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Case Report

Microbiology Section

Neonatal Septicaemia Caused by Vancomycin Resistant *Enterococcus Faecium*-A Case Report

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ABSTRACT

Neonatal bacterial sepsis is one of the major causes of morbidity and mortality in neonates. 10% cases of neonatal bacteraemia and septicaemia are caused by *Enterococci*. The increasing incidence of Vancomycin resistant *enterococci* (VRE) is of particular concern because of limited treatment options and increased mortality. We report here a case of neonatal sepsis in a premature baby caused by vancomycin resistant *Enterococcus faecium* Van A phenotype from a tertiary care Hospital in South India. A preterm baby boy with low birth weight was admitted to the NICU with Respiratory distress and meconium aspiration. On 5th day the baby succumbed to death and a final diagnosis of respiratory distress and meconium aspiration with sepsis was made. Blood cultures sent yielded vancomycin resistant *Enterococcus faecium* (minimum inhibitory concentration ≥ 256 µg/ml). It was confirmed as *Enterococcus feacium* Van A phenotype by Automated Vitek system.

Keywords: Neonatal septicaemia, VRE

CASE REPORT

A preterm baby boy with birth weight of 1.75 kg was born to a Primigravida by normal delivery at 34 wks of gestation at Vani Vilas Hospital attached to Bangalore Medical college and Research Institute, Bangalore, in January 2014. The mother was diagnosed with Pregnancy induced Hypertension on admission. It was a High risk pregnancy with premature rupture of membranes. The baby cried immediately after birth, however developed respiratory distress with meconium aspiration and was shifted to NICU. The temperature was 36.5^{0}C, heart rate 80/min, Respiratory rate 70/min, perfusion <3 sec. Systemic examination of CVS,CNS & reflexes were normal.

The baby was started on empirical antibiotics inj. ampicillin (60mg, 8th hourly) & inj. gentamicin(15 mg,24th hourly) initially, however in view of poor response the same were switched over to parenteral ceftriaxone (175mg,IV,12th hourly), Vancomycin (25mg,12th hourly) & amikacin (25 mg, 24th hourly). Despite therapy, there was no clinical improvement, respiratory distress worsened, baby developed cyanosis with decrease in SpO_2 to 70% and perfusion >3secs. The baby was intubated and placed on mechanical ventilation for respiratory failure. The investigations revealed normocytic normochromic blood picture with thrombocytopenia and reactive CRP. The respiratory course continued to deteriorate with worsening saturation and inspite of intensive neonatal care baby succumbed to death on 5th day. A final diagnosis of Respiratoy distress syndrome with Meconium aspiration syndrome with septic shock was made.

Blood cultures sent on 3rd day yielded *Enterococcus faecium*. The identification of the isolate was done by standard methods [1,2]. Antibiotic sensitivity by standard Kirby-Bauer disc diffusion method, showed the isolate to be resistant to penicillin(10 units), erythromycin (15µg), high level gentamicin (120µg), ciprofloxacin (5µg), vancomycin (30µg) and teicoplanin (30µg) but susceptible to linezolid (30µg). The isolate possessed high-level resistance to vancomycin; the minimum inhibitory concentration (MIC) of the strain to vancomycin was ≥256 µg/ml by E test (BioMërieux). The identification and sensitivity of the isolate were confirmed by Automated system (BioMërieux-Vitek, USA). Based on its high-level resistance to vancomycin and resistance to teicoplanin, the strain was designated as belonging to Van A phenotype.

DISCUSSION

Enterococci have evolved over the past few decades from being harmless intestinal commensals of little clinical significance to becoming the second or third most common pathogens associated with nosocomial infection. Among various species of *Enterococcus*, *E.feacalis* and *E. faecium* are the most common human pathogens. Serious *enterococcal* infections are often difficult to treat since the organisms exhibit intrinsic resistance to penicillinase susceptible penicillin (low level), penicillinase resistant penicillins, cephalosporins, lincosamides, nalidixic acid, low level of aminoglycoside and low level of clindamycin. They have a tremendous capacity to acquire resistance to penicillin by β-lactamases, vancomycin, chloramphenicol, erythromycin, high level of clindamycin, high level aminoglycosides (HLAR), tetracycline and fluroquinolone, thus drastically limiting therapeutic options [3,4]. *Vancomycin resistant Enterococci* (VRE) sepsis is emerging as a significant problem in the intensive care setting. The infection can be acquired from the carrier mother or as cross infection from the hospital (nosocomial) [5]. The treatment at any age is challenging, but there is a dearth of information on the cause of infection and its treatment in premature infant. Moreover the transfer of plasmids carrying resistance genes to *Staphylococcus aureus* is a matter of grave concern.

