

# Hospital-Acquired Vancomycin-Resistant *Enterococci*: Now Appearing in Kuala Lumpur Hospital

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## Summary

Hospital-acquired vancomycin-resistant enterococci (VRE) were first reported in the late 1980s and have since been an increasing problem worldwide. Kuala Lumpur Hospital thus far, to the best of our knowledge has been spared from this pathogen. We describe the first confirmed case of *Enterococcus faecium* exhibiting the van A phenotype in our hospital, in a patient with chronic renal failure who was successfully treated with linezolid. The microbiology laboratory plays an important role in the identification and detection of VRE.

**Key Words:** Vancomycin-resistant enterococci (VRE), Hospital-acquired, Chronic renal failure, Linezolid

## Introduction

Enterococci have long been known as important causes of endocarditis and in 1970s began to be recognized as common causes of hospital-acquired infections mainly recovered from hospital-acquired urinary tract and wound infections. Two of the most common of these microorganisms are *E. faecalis* and *E. faecium*. By virtue of the fact that these organisms that are frequently resistant to commonly used antibiotics, the emergence of vancomycin-resistant enterococci that occurred nearly 30 years after vancomycin was introduced, is bound to occur. Vancomycin-resistant enterococci (VRE) were first reported in 1988 in Europe. More patients with VRE have been detected world-wide ever since and these pathogens continue to pose therapeutic challenges in the management of patients. Gastrointestinal tract colonization is believed to precede VRE infections in many patients. High risk patients include those in intensive care units, those with chronic renal failure or cancer, organ transplant recipients and those with a history of vancomycin usage<sup>1</sup>.

The first case of hospital-acquired VRE in Malaysia was first described in 1996 from University Malaya Medical Centre<sup>2</sup>. Kuala Lumpur Hospital thus far, to the best of our knowledge, has been spared from this pathogen. Here, we report the first confirmed isolation of VRE in a patient with chronic renal failure detected in our institution.

## Case Report

A 28-year old woman with a history of chronic renal failure was admitted for peritoneal dialysis and subsequently underwent haemodialysis. One week after admission, she developed acute pulmonary oedema with pneumonia and she had to be ventilated. Ceftazidime plus azithromycin were started empirically. She was extubated after four days but the fever persisted. Azithromycin was then replaced by cloxacillin.

The blood culture grew *Enterococcus faecium*. The organism was identified according to the following

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criteria: Gram positive cocci, catalase negative, Lancefield group D, pyrrolidonyl arylamidase positive. Vitek® GPI identified the organism as *Enterococcus faecium*. The organism was resistant to ampicillin and vancomycin and high level gentamicin resistance was also demonstrated. The MIC of the vancomycin was > 256 mg/l by E-test and resistant to teicoplanin by disc diffusion, consistent with the van A phenotype. The isolate was subsequently sent to the Institute for Medical Research where the presence of a van A gene was confirmed by polymerase chain reaction (PCR).

Upon knowing the culture result initially, the patient was treated with vancomycin but later was switched to linezolid treatment once VRE was confirmed. The clinician was alerted immediately and advised on control measures i.e. adherence to handwashing and compliance to contact isolation precautions. The patient responded well with a two-week course of linezolid at 600 mg 12 hourly. A repeat blood culture was negative for *Enterococcus faecium*.

### Discussion

Five phenotypes of vancomycin resistance; termed van A, van B, van C, van D, and van E are described. The van A and van B phenotypes are clinically significant as these phenotypes can be induced by vancomycin use. In the United States and Europe, the Van A-resistance phenotype is reported as the most common phenotype. Van A enterococcal isolates exhibit high-level resistance to both vancomycin and teicoplanin, while van B isolates have variable resistance to vancomycin and remain susceptible to teicoplanin. The van C phenotype is mediated by the chromosomal genes, which are constitutively present in *Enterococcus gallinarum* and *Enterococcus casseliflavus*. These genes confer relatively low resistance levels to vancomycin and are not transferable. Therefore, the definitive identification of enterococcal isolate to the species level is important as it has infection control implications.

The emergence of VRE in our institution is not unexpected. It is probable that other patients who have been colonized have not yet been detected.

Guidelines produced by the Hospital Infection Control Advisory Committee (HICPAC) of the CDC in the United States of America recommend that even hospitals without known cases should monitor for VRE. The question is: Should we do periodic screening especially in patients in the high risk groups? Patients treated with chronic ambulatory peritoneal dialysis are frequently given vancomycin as empiric treatment for peritonitis and catheter exit site infections. The HICPAC guidelines discouraged this practice unless there is strong evidence at the outset that the patient has an infection due to gram positive organisms and the prevalence of infections due to beta-lactam resistant gram positive organisms in the hospital is substantial<sup>3</sup>.

The exposure of patient's endogenous enterococcal flora to vancomycin is a known risk factor for the development of resistance<sup>1</sup>. In this patient, this is probably the case as she had been known to be exposed to vancomycin in the past. Vancomycin and ceftazidime have been used as first line empirical therapy in the renal unit in our institution but with the emergence of VRE, it has been changed to cloxacillin and ceftazidime.

In 2000, the FDA approved linezolid, the first in a new group of antimicrobial drugs called oxazolidone class. It acts by inhibiting bacterial protein synthesis at the 50s subunit. A study looking at the antibacterial activity of linezolid against VRE supports the use of linezolid for the treatment of VRE infections. The study found that MIC<sub>90</sub> of linezolid for VRE was 2mg/l<sup>4</sup>. Thus, while linezolid is an efficacious agent for chemotherapy of patients infected with vancomycin-resistant organisms, its use should be restricted in order to prevent an increase in linezolid-resistant organisms.

The patient had a successful outcome following treatment with linezolid and there was no evidence of enterococcal bacteraemia in the repeat blood culture. Infection control measures were effective in preventing the spread of the resistant *Enterococcus faecium*. Regular surveillance of enterococcal isolates and or the collection of rectal swabs of patients at high risk may be justified in the near future to determine the level of vancomycin resistance in our institution.

## References

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