American Journal of Infection Control 42 (2014) 1084-8

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Utility of routine surveillance blood cultures in asymptomatic allogeneic hematopoietic stem cell transplant recipients with indwelling central venous catheters at a comprehensive cancer center

Lior Nesher MD [a,b,*], Roy F. Chemaly MD, MPH [a], Dimpy P. Shah MD, PhD [a], Victor E. Mulanovich MD [a], Chitra Hosing MD [c], Kenneth V.I. Rolston MD [a]

[a] Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas - MD Anderson Cancer Center, Houston, TX
[b] Internal Medicine Division, Faculty of Health Sciences, Ben-Gurion University, Beer Sheba, Israel
[c] Stem Cell Transplantation and Cellular Therapy, Division of Cancer Medicine, The University of Texas - MD Anderson Cancer Center, Houston, TX

Key Words:
Surveillance
Blood culture
Asymptomatic
Transplant

Background: Many transplant centers obtain surveillance blood cultures (SBCs) from asymptomatic allogeneic hematopoietic stem cell transplant (allo-HCT) recipients with central venous catheters for early detection of potential blood stream infections. The aim of this study was to determine the utility of this practice.

Methods: We conducted a retrospective study of all patients who underwent allo-HCT to determine the frequency, clinical significance, and costs associated with SBCs.

Results: From 776 patients, 6,801 SBCs were obtained (median, 9 per patient). Most (96.89%) were negative. Of the 211 positive SBCs, 171 (81%) had minimal clinical significance. The remaining 40 positive cultures (19%) were considered potentially significant. The frequency of potentially significant SBCs was 5.1% for the entire cohort and 0.59% of all SBCs drawn.

Conclusion: All potentially significant cultures and some that were deemed to have minimal significance led to medical intervention, some of which were probably unnecessary. No adverse outcomes occurred in patients with positive SBCs for the first 30 days following the positive result, regardless of the pathogen isolated or the quantitative colony count. The frequency of clinically significant positive SBCs in asymptomatic adult allo-HCT recipients is very low. Routine use of this practice leads to some unnecessary medical interventions and added costs.

INTRODUCTION

Surveillance cultures from clinically relevant sites, especially in high-risk patients, have been advocated as a means of detecting colonization of pathogenic organisms prior to the onset of infection and may provide the basis for the early institution of appropriate antimicrobial therapy during periods of increased risk.[1] Older studies conducted in cancer patients receiving intensive remission induction chemotherapy failed to demonstrate the utility of routine screening with surveillance cultures from various sites (eg, nose, throat, urine, stools).[2] More recently, surveillance rectal cultures to detect intestinal colonization with vancomycin-resistant enterococci (VRE) have been shown to have high positive and negative predictive values for the development of subsequent VRE bacteremia in patients with hematologic malignancies and recipients of allogeneic hematopoietic stem cell transplant (allo-HCT). They also have been found to be useful in controlling outbreaks of blood stream infections (BSIs) caused by VRE in such patients.[3,4] Similarly, the detection of intestinal colonization with extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBLE) has been shown to be predictive for the subsequent development of BSI with these organisms in patients with underlying malignancies.[5,6] However, only a few patients (~30% with VRE, 6%-8% with ESBLE) who are colonized with potential

* Address correspondence to Lior Nesher, MD, Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas - MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 1460, Houston, TX 77030.
E-mail address: nesherke@bgu.ac.il (L. Nesher).

Conflict of interest: None to report.

0196-6553/$36.00 - Copyright © 2014 by the Association for Professionals in Infection Control and Epidemiology, Inc. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ajic.2014.07.004

pathogens go on to develop subsequent infection. Several studies have shown that only a small proportion of patients with central venous catheter (CVC) colonization go on to develop subsequent BSI. Currently, no reliable methods to identify colonized patients who are likely to develop a subsequent infection are available.[7] Additionally, other studies have demonstrated that routine surveillance blood cultures (SBCs) are not cost effective and add very little to the management of critically ill patients.[8-11]

BSIs are a frequent complication of, and a significant cause of, morbidity and mortality in patients undergoing allo-HCT.[1,12-16] Many factors contribute to the development of BSIs, including the type of underlying malignancy, intensity of antineoplastic therapy, degree and duration of neutropenia, and administration of corticosteroids or other immunosuppressive agents.[1,17] A major risk factor associated with the development of BSI is the presence of long-term CVCs.[18,19] The reported incidence of posttransplant BSI varies between 12.5% and 41%, with gram-positive organisms being isolated more frequently than gram-negative organisms.[14,20-22] A substantial proportion of these BSIs are considered to be CVC related.

