What Is the Source of Bloodstream Infection due to Vancomycin-Resistant Enterococci in Persons with Mucosal Barrier Injury?

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To the Editor

Persons undergoing treatment with cytotoxic chemotherapy or hematopoietic stem cell transplant (HSCT) are particularly vulnerable to bloodstream infections (BSIs). While performing surveillance for central line-associated BSIs (CLABSIs), many infections that result from gut translocation following mucosal injury are likely to be misinterpreted as catheter associated. These infections would not be amenable to CLABSI preventive efforts and can adversely affect publicly reported rates.1,2

While definite diagnosis of CLABSI requires catheter removal, an alternate method of differential time to positivity (DTP) has proved to have good sensitivity and specificity in diagnosis of CLABSI.3 Colonization with vancomycin-resistant enterococci (VRE) is increasingly being encountered among persons undergoing HSCT. Steinberg et al4 compared organisms causing CLABSI among neutropenic and nonneutropenic hosts and reported a higher occurrence of VRE-associated CLABSI in persons with neutropenia due to cytotoxic chemotherapy (16.7% vs 4.5%; P = .001). A unique pathogenesis of VRE bacteremia in transplant recipients heralded by massive gastrointestinal overgrowth of VRE has been demonstrated.5 While this might predispose to gut translocation and bacteremia, contamination of a patients' environment with subsequent exogenous entry of the organism into the bloodstream via catheter is a plausible mechanism of BSI as well.6

The National Healthcare Safety Network recognized the challenges of CLABSI surveillance among select hosts and created a distinct entity of mucosal barrier injury laboratory-confirmed bloodstream infection (MBI-LCBI), which is currently in the works; data collection began in January 2013. According to the proposed modifications, BSI caused by oral and gastrointestinal commensal organisms in HSCT recipients with severe diarrhea or grade 3 or higher gastrointestinal graft-versus-host disease (GVHD) and neutropenia...
(absolute neutrophil count less than 500 cells/mm$^3$) would meet criteria for MBI-LCBI. These modifications are based on expert opinion; no clinical evidence supporting this stratification exists.$^7$

To investigate the MBI-LCBI definition, we examined the pathogenesis of VRE-CLABSI among HSCT recipients using 2 distinct methods: molecular typing comparing gastrointestinal and blood isolates from the same patient$^1$ and DTP for concomitantly drawn blood through the catheter and percutaneously.$^2$ This retrospective study was conducted among adult allogeneic HSCT recipients at Memorial Sloan-Kettering Cancer Center from July 2011 until May 2013. Electronic medical records were reviewed to retrieve demographic, clinical, and laboratory information. Blood cultures were drawn as per Memorial Sloan-Kettering Cancer Center policy and procedures. For the central venous catheter (CVC), the needleless connector was disinfected, and 20 mL of blood was drawn. The same volume of blood was drawn percutaneously by aseptic technique. Blood culture bottles were incubated in the BACTEC 9240 automated blood culture system. DTP was defined as the difference in time for blood cultures drawn simultaneously through the CVC and from a peripheral vein to become positive. On the basis of previous studies, DTP was considered to indicate a CVC source if the blood culture drawn through the catheter became positive at least 120 minutes earlier than a culture drawn percutaneously.$^3$ Multilocus sequence typing (MLST) for VRE was performed as previously described.$^8$ The Memorial Sloan-Kettering Cancer Center institutional review board reviewed the study and granted a Health Insurance Portability and Accountability Act waiver of authorization.

Thirty-two patients had a positive blood culture for VRE during the study period. Among these, 10 patients had blood cultures drawn through the catheter only. Six had positive blood cultures from the catheter only, with negative peripheral blood cultures. Each of these was considered a true CLABSI. One patient had a positive culture drawn via periphery with a negative blood culture drawn via catheter. Fifteen patients had positive blood cultures drawn from catheter and periphery, 3 were not concomitantly drawn, and 1 patient had received linezolid; these were excluded. Among the remaining 11 patients, mean age was 55.6 years, and 6 were male. Acute myelogenous leukemia was the most common underlying disease ($n = 9$). Seven patients had received T-cell-depleted transplants, 3 had received unmodified transplants, and 1 person had received a cord graft. Ten of 11 patients were in the early posttransplant period at the time of VRE bacteremia (range, 6–16 days posttransplant). One person was day +185 after transplant; none had any clinical evidence of GVHD, and 10 of 11 were neutropenic. Three patients had more than 1 catheter type at the time of infection. The most common catheter types were Hickman ($n = 6$) and nontunneled triple lumen ($n = 4$). Two patients each had a MediPort and peripherally inserted central catheters. The DTP was calculated for 11 evaluable patients and predicted that 2 (18%) had CLABSI (Figure 1). VRE colonization was detected before onset of bacteremia in all patients. MLST typing of strains obtained from stool and blood showed concordance for all 11 patients. Six unique ST types were isolated (ST 280, 203, 412, 419, 17, and 436).

In our study, we used VRE as a representative organism among HSCT recipients for several reasons. See et al$^7$ report VRE among the most common organisms reported to cause BSI in patients who met the MBI criteria. VRE is the only organism for which gastrointestinal
overgrowth under antibiotic pressure has been demonstrated and recently shown to precede bloodstream invasion in HSCT recipients. Finally, empiric use of VRE active agents is not routine among HSCT recipients, reducing the likelihood of false negative results on blood culture. Our findings show that the majority (82%) of cases of VRE BSI early after HSCT—a period of neutropenia and mucositis resulting from a preparative regimen—likely resulted from gastrointestinal translocation. The findings from our study support the current National Healthcare Safety Network initiative to distinctly categorize high-risk patients with MBI and BSI due to gastrointestinal commensal organisms. Exclusion of this category when reporting CLABSI among high-risk patients will improve accuracy of reported rates to develop reliable benchmarks.

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REFERENCES


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FIGURE 1.
Time to positivity (minutes) for blood cultures drawn via catheter and percutaneously (peripheral) from 11 hematopoietic stem cell transplant recipients with bloodstream infection due to vancomycin-resistant enterococci.