Clinico-Microbiological Investigation of Catheter Associated Urinary Tract Infection by Enterococcus faecalis: vanA Genotype

ABSTRACT

Prolonged hospitalization and exposure to third generation cephalosporins are reported to facilitate the acquisition and colonization of Vancomycin Resistant Enterococci (VRE). Though VRE is not uncommon in India, urinary tract infection with a vanA genotype is a cause of serious concern as VRE co-exhibit resistance to aminoglycosides. In India, majority of the VRE isolates recovered from hospitalized patients include Enterococcus faecalis. We report a case of catheter associated urinary tract infection by an endogenous, multidrug resistant E. faecalis of vanA genotype following prolonged hospitalization, ICU stay, catheterisation and exposure to 3G cephalosporin and metronidazole. The patient responded to linezolid therapy.

CASE REPORT

A 23-year-old male, a resident of Kanchipuram district (Tamil Nadu, India) presented to the Emergency Department of SRM Medical College Hospital, Katankulathur, a tertiary care centre with clinical signs of degloving injury of the left lower limb, over thigh, left aspect of knee, lateral aspect of leg and anterolateral aspect of ankle following a road traffic accident. Wound debridement was done under spinal anesthesia on the day of admission. Routine laboratory investigations were performed. Results from haematological tests revealed the following values: Haemoglobin - 9.1g dl⁻¹, Total Count - 5600 cells/µl, Differential Count: N-87%, L-9%, E-3%, M-4%, Random blood glucose - 120 mg/dl, Urea-14mg/dl, Creatinine-0.7 mg/dl. Serum electrolytes: Na-134 mEq/L⁻¹, K-9.8 mEq/L⁻¹, Cl-106 mEq/L⁻¹, HCO₃⁻20 mEq/L⁻¹.

On the 11th day of admission, flap cover with superficial skin graft was performed and the patient was shifted to surgical ICU. Post surgery, the patient received cefaperazone-sulbactam-1.5g IV, gentamicin -80 +mg IV-BD, metronidazole 100 mg-TD, Dynaper IM surgery, the patient received cefaperazone-sulbactam-1.5g IV, amikacin, gentamicin, imipenem, meropenem, vancomycin and linezolid but susceptible to linezolid and tigecycline. Screening for high level aminoglycoside resistance (HLAR) revealed that the isolate harboured vanA genotype following prolonged hospitalization, ICU stay, catheterisation and exposure to 3G cephalosporin and metronidazole. The patient responded to linezolid therapy.

The isolate exhibited high level resistance to gentamicin and hence, genotyping was performed by multiplex PCR. Five common aminoglycoside resistance genes aac(6’)-Ie-aph(2”)-Ia, aph(2”)-Ib, aph(2”)-Ic, aph(2”)-Id and aph(3’)-IIIa were analyzed using previously described primers [2]. Analysis of the PCR product revealed that the isolate harboured aac(6’)-Ie-aph(2”)-Ia and aph(3’)-IIIa. The high level gentamicin resistance (MIC ≥ 512 µg/ml) and the dual presence of AGMEs - aac(6’)-Ie-aph(2”)-Ia and aph(3’)-IIIa revealed that the isolate was resistant to synergism with the cell wall active agents.

Biofilm forming ability of the enterococcal strain was assessed by the tissue culture plate method. Safranine (0.1%) was used to stain the adherent bacterial cells. The presence of Esp gene encoding Enterococcal surface protein (Esp) was assessed by PCR using previously described primers [3]. The current isolate was found to exhibit moderate in-vitro biofilm formation nevertheless, Esp was not detected. According to the antibiogram, the patient was treated with linezolid 600mg IV. The patient responded to therapy, 2 days later patient was shifted from the ICU to plastic ward and the closed bag system was removed.

DISCUSSION

The patient is likely to have acquired VRE during his stay at SICU, concurrently the other patients hospitalised at the SICU were not infected with VRE. Previous studies document that prolonged hospitalization, ICU stay, catheterisation, exposure to antibiotics especially, the third generation cephalosporins, fluoroquinolones, anti-anaerobes are the potential risk factors for nosocomial colonisation and infection with VRE [4-6]. In this case, the selection pressure exerted by the broad spectrum antimicrobial especially the third generation cephalosporin is likely to have promoted the emergence of VRE and the anti-anaerobic drug; metronidazole is likely to have facilitated the colonization and persistence of VRE.
Recent Indian studies have reported that the majority of the VRE isolates recovered from hospitalized patients were found to be *E. faecium* [7–9]. However, we report a case of vancomycin resistant *E. faecalis* CAUTI. Also, catheterization had promoted the formation of biofilm and the concomitant entry of the endogenous VRE into the urinary tract resulting in catheter associated UTI (CAUTI).

vanA and vanB genotypes are reported to be the predominant among the glycopeptide-resistant genotypes in *Enterococci* [10]. vanA positive isolates are inducibly resistant with high MICs (> 64 µg/ml) of vancomycin and teicoplanin while, vanB isolates exhibit inducible resistance to vancomycin with an MIC of (32-64 µg/ml) but are susceptible to teicoplanin. The vanA operon can easily be transferred through acquired resistance. *E. faecalis* isolated from this patient exhibited glycopeptide resistance of the vanA phenotype.

Aminoglycosides are the most frequently prescribed antibiotics in clinical practice as they possess good pharmacokinetics and exhibit synergism with beta-lactams and glycopeptides. Production of aminoglycoside-modifying enzymes (AGMEs) is reported to be the major mechanism involved in aminoglycoside resistance. This isolate was found to harbour aac(6')-Ie-aph(2')-Ia and aph(3')-IIa. The latter encodes the aminoglycoside phosphotransferase, APH(3')III which confers high-level resistance to kanamycin while, the former encodes AAC(6')-APH(2')-Ia, a bifunctional enzyme that confers resistance to all clinically available aminoglycosides except streptomycin.

Multidrug resistance is a matter of great concern among nosocomial uropathogens with the associated increase in the health care cost compared to the community strains. Currently, the use of synergistic combinations of a cell wall-active agent, a penicillin or a glycopeptide, with an aminoglycoside is claimed to be optimal in the treatment of enterococcal infections [11]. However, certain *Enterococci* have acquired resistance genes that encode AGMEs, which eliminate this synergistic bactericidal effect. This isolate was found to exhibit high level aminoglycoside resistance and was resistant to synergism with cell wall active agents.

Biofilm formation along all surfaces of the catheter is reported to be a major factor that promotes catheter associated UTI (CAUTI). Enterococcal surface protein (Esp) is reported to enhance biofilm formation [3]. Also, biofilm specific counterparts are reported to exhibit enhanced antibiotic tolerance [12]. This isolate was capable of forming in-vitro biofilm but did not harbour Esp. This is in line with the recent finding which has documented that Esp independent biofilm formation can occur in *Enterococci* [13].

Taking into account the possibility of VRE associated UTI among hospitalized, non-ambulatory patients, empirical treatment for UTI with vancomycin needs to be administered with caution. Previous Indian reports have documented increased case fatality among catheterized patients who developed bacteremia and sepsis caused by VRE of urinary origin [14].

CONCLUSION

Prompt diagnosis, identification of the aetiology of UTI and the antibiotic resistance pattern of the isolate is critical in the management of UTI. Prudent use of third generation cephalosporins could prevent the emergence of VRE and linezolid is currently effective in the treatment of UTI caused by VRE with a vanA genotype.

REFERENCES