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Full Length Article

Source, pattern and antibiotic resistance of blood stream infections in hematopoietic stem cell transplant recipients

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KEYWORDS

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Abstract Mucositis developing as a result of myelo-ablative high dose therapy administered prior to hematopoietic stem cell transplantation (HSCT) is associated with the risk of bacteremia. The aim of the present study was to detect the pattern of bacteremia coinciding with the present practice of HSCT, to study the contribution of health-care associated infection (HAI) to the pattern of infection, in the context of the problem of antibiotic resistance in HSCT recipients.

Patients and methods: This is a retrospective, single center study including patients who developed febrile neutropenia (FN) among HSCT recipients in one year duration.

Results: Ninety FN episodes were recorded in 50 patients. Out of 39 positive blood cultures, Gram negative rods (GNR) were the predominant pathogens, constituting 67% ($n = 26$) of isolated organisms, while 33% of infections were caused by gram positive cocci (GPC) ($n = 13$). Bacteremia was significantly associated with central venous line (CVL) infections and gastroenteritis (diarrhea and vomiting) with a p-value 0.024, 0.20 and 0.0001, respectively. Multi-drug resistant organisms (MDROs) were identified in 27 (69%) of the 39 positive blood cultures.

Conclusion: In one year duration, gram negative pathogens were the predominant causes of infection in HSCT recipients with high rates of MDROs in our institution. Gastroenteritis and central venous line infections are the main sources of bacteremia.

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Introduction

Despite the advances in conditioning, supportive care and prophylaxis, infection remains a major cause of morbidity and mortality in HSCT due to continued development of antimicrobial resistance and the emergence of new pathogens [1].

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On investigating normal microflora and their role in maintaining the micro biome it was found that they may prevent colonization of pathogenic microorganisms including MDROs. This is achieved by many ways either competition of space and resources or a complex immunologic and biochemical interactions. The overuse and empirical introduction of antibacterial agents may play a role in the appearance of MDROs. The new approach now is to maintain an intact micro biome through the usage of micro biome-sparing antimicrobial therapy and discovering ways to augment host protective mechanisms thus maintaining a healthy micro biota [2].

The most predominant type of bacterial infection when patients are neutropenic is bacteremia. The main sources of bacterial infection include central venous cathetes, oral flora and gut flora via bacterial translocations [3]. Health-care associated infections (HAI) present evolving challenges to the successful management of infectious complications in this expanding patient population. Therefore, the aim of the present study was primarily to detect the pattern of bacteremia in HSCT patients coinciding with the present practice of HSCT, to study the contribution of HAI to the pattern of infection, and, to investigate the problem of antibiotic resistance on the course and outcome in transplant patients in our institution in one year duration.

Patients and methods

This is a retrospective, single center study conducted at the Microbiology laboratory of the clinical pathology department in collaboration with the Bone Marrow Transplant unit, at The National Cancer Institute of Cairo (NCI), Egypt, in one year duration. During the period extending from the first of January till the end of December 2009, 80 patients had undergone HSCT for different hematological malignant disorders. The study was approved by Ethics Committee of NCI and an informed consent was obtained from all participants.

During this period, 90 bacteremic episodes were recorded in 50 patients only who showed neutropenia and fever. Their data included were age, diagnosis, state of disease, clinically documented infection (CDI) especially central venous line (CVL) and lower respiratory tract infections (LRTI), duration of episode, and broad spectrum antibiotics given with the need of shift to second line. All patients were hospitalized during the study period and if a patient developed fever >48 h after hospitalization the case was considered febrile neutropenia.

Definitions

In the context of HSCT, fever was defined as a single oral temperature of 38.3 °C, or a temperature more or equal to 38.0 °C for 1 h at 2 times with a minimum interval of 12 h. Neutropenia described an absolute neutrophil count (ANC) $<0.5\times10^9$/L or $<1.0\times10^9$/L, with decline predicted over the next two days [4]. Lower respiratory tract infections were defined as any new infiltrate arising within 48 h before or after the onset of fever and neutropenia.

Microbiology

Two blood culture sets were usually drawn from each patient within the first day of fever from two separate veins. If the cannula site, portacath, or central venous catheter (CVC) was suspected as the source of infection, a blood sample was obtained from it as well. Collected blood was directly injected into Bactec® (Becton Dickinsion, USA) culture vials and they were incubated in the Bactec 9050® incubator. When the blood culture revealed a potential contaminant, another positive blood culture, or other clinical evidence of ongoing blood stream infections (BSI), such as rigors, hypotension, or documented infection at a second site with the same organism, was required for confirmation of true infection. Identification of isolates was carried out utilizing MicroScan® dried gram negative MIC/Combo and dried gram positive MIC/Combo panels Siemens Healthcare Diagnostics Ltd. (Sir William Siemens Sq. Frimley, Camberley, UK GU16 8QD) for gram-negative and gram positive organisms. The panel of antibiotics used for gram negative included: amikacin, amoxicillin-clavulanate, ampicillin-sulbactam, cefepime, norofloxacin, ceftazidime, cefotaxime, ciprofloxacin, levofloxacin, gentamicin, tobramycin, imipenem and meropenem. For gram positives the following panel was used amoxicillin-clavulanate, oxacillin, cefepime, cefotaxime, ciprofloxacin, levofloxacin, clindamycin, imipenem, linezolid and vancomycin. Antimicrobial susceptibility testing both manual using antibiotic disk on Muller Hinton agar using petri dishes at 37 °C for 24–48 h. [5], and automated testing using minimal inhibitory concentration (MIC) by the Microscan was determined by using the criteria established by the National Committee for clinical laboratory standards (CLSI) [6]. The multidrug resistant organism phenotype was defined as diminished susceptibility to $\geqslant3$ antibiotics of the antibiotic groups [7].

Management

According to NCI guidelines, empirical treatment was given to F&N patients after withdrawal of blood samples for blood cultures. The first line of empirical regimen included a third generation cephalosporins and amikacin double agent antimicrobial therapy for 3 days, antibiotics were continued if the patient showed response. If fever persisted, treatment was given according to microbiological results and/or clinical examination necessitating shift or addition of antibiotics; whereas if culture results were not indicative, a carbapenem and antifungal were given. Both antibiotics were continued until the patient became afebrile and ANC exceeded 0.5×10^9/L. After recovery, the patients with persistent fever or clinical symptoms related to the infectious episode were placed under close follow up for 2 weeks for verification.

Statistical methods

Data were analyzed using SPSSwin statistical package version 17. Chi-square test or Fisher's Exact test was used to test the relation between qualitative variables. A p-value less than 0.05 was considered significant. All tests were two tailed.

Results

Patient characteristics

In the period from January first to the end of December 2009, blood stream infections were detected in 39 of 90 (43%) febrile