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Original Contribution

Bacteremia in nonneutropenic pediatric oncology patients with central venous catheters in the ED☆,☆☆,★

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ABSTRACT

Objective: To examine clinical characteristics associated with bacteremia in febrile nonneutropenic pediatric oncology patients with central venous catheters (CVCs) in the emergency department (ED).
Background: Fever is the primary reason pediatric oncology patients present to the ED. The literature states that 0.9% to 39% of febrile nonneutropenic oncology patients are bacteremic, yet few studies have investigated infectious risk factors in this population.
Methods: This was a retrospective cohort study in a pediatric ED, reviewing medical records from 2002 to 2014. Inclusion criteria were patients with cancer, temperature at least 38°C, presence of a CVC, absolute neutrophil count greater than 500 cells/μL, and age less than 22 years. Exclusion criteria were repeat ED visits within 72 hours, bloodwork results not reported by the laboratory, and patients without oncologic history documented at the study hospital. The primary outcome measure is a positive blood culture (+BC). Other variables include age, sex, CVC type, cancer diagnosis, absolute neutrophil count, vital signs, upper respiratory infection (URI) symptoms, and amount of intravenous (IV) normal saline (NS) administered in the ED. Data were analyzed using descriptive statistics and a multiple logistic regression model.
Results: A total of 1322 ED visits were sampled, with 534 enrolled, and 39 visits had +BC (7.3%). Variables associated with an increased risk of +BC included the following: absence of URI symptoms (odds ratio [OR], 2.30; 95% CI, 1.13-4.69), neuroblastoma (OR, 3.65; 95% CI, 1.47-9.09), "other" cancer diagnosis (OR, 4.56; 95% CI, 1.93-10.76), tunneled externalized CVC (OR, 5.04; 95% CI, 2.25-11.28), and receiving at least 20 mL/kg IV NS (OR, 2.34; 95% CI, 1.2-4.55). The results of a multiple logistic regression model also showed these variables to be associated with +BC.
Conclusion: The absence of URI symptoms, presence of an externalized CVC, neuroblastoma or other cancer diagnosis, and receiving at least 20 mL/kg IV NS in the ED are associated with increased risk of bacteremia in nonneutropenic pediatric oncology patients with a CVC.

1. Introduction

Fever is the primary reason pediatric oncology patients present to emergency departments (EDs) in the United States and is often the heralding symptom of a life-threatening infection [1]. The incidence and risk of bacteremia in febrile neutropenic pediatric oncology patients has been well described in the literature [8-10]. The same is not true, however, for nonneutropenic pediatric oncology patients, who represent a considerable portion of patients evaluated in the ED. It has been reported that 0.9% to 39% of febrile nonneutropenic oncology patients with fever are bacteremic [2-6], yet very few studies have investigated infectious risk factors in this specific patient population [2,7]. Consequently, clinical management strategies for febrile nonneutropenic patients vary greatly among providers [6].

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Central venous catheters (CVCs), such as Broviac® (Bard Access Systems Inc, Salt Lake City, Utah), Port-a-Cath® (Smiths Medical, St Paul, Minnesota) (port), and peripherally inserted central catheters (PICCs), are routinely used to facilitate chemotherapy, fluid administration and blood draws in pediatric oncology patients, but these devices are associated with significant morbidity and mortality [2,7,11-14]. Since the standardization of their use, rates of bacteremia among pediatric oncology patients have increased [3,4]. Central line–associated blood stream infections among inpatient pediatric hematology oncology patients ranges from 2.3 to 4.6 infections per 1000 catheter-days [4]. There are 3 times more central line–associated blood stream infections in the ambulatory setting compared with the inpatient setting [4]. Because of the elevated risk of infection inherent to oncology patients undergoing immunosuppressive therapy, and particularly those with CVCs, it is vital that emergency physicians have a clear understanding of the clinical factors associated with bacteremia in nonneutropenic as well as neutropenic hosts to provide optimal care to this vulnerable patient population.

The aim of this study is to examine clinical characteristics associated with a higher risk for bacteremia in nonneutropenic pediatric oncology patients with CVCs evaluated for fever in the ED.

2. Methods

2.1. Study design and setting

This retrospective cohort study was conducted at a large, urban academic children's hospital in Los Angeles, California, where more than 400 newly diagnosed cancer patients are treated each year. The study hospital ED sees approximately 82,000 patients annually, for a wide variety of medical and traumatic diagnoses. The institutional review board at the study hospital approved the current study.

