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Single Positive Commensal Blood Culture in hospital setting is associated with higher mortality after hematopoietic stem cell transplantation

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ABSTRACT

Background: Single positive staphylococcal blood culture in a hematopoietic stem cell transplantation (HSCT) recipient is generally regarded as contamination. Such a blood culture (BC) does not fill the criteria for Laboratory-Confirmed Bloodstream Infection (LCBI) and could be described as Single Positive Commensal Blood Culture. The aim of this retrospective cohort analysis was to determine the clinical significance of SPCBC in HSCT recipients. **Methods:** 206 patients transplanted between 2007 and 2013 were followed until January 2015. **Results:** The 100-day survival for patients without positive BC was 99.6% compared with 83.9% for LCBI and 82.8% for SPCBC ($p = 0.0036$). The 5-year overall survival (5yOS) was 67.1% for patients without positive BC, 44.9% for LCBI, 34.0% for SPCBC ($p < 0.0001$). The per-day risk of developing SPCBC was identical in autologous and allogeneic transplantation. SPCBC remained a significant factor for reduced 5yOS after HSCT in the univariate analysis (HR 2.52, 1.26–5.02, $p = 0.0001$) as well as in the multivariate analysis (HR 2.21, 1.26–3.87, $p = 0.006$). SPCBC consisted solely of different *Staphylococcus* species with dominance of *Staphylococcus epidermidis* (64% of SPCBC). **Conclusion:** To our knowledge this is the first report that specifically shows that short- and long-term survival after HSCT is significantly lower in patients who experience an episode of SPCBC with *Staphylococcus* spp. during HSCT hospitalization.

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Introduction

Bloodstream infections (BSI) are a major risk of severe complications for patients after hematopoietic stem cell transplantation (HSCT) [1–4]. *Staphylococcus* spp. bacteria are part of the normal skin flora and are regarded as one of the leading causes of nosocomial infections [5, 6]. Even though *Staphylococci* are found in a significant proportion of blood cultures collected from patients after HSCT, their presence is often underestimated. Moreover, there are no separate analyses of survival of patients with staphylococcal BSI after HSCT in current studies [1–3]. The role of staphylococcal BSI is more acknowledged in neonatal late onset sepsis, which is most often associated with indwelling medical devices [7]. In infants with very low birth weight, mortality rates for *Staphylococcus epidermidis* BSI, for example, range from 1.5% to 10.2%, showing that bloodstream infection by this pathogen cannot be simply regarded as a “contamination”.

European Centre for Disease Prevention and Control (ECDC) and Centres for Disease Control and Prevention (CDC) diagnostic criteria of Bloodstream Infection (BSI), Laboratory-Confirmed Bloodstream Infection (LCBI) or Central Line Associated Bloodstream Infection (CLABSI) require at least two positive blood cultures with common skin contaminant, e.g. *Staphylococcus* spp., for the diagnosis to be established [8, 9]. A single positive culture with *Staphylococcus epidermidis* in HSCT patient (with or without symptoms of infection) under current guidelines is not classified as BSI or LCBI. For the purpose of this analysis we classified those cases as Single Positive Commensal Blood Cultures (SPCBC) – a definition that would include all cases of patients with single commensal cultures, with or without other clinical symptoms of infection.

Due to the clinical characteristics of some patients with SPCBC during the HSCT hospitalization, we hypothesized that SPCBC within this group of patients might influence the outcome of transplantation.

In this publication, we show that the HSCT patients who have an episode of SPCBC (i.e. a single positive blood culture of *Staphylococcus* spp.) during the transplant hospitalization, have significantly higher short- and long-term mortality. While all of those cases did not fulfil the criteria for BSI, LCBI or CLABSI, we were able to show their significant influence on outcome after HSCT.

Patients and methods

This study was a retrospective cohort analysis of consecutive adult patients who underwent autologous or allogeneic haematological stem cell transplantations at the Department of Haematology, Oncology and Internal Medicine of the Medical University of Warsaw.

In 2006 we set up an electronic medical record system for storing the hematopoietic stem cell transplantation recipients' information. It recorded data necessary for EBMT and CIMBTR reports and excerpts from patients' discharge summaries – including significant microbiological data – that could be systematically evaluated. This allowed us to gather

clinical information about patients after standard hematopoietic stem cell transplantation which exceeded the basic standards required for EBMT and CIMBTR data reporting.

Patients' data were collected and entered into the database between December 2006 and March 2013. After concluding an internal audit that excluded incomplete or incompatible records, we began the final analysis. Patients' outcomes were followed until their death or the cut-off date of December 31, 2014. Response to therapy, relapse, and survival data were updated continuously. No patients were lost to follow-up. All the information concerning demographics, type of underlying disease, transplant type, and survival was noted. All patients gave written, informed consent allowing the use of their medical records for research. The study was approved by Local Institutional Ethics Board.

Prophylaxis and management of infections

Patients received standard antimicrobial prophylaxis with ciprofloxacin, antiviral prophylaxis with acyclovir, and antifungal prophylaxis with fluconazole during the HSCT hospitalization. Central venous catheters were placed on the first day after admission to the hospital and were removed on the day of discharge. Non-tunnelled double lumen central venous catheters were placed in subclavian vein as a standard in HSCT patients. In cases where CVC had to be removed because of infections, the next CVC has been inserted on the same or next day.

In case of fever (pyrexia of 38 °C) or other signs or symptoms of infection, prophylactic antibiotics were stopped and blood cultures were taken. Patients were treated with broad-spectrum intravenous antibiotics at the discretion of the attending physicians until the results of the bacterial cultures were known. The first line antibiotic therapy standard of the centre was piperacillin/tazobactam with amikacin. Other antibiotics were introduced according to the results of the bacterial cultures. If the patient developed signs of septic shock or the symptoms persisted more than 48 h, meropenem or imipenem/cylastatin were added. Fungal infection diagnostic and treatment has been initiated in cases of persistent fever (>96 h), suspected or confirmed fungal infection. In cases of CMV reactivation patients were treated with ganciclovir or other antivirals. Antibiotics were modified according to the susceptibility of all organisms isolated.

Bloodstream infection

All blood cultures (BC) were obtained in response to clinical suspicion of infection, usually fever (pyrexia of 38 °C), malaise, or rash near the site of central venous catheter insertion, or after physician's request (usually when other clinical signs made infection probable). As a standard two sets (aerobic and anaerobic) of blood cultures were taken – one from periphery and one from central line. If there was no bacterial growth and fever persisted subsequent sets of BC were taken.

Blood specimens were tested using BD BACTEC bottle culture qualitative test. Kirby-Bauer disc diffusion test was

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