The case described here has several risk factors for acquisition of VRE like those reported earlier. The neonate had Immunosuppression or debilitation because of prematurity, respiratory tract instrumentation, ICU stay and use of broad spectrum antibiotics especially third generation cephalosporins [6,7]. The VRE strain in the present case was isolated from blood culture which may have contributed to the fatal outcome with underlying predisposing conditions.

Enterococci are among the first bacteria to colonize the neonatal gastrointestinal tract either through oral ingestion of breast milk or from the vaginal and gastrointestinal flora of the mother during the birth passage [7]. The present case is early onset sepsis and the baby would have acquired *enterococci* from the vaginal flora of the mother. Use of Broad spectrum antibiotics in the present case may have resulted in antibiotic selection pressure on the bowel inhabitants resulting in increased survival and overgrowth of the resistant population. VRE may thus have colonized the GIT or skin and subsequently resulted in infection. VRE may spread through direct contact with contaminated environmental surface and hands

of health care workers [3]. We can only speculate about the source of this strain, as neither the skin/ rectal swabs of the neonate nor could maternal blood culture, vaginal swab culture or screening of stool for *Enterococci* be done. The skin or rectal swabs could not be taken as the baby succumbed to death even before the culture report of the isolation of VRE could be communicated to the attending paediatrician.

It is important to speciate *enterococcal* isolates from clinical samples because, while most isolates of *E. faecalis* are inhibited by concentrations of penicillin or ampicillin (1 to 8 µg/ml) easily achievable in humans, isolates of *E. faecium* are more resistant to penicillins, requiring an average of 16 to 64 µg/ml to inhibit growth, although some isolates are even more resistant. *Enterococcus faecium* strains as compared to *E. faecalis* display a higher degree of drug resistance to multiple other antibiotics as well, including ampicillin, gentamicin, ciprofloxacin, vancomycin and teicoplanin [8,9]. Failure to recognize the resistant strains may result in inadequate antibiotic therapy with its attendant morbidity and mortality.

Seven types of glycopeptides resistance have been described among *enterococci*: Van A and Van B are considered the most clinically relevant phenotypes and are usually associated with *E.faecalis* and *E.faecium* isolates. Van A phenotype confers high level resistance to vancomycin(MIC>64mcg/ml) and teicoplannin(MIC>32 mcg/ml)and is usually seen in *E.faecium* [7]. In India, VanA VRE has been reported mainly in *E. faecalis* [10-12]. Mohanty et al., first documented isolation of vancomycin- resistant *E. faecium* of VanA phenotype from a 3-year-old child with PDA in India [3].

The primary therapeutic options for patients with VRE infection include quinupristin/dalfopristin and Linezolid, but the use of quinupristin/dalfopristin is limited because of its adverse effects profile, need for a central line and because of its lack of coverage against *Enterococcus faecalis*. Linezolid is active against *E. faecium* and *Enterococcus faecalis*. Hapnes et al., reported a case of Vancomycin resistant *Enterococcus faecium* in a 10 d old infant who was successfully treated with Linezolid [13]. Vidya mave et al., have studied the effectiveness of Daptomycin in treatment of vancomycin resistant *enterococcal* bacteraemia and concluded that in the case of patients intolerant to linezolid, daptomycin may be considered as an alternative for the treatment of VRE bacteraemia [14]. Beneri et al., reported a case of persistent bacteraemia with Vancomycin resistant *E.faecium* in a neonate successfully treated with daptomycin containing regimen [15]. The choice of antibiotics should also be based susceptibility reports, type of infection being treated (endocarditis versus urinary tract infection), the severity of the infection and clinical response to the regimen chosen.

CONCLUSION

In India, Van A VRE has been reported mainly in *E.faecalis*. There are very few case reports of Neonatal sepsis caused by Vancomycin resistant *Enterococcus faecium* which made us report this case stressing the need for strict enforcement of infection control practices. The Microbiology Laboratory plays a pivotal role in early detection and reporting of VRE. In addition, close liaison between the clinicians and the microbiologists will facilitate a significant reduction in mortality and morbidity caused by VRE. The emergence & spread of these pathogens can be significantly curtailed if appropriate infection control procedures, strict enforcement of antibiotic policies and screening programs are implemented immediately.

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