Early identification of allo-HCT recipients at potential risk for developing a CVC-related BSI is a desirable goal. Consequently, many hematopoietic stem cell transplant (HCT) centers, including ours, obtain weekly SBCs. The rationale behind this approach is that prior knowledge of organisms colonizing CVCs in such patients may facilitate the administration of appropriate antimicrobial therapy if a subsequent BSI develops. Additionally, many allo-HCT patients have a blunted inflammatory response and may remain asymptomatic despite having occult or overt bacteremia, and SBCs might provide useful information. Nevertheless, the evidence regarding the utility of routine SBCs in this setting is mixed. There is some evidence that SBCs may be useful in allo-HCT recipients during the initial preengraftment period of profound neutropenia and in patients receiving corticosteroids.[23,24] However, SBCs are not recommended in the absence of clinical signs and symptoms in immunocompetent individuals, and their utility has been questioned in some studies conducted in pediatric HCT recipients, especially those without neutropenia.[25,26] Currently, no guidelines exist for the management of asymptomatic patients with positive SBCs. Because the practice of obtaining SBCs has become a standard of care at many institutions, including ours, we conducted a retrospective study to determine the frequency and clinical significance of positive SBCs and whether or not they are useful in predicting subsequent BSI. We also documented the various therapeutic interventions that were implemented based on the results of these SBCs, the outcomes of patients with positive SBCs, and the costs associated with the performance of SBCs.

METHODS

This study was approved by the Institutional Review Board at the University of Texas - MD Anderson Cancer Center (protocol no. PA11-1180). Patients were identified using the stem cell transplantation and cellular therapy departmental registry. The medical records of study patients were reviewed retrospectively. Data retrieved included demographic data (eg, age, sex, underlying malignancy), type of allo-HCT, antimicrobial prophylaxis, usage of corticosteroids or other immunosuppressive agents, number of SBCs, presence of neutropenia on the day of the positive culture, and time in days from CVC insertion to positive SBC. In patients with a positive SBC, additional information (eg, microbiologic data, clinical course, management) and outcome of the episode was also retrieved. All patients had a nontunneled, nonantibiotic-coated CVC placed prior to transplantation. Routine weekly SBCs were obtained starting 1 day prior to transplantation and usually lasting until 100 days posttransplant, or as long as the CVC was in place. This study included only SBCs obtained from asymptomatic patients with a normative temperature ($<38^{\circ}$C). We excluded patients in whom the treating physician suspected an infectious process at the time the cultures were drawn. All patients received prophylactic antibiotics while they were neutropenic, with fluoroquinolones being administered most often. In all cases, SBCs were drawn from the CVC, whether the patients were hospitalized or not, using aseptic techniques and placed into 2 sets of blood cultures: (1) standard blood culture vials using the BACTEC system (Becton Dickinson, Franklin Lakes, NJ) for qualitative blood cultures,[27] and (2) using the lysis-centrifugation system (Isolator, Wampole Laboratories, Cranbury, NJ) for quantitative blood cultures as previously described.[28] In patients with multiple lumen CVCs, SBCs were obtained from each lumen. Patients with positive SBCs were managed according to current standards of care at our institution.

All reported positive cultures were included in this study regardless of the type of pathogens recovered, and they were divided into 1 of 3 predefined groups based on current recommendations for catheter-related infections.[29]

- Group 1: this group included patients with $\leq$10 colony-forming units (cfu)/mL on quantitative SBCs that were positive for common skin inhabitants and low virulence pathogens (eg, coagulase negative staphylococci, *Corynebacterium* spp, *Bacillus* spp, *Micrococcus* spp). This group was considered to be at low risk for the subsequent development of bacteremia.
- Group 2: this group included patients with >10 cfu/mL on quantitative SBCs that were positive for common skin inhabitants and low virulence pathogens (eg, coagulase negative staphylococci, *Corynebacterium* spp, *Bacillus* spp, *Micrococcus* spp). This group was considered to be at some risk for the subsequent development of bacteremia.
- Group 3: this group included all patients with positive SBCs not included in the previous 2 groups regardless of colony count or organism isolated. This group was considered to have a substantially higher risk for the development of bacteremia than the previous 2 groups.

We also ascertained the cost associated with the performance of SBCs.

Statistical analysis

We summarized the baseline demographic data, which included means, medians, and ranges, for continuous variables and frequency for categorical variables. We also determined the incidence of positive cultures or yield of routine SBCs for the study period. One-way analysis of variance test, χ^2 test, and Fisher exact test were used to assess differences between the 3 groups with respect to demographic and clinical characteristics when appropriate. Any statistical differences between the outcomes of the 3 culture groups were also assessed by these tests. Unadjusted and adjusted odds ratios with 95% confidence intervals were also calculated for each clinical characteristic that may be a potential risk factor for pathogenic culture (group 3) compared with nonpathogenic culture (group 1 and 2 combined) using logistic regression analysis. We used 2-tailed tests with alpha = .05 for statistical significance. All statistical analyses were performed using Stata software version 10.1 (StataCorp, College Station, TX).

RESULTS

During the study period, a total of 794 patients underwent allo-HCT. Of these, 18 were excluded because of the development