



VANCOMYCIN RESISTANT *ENTEROCOCCUS FAECALIS* CAUSING DIARRHEA IN RENAL TRANSPLANT PATIENT

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ABSTRACT

Enterococcus faecalis is a commensal organism of the intestinal tract. However, it may be a causative agent of diarrhea in elderly and immunocompromised patients. Here we report a case of a 33 years female who presented with diarrhea few days after her renal transplant. She was on corticosteroids, cotrimoxazole, valacyclovir, ceftriaxone and metronidazole. However, she was having diarrhea for 12 days. Three consecutive stool sample was processed for culture on MacConkey agar which revealed *Enterococcus faecalis* as the predominant organism. The organism was identified on the basis of biochemical tests. *Enterococcus faecalis* which was isolated in her stool sample was resistant to most of the antibiotics including vancomycin, however it was sensitive to linezolid. The resistance of the isolate to vancomycin was confirmed by minimum inhibitory concentration (MIC) testing by agar dilution method which showed that MIC was more than 16 mcg/ml. On the background of immunosuppressive state of the patient, predominant colony of *E. faecalis* on repeated culture, negative test for toxin analysis for *C. difficile* and improvement of the patient on third day of linezolid therapy, vancomycin resistance *Enterococcus faecalis* was considered the causative agent of her diarrhea. Stool culture on the third day of linezolid and on follow up after seven days revealed no growth of *Enterococcus* species. Vancomycin-resistant *Enterococci* are organisms renowned for their ability to cause infections with limited treatment options and may cause diarrhea in immunocompromised patients. So, diarrhea not responding to commonly used antimicrobial agent should be searched for vancomycin-resistance *Enterococci* for proper management of the patient.

KEYWORDS: Vancomycin Resistance *Enterococci*, Renal transplant, diarrhea, immunocompromised, Nepal.

BACKGROUND:

Enterococcus faecalis are commensal microorganisms that act as opportunistic pathogens, particularly in elderly patients with serious underlying disease or immunocompromised patients¹. They are frequent causative agents of both nosocomial and community acquired infection in transplant patients. In the past two decades, resistance of *E. faecalis* to glycopeptides has emerged in an epidemic fashion and is now endemic in many countries².

CASE PRESENTATION:

A 33 years female was admitted in nephrology ward of TUTH on 21st September, 2015 for renal transplantation. After few days of her renal transplant, she developed diarrhea and she was on corticosteroids, cotrimoxazole, valacyclovir, ceftriaxone and metronidazole however, she was having diarrhea for 12 days. The stool sample was processed for routine microscopic examination and culture. Wet mount and iodine mount of stool sample revealed few pus cells, plenty of undigested food particles but no parasites, no fungi and no RBC. Occult blood test was negative. Stool culture was done on MacConkey agar (fig.1). The sample was repeatedly collected for three consecutive days for microscopic examination and culture. On repeated culture, predominant organism was small lactose fermenting colonies, identified as *E. faecalis* on the basis of gram stain and biochemical tests [Gram positive cocci in short chain and pair on Gram stain, Catalase test negative, non-motile in sulphite indole motility (SIM) test (fig.2), Bile esculin hydrolysis test positive (fig.3), able to grow in 6.5% NaCl, it can ferment sorbitol (fig.4) but cannot ferment raffinose (fig.5) and arabinose (fig.6)]. On the background of immunosuppressive state of the patient and predominant colony of *E. faecalis* on repeated culture and negative test for toxin analysis for *C. difficile* (fig.7). *E. faecalis* was considered pathogenic organism and was processed for antibiotic sensitivity testing³ by Kirby Bauer method (fig. 8, 9) and Stokes method (fig.10) which revealed resistance to most of the antibiotics like Amoxycillin, high level gentamicin, ciprofloxacin, clindamycin, erythromycin, ceftioxin, amoxicillin-clavulanic acid, ceftriaxone, ticoplanin and vancomycin except linezolid. The resistance of the isolate to vancomycin was confirmed by minimum inhibitory concentration (MIC) testing by agar dilution method which showed that MIC was more than 16 mcg/ml. So, the patient was started on linezolid 600mg twice daily with continuation of her all drugs. On third day of linezolid therapy, diarrhea was resolved and she got improved. So it was concluded that the vancomycin resistant *Enterococcus faecalis* was responsible for diarrhea in this renal transplant patient. She was discharged with linezolid (to complete the standard course) and all others previous drugs. Stool culture on the third day of linezolid and on follow up after seven days revealed no growth of *Enterococcus* species.

