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# Vancomycin Resistant Enterococcal Sepsis in An Acute Myeloid Leukemic Patient

Abdul Sattar, Shahid Ahmed Abbasi, Irfan Ali Mirza, Nasrullah Malik, Parvez Ahmed\* and Farah Faqir

## ABSTRACT

Neutropenic fever is an important cause of morbidity and mortality during therapy of acute myeloid leukemia. Patients with acute myeloid leukemia are at increased risk of acquiring vancomycin resistant enterococcal infection and its treatment remains problematic. Vancomycin therapy for more than 7 days is usually associated with inducible vancomycin-resistant enterococcal infections. We report a case of vancomycin resistant enterococcal sepsis in a patient of acute myeloid leukemia.

**Key words:** *Enterococcus. Vancomycin. Resistance. Sepsis. Acute myeloid leukemia.*

## INTRODUCTION

Bloodstream infections are major causes of morbidity and mortality in patients of acute myeloid leukemia (AML) undergoing chemotherapy. These patients are susceptible to a wide variety of infections due to prolonged and severe neutropenia.<sup>1</sup> This contributes to delayed administration of chemotherapy, increased length of hospitalization, and healthcare expenditure. Risk factors include the widespread use of empiric antimicrobial therapy, increasingly intensive chemotherapeutic regimens and frequent use of central venous catheters.<sup>2</sup> Enterococci are common cause of bloodstream infections. First case of vancomycin-resistant enterococcus (VRE) was reported in 1980s followed by several such reports throughout the world.<sup>3</sup> Vancomycin resistance has appeared preferentially in *E. faecium*, which is inherently more resistant to multiple drugs, making therapy extremely problematic.<sup>3</sup> History of vancomycin therapy for more than 7 days is significantly associated with VRE colonization.<sup>4</sup> Recently, the incidence of VRE-related infection has been on the rise, and its treatment has become a serious issue during the pre-engraftment period.<sup>5</sup> Patients with AML represent a high-risk population for development of VRE infection.<sup>6</sup> Bielorai *et al.* reported a case of VRE septicemia in a neutropenic patient.<sup>7</sup> To the best of our knowledge, there is no report of VRE sepsis in acute myeloid leukemic patients from Pakistan. We report a case of VRE septicemia from bone marrow transplant centre.

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## CASE REPORT

A 25-year-old male patient, who was a known case of AML M3 was admitted in the Bone Marrow Transplant Centre, Rawalpindi, with a 5 month history of anal fistula along with painful bleeding per rectum and mild to moderate fever. His vital signs and pertinent laboratory investigations included, a blood pressure of 110/70 mmHg, pulse rate of 90/minute, Hb of 6.6 gm/dL, WBCs count of  $8.3 \times 10^9/L$  and platelet count of  $28 \times 10^9/L$ . His treatment was started with injection ceftriaxone 2 gm I/V BD, injection amikacin 1 gm I/V OD, injection metronidazole 400 mg I/V TDS and tablet prednisolone 50 mg per day on the day of admission.

Next day chemotherapy was started with capsule ATRA 70 mg/day (day 1 to day 30), Injection Indurubicin 15 mg in 100 ml normal saline I/V over 30 minutes (on days 2, 4, 6 and 8). On the 8th day, patient complained of sore throat and tablet moxifloxacin 250 mg BD was started. On the 11th day, patient had fever of  $100^\circ F$  and injection piperacillin-tazobactam was initiated. On the 14th day, high grade fever still persisted and injection amphotericin B was started. On the 15th day due to persistence of high grade fever, his chemotherapy was withheld. When on the 17th day, his clinical condition did not improve, injection teicoplanin was started. On the 18th day patient was severely myelosuppressed and toxic with high grade fever, therefore blood for culture/sensitivity was sent. Gram staining of blood showed gram-positive cocci in chains. On the 19th day blood culture yielded growth of enterococci. On the 20th day, antimicrobial susceptibility of the organism showed that isolate was resistant to vancomycin and sensitive to tigecycline and linezolid by disc diffusion method. Confirmation of VRE was done by determining MICs using E Strip (Ab biodisk). On the basis of sensitivity report tigecycline 100 mg I/V stat followed by 50 mg BD and tablet linezolid 600 mg BD were started. After 2 days of therapy, patient improved and temperature came

down to 99°F. On 4th day of therapy patient became completely afebrile.

## DISCUSSION

Acquisition of nosocomial pathogens resistant to multiple antibiotics represent a threat to patient's safety. The emergence of acquired resistance to vancomycin has been particularly problematic as it often occurs in enterococci that are also highly resistant to ampicillin and aminoglycosides.<sup>3</sup> Since the first report in 1988, nosocomial VRE infections have become a major problem in Western countries. In Pakistan the first case of VRE was reported in 2002 from a tertiary care hospital in Karachi, in a patient of neonatal sepsis. In 2004 another case of VRE was reported from AFIP Rawalpindi, in a renal transplant patient.<sup>8</sup> Transplant recipients, patients in ICU, haematology units or long-term care facilities are all at high risk of VRE infection and colonisation.<sup>9</sup> Vancomycin-resistant enterococci are significant nosocomial pathogens in patients with haematologic malignancies. Due to the effect of chemotherapy the patient in the present case report was neutropenic, hence the chances of acquiring VRE infection were increased. Worth *et al.* showed that there are more chances of VRE infection with neutropenia of more than days.<sup>2</sup> Several studies have shown that long-term use of glycopeptides can lead to development of resistance. This patient was on injection teicoplanin for 6 days. Another risk factor for VRE sepsis in this case was AML.

In outbreak of VRE infection at a tertiary cancer hospital in USA, AML was among the risk factors for VRE infection.<sup>6</sup> As VRE has ampicillin and high level aminoglycoside resistance (HLAR), these are the most difficult organisms to treat. The VRE isolated in this case was sensitive only to linezolid and tigecycline. Currently, linezolid is the only oral agent approved by the FDA for treatment of infections caused by VRE.<sup>10</sup> This patient was also successfully treated with linezolid and tigecycline.

It is concluded that risk stratification for development of VRE infection is possible for patients with haematologic malignancy. Patients with AML represent a high-risk population, and targeted prevention strategies must include improved antibiotic stewardship, particularly judicious use of vancomycin therapy.

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