP steadily declined to $15\ mg\ l^{-1}$ after 10 days (Figure 1).

CRE bacteraemia, delay in initiating appropriate antimicrobial treatment and medication toxicity had significant impact on our patient. Her rehabilitation was interrupted for 14 days during which time she suffered significant deconditioning, resulting in an adverse emotional impact and a morbid fear of future infections.

DISCUSSION

The rates of urinary tract infections (UTIs) and other infections or colonisations are high in spinal cord injury patients and antibiotic treatment is regularly needed.[6–8] Carbapenems are the last line of treatment for serious infections caused by multi-resistant *Escherichia coli*,[9] Klebsiella species and other Enterobacteriaceae.[10] Carbapenemases are carbapenem-hydrolysing beta lactamases that confer resistance to a broad spectrum of beta-lactam substrates, including carbapenems. Many carbapenemases reside on mobile genetic elements and have the potential for widespread transmission to other bacteria. Furthermore enterobacteriaceae, which harbour such coding genes, can spread from person to person. Enterobacteriaceae cause infections at a high frequency and resistant infections are associated with high mortality.[11]

The toxicity of medications available for the treatment of CRE infection is a significant challenge.[1,4,5] Colistin was initially used in the 1950s and was never subjected to modern approval regulations. It was also the last-line therapy for this infection and highlights the dearth of new classes of antimicrobials in the last decade. There is a relative lack of experience in using colisitin at safe doses. There is some concern about increased nephrotixicity with larger single loading doses (dose dependent)[1,4] which may have been a factor in our patient. It is difficult to determine the relative contribution of colistin to development of acute renal failure in our patient in the context of urosepsis and use of other nephrotoxins (amikacin).

Furthermore this case followed by others prompted an intensive focus on infection control practice in the unit to minimise transmission and colonisation (Table 1). A targeted CRE education and surveillance programme was instituted to control the spread of CRE in the unit. Strategies included:

1. Screening swabs of all patients admitted to the unit: relying solely on clinical cultures did not detect the majority of CRE carriers in our unit and active surveillance of patients at high risk of CRE carriage was needed. Screening of all admissions to the unit with rectal swabs and isolation with contact precautions were strictly enforced.
2. Appropriate use of personal protective equipment (PPE) and hand hygiene techniques by staff and visitors: intense focus on use of PPE with high risk patients and hand hygiene education and compliance rates were rigorously enforced. Patients were asked to use hand hygiene techniques when touching shared equipment which could not be easily disinfected.
3. Minimisation of equipment sharing between patients: hoist slings in particular were manadated for individualised use. Shared equipment and room surfaces were disinfected at least daily and also after each use. High-risk areas were identified as the gymnasium, mobility and seating equipment, sling hoists and commode chairs for which enhanced cleaning and disinfectants were instituted.
4. Common patient areas including the patient lounge and kitchen were reviewed as potential risk areas: visitors and family were asked to use PPE (gloves and gown) while using these facilities.

Since the introduction of the CRE surveillance and infection control enhancement programme, there have been no clinical CRE isolates in our unit in the last 18 months.

CONCLUSION

We present our experience with the management of CRE bactaeraemia in a spinal rehabilitation unit and the enhanced focus of infection control and surveillance strategies required to successfully contain risk of transmission.

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COMPETING INTERESTS

The authors declare no conflict of interest.

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