2.2. Study subject identification

An electronic query was performed to identify ED visits between 2002 and 2014 with a documented chief concern of fever, and an associated *International Classification of Diseases, Ninth Edition* oncology diagnosis code in the patient's record. Inclusion criteria included a diagnosis of cancer, fever reported from home or body temperature recorded in the ED of at least 38°C, presence of a CVC, absolute neutrophil count (ANC) greater than 500 cells/μL, and age less than 22 years. If a patient presented to the ED multiple times within 72 hours, only the first visit was included in the study. Other exclusion criteria were bloodwork results not reported by the laboratory and patients without oncologic history documented at the study hospital.

2.3. Data collection

An electronic data collection form was created for the study using Research Electronic Data Capture (REDcap). All data collectors were trained in its use before initiation of the study. RLM and CL independently transcribed constituent variables only from ED visits into the data collection form. Specifically, this included the transcription—without subjective interpretation—of vital signs, laboratory results, amount of IV NS administered by the nurse, and symptoms circled by the physician in a standardized preprinted review of systems within the physician's paper charting. Based on their independent review of 75 identical medical records, the 2 reviewers demonstrated a 6.6% proportion of error. LLI, a pediatric hematology oncology fellow, was the sole data extractor for oncology-specific data, including the oncologic diagnosis and details of the patients' oncologic treatment course. Continuous variables from the ED and oncology data were later recoded into categorical or binary data for analysis. Aggregate variables were coded by RLM.

2.4. Outcome measures

The primary outcome variable for the analysis is a positive blood culture (+BC), which is defined as a blood specimen with microbiology laboratory–confirmed bacterial species growth, and is either a high-risk organism or a lower-risk organism [15] that is also identified on a repeat blood culture. Blood samples in which a lower-risk organism grows from an initial blood culture sample from the ED, but not from a repeat blood culture, are considered negative. The results of the analysis refer to the outcome of each ED visit. Independent variables studied include age, sex, CVC type, cancer diagnosis, weeks since last chemotherapy (intravenous [IV] and/or oral administration), ANC, maximum heart rate and minimum systolic blood pressure in triage and in the ED, and the amount of IV normal saline (NS) administered to the patient in the ED. Tachycardia and hypotension are based on age-adjusted ranges for heart rate and blood pressure [16-18]. Upper respiratory infection (URI) symptoms were defined as the presence of rhinorrhea or nasal congestion and cough on review of systems in the ED.

2.5. Analysis

The study was powered to 80% to detect an effect size greater than 6.3%, based on the most recent bacteremia rate in nonneutropenic pediatric oncology patient published in the literature [2]. The differences in distribution of these selected clinical characteristics between negative blood culture and +BC groups were examined. Two-sample *t* test was used for comparing means between 2 groups, whereas Wilcoxon rank sum test was used for comparing the nonnormal distributed variables. χ^2 Test was used when an expected frequency of the categorical variable was 5 or more, and Fisher exact test was used when an expected frequency of the categorical variable was less than 5.

Because there is little information of the known risk factors in the nonneutropenic pediatric oncology population, a multiple logistic regression model using the stepwise and likelihood ratio test assessed potential risk factors for their associations with +BC and retained important covariates in the model. The amount of IV NS administered to the patient in the ED was analyzed as a dichotomous variable, less than 20 mL/kg vs at least 20 mL/kg, which clinically corresponds to pediatric patients not receiving a bolus in the ED vs those receiving at least 1 bolus (a bolus is defined as at least 20 mL/kg of IV NS). The results are summarized as odds ratios (ORs) with 95% confidence intervals (CIs) and *P* values. Statistical significance was set at 2-sided 5% level throughout the analysis.

3. Results

3.1. Study subjects

One thousand three hundred twenty-two ED visits were sampled; 534 were included in the study. Of the excluded patients, 361 had an ANC less than 500, 195 did not have a CVC, 80 were not primary oncology patients of the study hospital, 12 had unavailable or equivocal blood culture results, 7 did not have an ANC reported, 5 were repeat ED visits within 72 hours, and 128 were excluded for a combination of the aforementioned reasons.

3.2. Results

Table 1 describes patient characteristics of the study population. The proportion of the male patients in this study was 56.5% and that of female patients was 43.5%. More than half of the patients had a diagnosis of acute lymphoblastic leukemia (ALL).

The bacterial species isolated from the blood culture specimens are displayed in Tables 2a, 2b, and 2c. There were 39 +BC, for an overall observed bacteremia rate of 7.3%. At the study hospital, *Pseudomonas* species, coagulase-negative staphylococcus, *Staphylococcus epidermidis*,