Isolation of β-lactamase positive vancomycin resistant *Enterococcus faecalis*; first case in Australia

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Abstract

An increasing number of clinical isolates of vancomycin resistant enterococci (VRE) have been reported in the literature since 1988. Only a few cases of β-lactamase producing VRE have been described worldwide. This article reports the first case of β-lactamase positive VRE in Australia. This strain of *Enterococcus faecalis* was isolated from a patient with non-Hodgkin’s lymphoma who subsequently underwent a bone marrow transplant. Screening of all ward contacts did not detect any further case of β-lactamase producing VRE. With the development of multiple antibiotic resistance in enterococci, additional infection surveillance protocols have been implemented in the hospital. These include routine screening of ‘at risk’ patients, instigating relevant infection control measures for management of VRE positive patients and controlling the usage of vancomycin in order to limit the development of resistant isolates. Commun Dis Intell 1999;23:237-239.

Introduction

Enterococci are intrinsically resistant to a wide range of antibiotics. Traditionally, vancomycin and amoxycillin are the drugs of choice for treatment of enterococcal disease, however, the choice of therapeutic options has been markedly reduced with the emergence of β-lactamase producing, vancomycin resistant strains of enterococci.* Since the first reported case of vancomycin resistance in enterococci in Britain in 1988, further cases have occurred throughout Europe and America. In Australia, vancomycin resistant enterococci (VRE) were first detected in 1994.7 It was not until 1996* that VRE were first detected at the Royal Brisbane Hospital (RBH).

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This article documents the first reported case of β-lactamase production in a vancomycin resistant isolate of enterococcus in Australia.

Case report
A 28 year old male was diagnosed with non-Hodgkin’s lymphoma in April 1996. He received a bone marrow transplant in March 1997. Subsequently the patient developed a number of febrile episodes (up to \(40.2^\circ\text{C}\)) in the period preceding his death on 25 March 1997.

During March 1997, the laboratory investigations revealed severe neutropaenia and thrombocytopaenia. \textit{Staphylococcus aureus} was cultured from peripheral blood and the lumen of his Hickman’s catheter. Cytomegalovirus was cultured from his urine. Faecal specimens were positive for \textit{Clostridium difficile} toxin A. A β-lactamase positive \textit{Enterococcus faecalis} (\textit{E. faecalis; VanB phenotype}) was isolated from his faeces on 23 March 1997.

In the four months from December 1996 to March 1997 the patient was treated with acyclovir, amphotericin B, ceftazidime, co-trimoxazole, ciprofloxacin, gentamicin, imipenem, metronidazole, netilmicin, piperacillin, tetracycline, ticarcillin-clavulanic acid and tobramycin. During the same period, five courses of vancomycin were administered, three of these between January and March.

Methods and Results

Laboratory investigations

\textit{Enterococcus faecalis} was grown following routine screening of his faeces on Enterococcusel (ESEL) agar (BBL) which contained 6mg/L vancomycin. Identification tests included aesculin hydrolysis, gram stain, motility, pyrrolidonyl arylamidase (PYR) activity and Strep API (bioMérieux). Vancomycin resistance was determined by the \textit{E} Test\textsuperscript{TM} (AB Biodisk, Sweden) method. The minimum inhibitory concentration (MIC) of vancomycin was 48 mg/L. The isolate was susceptible to teicoplanin with an MIC of 0.15 mg/L. These results classified the organism as a VRE with a VanB phenotype. The organism was referred to the Women’s and Children’s Hospital, Adelaide, Australia for genotypic analysis. The identification of the organism was confirmed using a multiplex polymerase chain reaction (PCR) assay based on specific detection of genes encoding D-alanine: D-alanine ligases; and PCR primers to 330 base pair fragments following direct amplification were used to confirm the VanB genotype. Additional antibiotic susceptibility testing using agar dilution also showed the organism to be resistant to 500 mg/L gentamicin. The Nitrocefin test (Oxoid) for β-lactamase was positive after 15 minutes.

