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Bloodstream infections in neutropenic patients with cancer: Differences between patients with haematological malignancies and solid tumours

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Summary *Objectives:* We sought to identify the characteristics, aetiology, antibiotic resistance and outcomes of bloodstream infection (BSI) in neutropenic patients with haematological malignancies (HM) and in those with solid tumours (ST) and assess their impact on empirical therapy and outcomes.
Methods: All episodes of BSI in neutropenic patients with HM and ST were prospectively recorded and compared.
Results: Of 579 episodes of BSI, 493 occurred in patients with HM and 86 in patients with ST. An endogenous source and catheter-related infection were more frequent in patients with HM,

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whereas pneumonia and urinary tract were more common in the ST group. BSI was mainly due to Gram-negative bacilli. Coagulase-negative staphylococci were more frequent in patients with HM, while *Pseudomonas aeruginosa* was more common in patients with ST and was the leading cause of pneumonia. Multidrug-resistant Gram-negative bacilli (MDRGNB) were more frequently isolated in haematological patients who more often received inadequate empirical therapy than those with ST. Case-fatality rates were higher in patients with ST.

Conclusions: We identified significant differences in BSI in neutropenic patients with HM and ST. MDRGNB were more often isolated in patients with HM. Pneumonia due to *P. aeruginosa* was particularly frequent among patients with ST. Case-fatality rates were higher in patients with ST.

Introduction

Bloodstream infection (BSI) remains a major complication in cancer patients, delaying the administration of chemotherapy, reducing the dosages than can be applied, and lengthing hospital stay. BSI may lead to suboptimal treatment and increase mortality rates.[1–3] The available epidemiological data for BSI in neutropenic cancer patients are mainly derived from studies involving patients with haematological malignancies and stem cell transplant recipients.[4,5]

Myelosupressive cytotoxic chemotherapy and some malignancies themselves lead to immunosuppression and an increased risk of infection. The role played by the rapid institution of empirical antibiotic therapy for febrile neutropenia in reducing mortality is now undisputed.[6] It is well known that appropriate empirical antibiotic treatment has a large and significant impact on survival following BSI, especially among neutropenic patients.[7,8]

In recent years, a shift from Gram-positive to Gram-negative organisms has been documented in the aetiology of BSI in febrile neutropenic patients with haematological malignancies.[9] This change is probably due to modifications in the management of these patients (including maximal barrier measures implemented at the time of catheter insertion and better catheter care), the reduced frequency of severe mucositis and the discontinuation of quinolone prophylaxis in some institutions, which had led to a decrease in viridians group streptococci but an increase in Gram-negative bacilli (GNB). An issue of particular concern is the increasing incidence of multidrug resistance among GNB which is becoming a significant therapeutic problem worldwide.[10]

BSI in neutropenic patients with solid tumours seems to be an under-reported complication. These patients are empirically treated with the same antibiotic regimen as neutropenic patients with haematological malignancies.[2] Of note, information regarding the aetiology of BSI in patients with solid tumours is scarce,[11,12] and at present, there are no comparative studies of BSI in these two distinct populations.

The aim of this prospective study was to identify differences in the characteristics, aetiology, antibiotic resistance and outcomes of BSI in neutropenic patients with haematological malignancies and those with solid tumours. We also sought to assess their potential impact on empirical antibiotic therapy and clinical outcomes.

Patients and methods

Setting, patients and study design

From January 2006 to April 2013, we conducted a prospective observational study at a 200-bed university referral cancer centre in Barcelona, Spain. From all episodes of BSI occurring in hospitalized neutropenic adult patients with cancer, information on baseline characteristics, clinical features, antimicrobial resistance, empirical antibiotic therapy and outcome was recorded in a specific database. We compared the episodes that occurred in neutropenic patients with haematological malignancies and haematopoietic stem cell transplant recipients with those occurring in neutropenic patients with solid tumours.

Our Microbiology Laboratory reports all the positive results of blood cultures daily to an infectious disease physician. All patients are followed up, and changes in antimicrobial treatment are advised when necessary. Information regarding these episodes are prospectively collected and recorded in a specific database.

From January 2006 to June 2011 no universal antibacterial prophylaxis was given to prevent bacterial infections during neutropenia. After July 2011, ciprofloxacin was given to all patients receiving an allogeneic transplantation in an attempt to prevent polyomavirus BK virus-associated hemorrhagic cystitis.[13] Empirical antibiotic therapy for febrile neutropenia was mainly cefepime (or imipenem) plus amikacin.

The study was approved by the ethics committee of our institution.

Definitions

Neutropenia was defined as an absolute neutrophil count $\leq$500 neutrophils/μL. Prior antibiotic therapy was defined as the receipt of any systemic antibiotic for $>$48 h in the previous month. BSI was considered to be nosocomially acquired, healthcare related or community acquired, applying the criteria described previously.[14]

Corticosteroid therapy was recorded when a patient was receiving corticosteroids at the time of the episode of the BSI or in the previous month. Shock was defined as a systolic

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