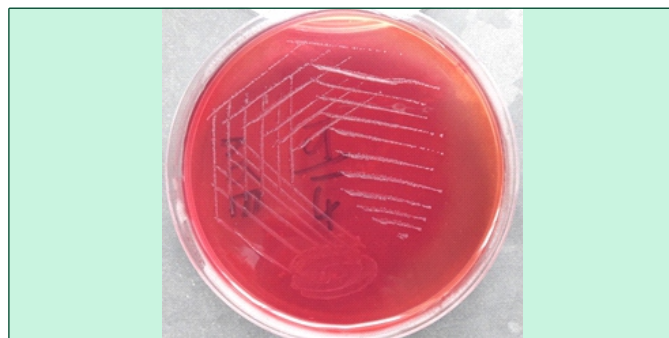


Fig.1: *Enterococcus faecalis* colonies on MacConkey agar plate



Fig. 2: Motility test using SIM agar³



Fig. 3: Bile esculin hydrolysis test³



Fig. 4: Sugar utilization test sorbitol³

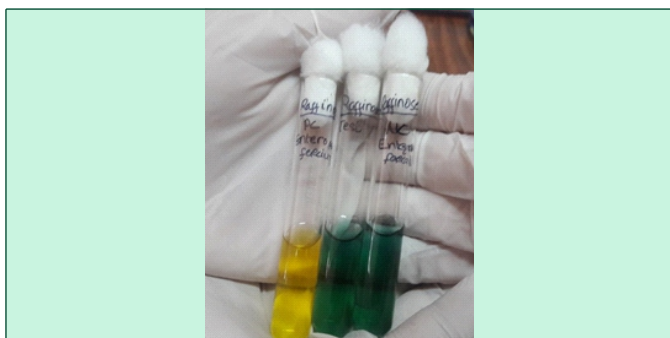


Fig. 5: Sugar utilization test raffinose³



Fig. 6: Sugar utilization test arabinose³



Fig. 7: A negative test of toxin analysis of *C. difficile*

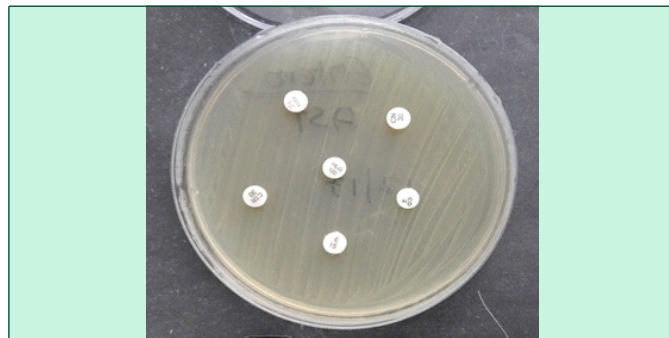


Fig. 8: Antibiotic susceptibility testing showing resistance to all drugs



Fig. 9: Antibiotic Susceptibility testing showing sensitivity to linezolid and resistance to vancomycin



Fig. 10: Stokes method (comparative disc diffusion test)³ showing vancomycin, teicoplanin and amoxycillin resistant *E. Faecalis* (test organism) and sensitive to linezolid whereas *Enterococcus faecalis* ATCC 29212 sensitive to vancomycin, teicoplanin, amoxycillin and linezolid

DISCUSSION:

To our knowledge, this is the first case reported of vancomycin-resistant *Enterococci* causing diarrhea in renal transplant patient from Nepal. *Enterococci* are natural inhabitants of the oral cavity, gastrointestinal tract (GIT) and the female genital tract in both humans and animals. These days, they have emerged as an opportunistic pathogen causing nosocomial infections^{4,5}. The increasing use of antineoplastic and immunosuppressive agent has become the major reason for nosocomial infection due to *Enterococcus* species⁵. They cause urinary tract infections, bacteremia, endocarditis and are also recovered from infections of the abdomen, the pelvis, the biliary tract, and wounds⁶. There are two main species – *E. faecalis* and *E. faecium* responsible for human enterococcal infections⁵. Relative to the streptococci, enterococci are intrinsically resistant to many commonly used antimicrobial agents like cephalosporins, clindamycin⁷. As such, the emergence of resistance to the most common anti-enterococcal antibiotics like ampicillin, aminoglycosides and most importantly glycopeptides like vancomycin has made the treatment of these infections a real challenge for clinicians⁸. According to CLSI (2014) *E. faecalis* and *E. faecium* is considered resistant to vancomycin when the MIC of *enterococcus* for vancomycin is ≥ 16 . Newer antibiotics like linezolid, daptomycin, dalbapristin-quinupristin, tigecycline are drug of choice for vancomycin resistant *Enterococci*⁴. Both *E. faecalis* and *E. faecium* can survive in hospital environment and colonize patients⁵. They also have the ability to acquire resistance to most of the currently available antibiotics and also transfer vancomycin resistant genes to other organisms⁸. Due to these properties, they can easily persist and spread in the hospital environment. So proper hand washing, disinfection of the wards, isolation of the patient and carrier should be carried out in the hospital setting to prevent spread of vancomycin resistant *Enterococci*.

CONCLUSION:

Vancomycin-resistant Enterococci are organisms renowned for their ability to cause infections with limited treatment options. They may cause diarrhea especially in immunocompromised patients. So, diarrhea not responding to commonly used antimicrobial agent should be searched for vancomycin-resistance Enterococci for proper management of the patient.

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