Infection control

Following the bone marrow transplant, the positive patient was nursed in a single room in the Oncology ward. Barrier nursing techniques were implemented. The patient subsequently died two days after the specimen was sent to the laboratory, before the isolate was fully identified. Rectal swabs collected from all patients within the ward were culture negative for VRE. Environmental samples were collected from the walls, cupboards, bed frame, mattress and pillowcase in the single room. No VRE were isolated from any of the environmental samples. All horizontal surfaces, walls and the bed frame in the patient’s room were cleaned with neutral detergent solution.

Discussion

With the emergence of vancomycin resistance in enterococci, the choice of antibiotics for treatment of VRE infections is severely restricted. However, amoxycillin still remains a therapeutic option in cases of disease due to vancomycin resistant strains of \textit{E. faecalis}. With the emergence of β-lactamase producing strains of enterococci, amoxycillin becomes ineffective. Only a few cases of β-lactamase producing, vancomycin resistant \textit{E. faecalis} have been reported worldwide. Two other β-lactamase positive strains of enterococci have been isolated in Australia, however, this is the first documented case of β-lactamase production in a vancomycin resistant isolate.

The clinical history of the positive patient highlights many of the key ‘at risk’ criteria that one would expect for development of VRE infection. Firstly, the patient was diagnosed with non-Hodgkins lymphoma and was severely immunosuppressed prior to and following a bone marrow transplant. Secondly, during the course of his illness, he had been exposed to a wide range of broad spectrum antibiotics which would have the potential to promote colonisation by organisms such as enterococci. In addition to this, he had received five courses of vancomycin, three of which were in the two month period immediately preceding the detection of vancomycin resistant enterococci. The reason for the selection for β-lactamase production is not as clear cut. However, piperacillin and ceftazidime were used as prophylactic antibiotic cover during the period preceding his bone marrow transplant.

Since 1996, rectal swabs have been routinely collected on a weekly basis to screen all haematology/oncology and intensive care patients at Royal Brisbane Hospital for VRE. Similarly, any faecal sample submitted for routine microbiological investigation from patients in the Bone Marrow Transplant Unit are also screened for VRE. The samples are screened by plating on ESEL vancomycin medium. Colonies showing evidence of aeculin hydrolysis are subcultured for further identification tests. All enterococci are tested by the agar dilution method against a number of antibiotics including amoxycillin 2 mg/L, vancomycin 4 mg/L, gentamicin 500 mg/L and streptomycin 2,000 mg/L. β-lactamase tests are routinely performed on all enterococcal isolates. Any strain of enterococcus which is resistant to vancomycin at 4 mg/L has vancomycin and teicoplanin minimum inhibitory concentrations (MICs) determined using the \textit{E} Test\textsuperscript{TM} method.

On detection of VRE, the infection control unit is notified and screening of close ward contacts is undertaken. In this instance, all other patients within the ward were culture negative for VRE. Because enterococci can survive for long periods of time in the environment, it is recommended that environmental sampling be undertaken prior to cleaning to establish the extent of the potential contamination.
When VRE is isolated from a patient at RBH, he/she is transferred to a single room in the Infectious Diseases Unit. Rectal swabs are then collected weekly and screened for VRE until there are three consecutive negative samples. Meanwhile, his/her previous room is cleaned with a neutral detergent solution and the bedding and drapes are replaced. Swabs taken from various cleaned horizontal surfaces are then collected and screened for VRE prior to reuse.

Outbreaks of VRE infection are usually a result of dissemination of a single clone either via hospital personnel or contact with contaminated fomites. Implementation of strict infection control practices involving barrier nursing and isolation of positive patients is required to limit the outbreak. Failure to implement such precautions may result in the establishment of multiple endemic strains. Greatly increased usage of broad spectrum antibiotics including third generation cephalosporins and vancomycin have also contributed to escalating numbers of VRE isolates. With the emergence of β-lactamase producing VRE, therapeutic options are diminishing even further. Vancomycin usage should be restricted to limit the potential proliferation of VRE.

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References

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