Incidence, Clinical Features, Risk Factors and Outcome of Bacteremia due to Vancomycin-Resistant and Vancomycin-Sensitive Enterococcus Species Analyzed over a 7-Year Period in a Single Cancer Institution

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The aim of this study was to retrospectively compare the incidence, risk factors, and outcome in patients seen over a 7-year period at the National Cancer Institute in the Slovak Republic, with vancomycin-sensitive or vancomycin-resistant enterococcal bacteremia. The total incidence of enterococcal bacteremia at the National Cancer Institute increased from 5.1% in 1991 to 11.1% in 1993 and then decreased to 4.3% in 1995. Analysis of the 77 episodes of enterococcal bacteremia from 66 patients showed that 69 episodes from 60 patients were due to vancomycin-sensitive Enterococcus faecalis (group 1) and 8 episodes from 8 patients were due to vancomycin-resistant Enterococcus faecium (group 2). The features most frequently associated with enterococcal bacteremia were the insertion of a central venous catheter, neutropenia lasting more than 10 days, previous therapy with cephalosporins or vancomycin, previous prophylaxis with quinolones, and the incidence of superinfections. There was no difference in the clinical course or outcome between the 2 study groups. Previous therapy with aminoglycosides, cephalosporins or vancomycin, superinfections with other organisms, and the incidence of breakthrough bacteremia significantly correlated with patients with vancomycin-resistant E. faecium rather than patients with vancomycin-sensitive E. faecalis. The overall mortality was similar in both groups and averaged 32.5% for all enterococcal bacteremic patients. In this study, the major risk factors associated with cancer patients for developing vancomycin-resistant enterococcal bacteremia were previous therapy with aminoglycosides, cephalosporins or vancomycin, superinfections with other organisms and the incidence of breakthrough bacteremia.

Key words: enterococcal bacteremia, cancer, vancomycin resistance

INTRODUCTION

Escherichia coli and Staphylococcus spp. are the most commonly isolated pathogens from the blood of cancer patients, yet it is the third most common isolate, Enterococcus spp., which is associated with higher mortality in these patients.1,2 Vancomycin is the antibiotic of choice to treat enterococcal bacteremia, but the incidence of vancomycin-resistant strains, predominantly Enterococcus faecium, is increasing and represents an incidence of 10% to 16% of all enterococcal bacteremias in the US and 4% to 8% in Europe.2-5 E. faecium bacteremia occurs more frequently in neutropenic cancer patients with acute leukemia who are frequently pretreated with vancomycin, and it is also higher in centers using oral vancomycin for prophylaxis in bone marrow transplantation, intensive care units, for prophylaxis in central venous catheter insertion, or as empiric therapy for postantibiotic colitis.1,5

Enterococcus faecalis was once considered to have low pathogenicity, but it is now accepted that enterococci which arise from the gastrointestinal or urinary tract may cause serious infections particularly bacteremia or endocarditis.1,4 E. faecalis is responsible for 95% of all enterococcal bacteremias, however the proportion of bacteremias caused by E. faecium is increasing.4,6 Some studies have indicated that vancomycin-resistant E. faecium is associated with a higher mortality than E. faecalis.5,7 Therefore we retrospectively analyzed the incidence, risk factors, clinical features, patterns of resistance and outcome in cancer patients with enterococcal bacteremia seen at the National Cancer Institute, from 1989 to 1995, in the Slovak Republic.
PATIENTS AND METHODS

Study design
All cases of positive enterococci blood cultures from patients seen at the National Cancer Institute of the Slovak Republic during the period from January 1, 1989 to December 31, 1995 were included in this study. Seventy-seven episodes of enterococcal bacteremia were identified and the following patient characteristics were recorded: age, sex, type of malignancy, site of infection, enterococcal colonization at multiple sites, presence of other microbes, previous prophylaxis and/or antibiotic therapy, incidence of neutropenia (absolute neutrophil count less than 500/mm³ at the onset of bacteremia), venous or urinary tract catheter insertion, the incidence of hepatic disorders (3-fold elevation of hepatic enzymes and/or serum bilirubin), renal dysfunction (creatinine clearance below 0.7 mL/sec and/or a 20% increase in serum creatinine), or prior surgery or endoscopic procedures. The incidence of septic shock was included and was defined as sepsis associated with evidence of organ hypoperfusion and a systolic blood pressure that was less than 90 mm Hg or greater than 30 mm Hg less than the baseline value, or there was a requirement for intravenous fluids or vasopressors to maintain blood pressure. Mortality due to bacteremia was defined as death with clinical signs of active infection and positive blood culture, while death appearing up to 5 days after the isolation of enterococcal bacteremia, but not clearly associated with sepsis and/or shock was considered as a death with secondary bacteremia.

Blood samples were cultured with the use of an Isolator system (Dupont, Roche Laboratories, Bratislava, Czech Republic, from 1981 to 1992; Wampole Laboratories since 1993), and strains were analyzed with a Vitek Jr. system (Vitek Systems and Bio Merieux Europe, Vienna, Austria). The presence of E. faecium was confirmed by arabinose fermentation. Enterococcal bacteremia was confirmed by isolation of an Enterococcus species from 2 or more blood cultures, or from a single blood culture if there was a clinically-apparent source of infection. The bacteremia was considered polymicrobial if organisms in addition to Enterococcus species were isolated either from the same blood culture or from multiple cultures obtained during a single bacteremic episode. The source of the bacteremia was considered to arise from a culture-positive site or a clinically evident site of infection. If blood was the only culture-positive specimen and there was no evident source of infection, the source of bacteremia was considered unknown. A positive enterococcal blood culture appearing up to 10 days after initial improvement and/or cure was considered as a relapse. Vancomycin-resistance was defined as an MIC greater than 8 μg/mL.

Antibiotic policy in our center
Since 1990, the antibiotic policy at our cancer institu-