An 8-year survey of strains identified in blood cultures in a clinical haematology unit

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Abstract

The aim of our study was to determine the epidemiological profile and the antibiotic susceptibility of bacteria and fungi identified from blood cultures in the patients of the clinical haematology unit. A retrospective study was carried out over an 8-year period (2003–2010) in the clinical haematology unit of the Percy Military Medical Center. During this period, we collected 723 isolates: Gram-negative bacilli (70.8%) and Gram-positive cocci (18.7%). The four most commonly isolated species were *Escherichia coli* (18.5%), *Pseudomonas aeruginosa* (14.8%), *Stenotrophomonas maltophilia* (6.2%) and *Staphylococcus epidermidis* (5.4%). The rate of methicillin-resistant *Sthaphylococcus aureus* was 6.45% and that of coagulase-negative staphylococci 61.2%. No resistance to glycopeptides was observed. In *E. coli*, as in the Klebsiella-Enterobacter-Serratia group, a 27% resistance to fluoroquinolones was observed. Concerning *P. aeruginosa*, the phenotypes were distributed over penicillinase (23.4%) and cephalosporinase (13.1% were resistant to ceftazidime). The impermeability rate of imipenem was 9.3%. The aggressiveness and duration of haematological treatments explains why infections remain one of the main complications of neutropenia. The emergence of new or unusual bacteria is highly likely. Antibiotic selective pressure and long periods of hospitalization could explain the emergence of multiresistant bacteria. As a consequence, epidemiological surveillance is indispensable.

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Introduction

Infections are serious and frequent complications of cytotoxic chemotherapy-induced neutropenia. Seventy per cent of patients with agranulocytosis or who receive haematopoietic stem cells transplantation develop a fever [1]. The mortality rate is high: 5% in the case of bacteraemias associated with Gram-positive cocci (GPC) and 18% in the case of those associated with Gram-negative bacilli (GNB) [2]. For 30 years, the epidemiology of bacterial infections in these patients has evolved. In the seventies, and until the mid-eighties, the reports from the febrile neutropenic antibiotherapy study group of the EORTC (European Organisation for Research and Treatment of Cancer) showed that in 60% to 70% of cases, bacteraemia in this population was related to GNB [3]. By the end of the 1980s, the proportions reversed to a greater percentage of GPC, before tending towards a balanced situation following the year 2000. The study previously performed in the onco-haematology department of our hospital revealed the variability of these data [4]. Almost 10 years later, it appeared necessary to review the blood culture flora sampled in onco-haematology and to compare the results with the literature. Our aim was to improve the understanding of the impact of various therapeutic scenarios on the flora, and to optimize probabilistic antibiotherapy during episodes of febrile neutropenia.

Methods

We performed a retrospective study, between 1 January 2003 and 31 December 2010, in the Clinical Haematology Department of the Military Medical Centre Percy. This is a 23-bed department, with 10 rooms devoted to intensive care. It handles acute and chronic haematological malignancies and also undertakes procedures related to chemotherapy, autografting and allografting. All of the studied blood culture isolates were validated by the physician and communicated to the clinician. Ten millilitres of venous blood were inoculated into aerobic and anaerobic bottles using the BacT/Alert 3D system (BioMérieux®, Marcy l'Etoile, France). The bottles were incubated at 37°C with constant stirring for 6 days, before being considered as sterile. All positive cultures were subcultured on enriched media: blood agar, boiled blood agar, Sabouraud® agar and Schaedler® agar (BioMérieux®), under anaerobic conditions whenever necessary. An initial examination was carried out followed by another examination after Gram staining. Based on examination, a biochemical identification using the API system® (BioMérieux®) was inoculated directly from the blood culture broth. An antibiogram was also carried out, following the guidelines of the Antibiogramme Committee of the French Society for Microbiology (CA-SFM). An antifungigram was systematically carried out using the E-test® technique (BioMérieux®), whenever the isolate contained a fungus. The inhibition zone or E-test® diameters were read by a SIRSCAN® analyzer (i2a®, Perols, France).

The data were gathered using the 'epidemiological' module of the SIR® software (i2a®), with individualized analyses of the species and their resistance profiles. The bacteria belonging to commensal flora (coagulase-negative *staphylococcus* and *Corynebacteria* sp.) were retained if they were isolated at least twice with the same antibiotype. Duplicates (even isolates with the same sensitivity profile, isolated several times in the same patient over a period of at least 5 days) were excluded.

Patients

The colistin–amphotericin B combination is used in our hospital for selective digestive decontamination (SDD). During allogeneic bone marrow transplantation (BMT), patients receive primary antibioprophylaxis based on a combination of ciprofloxacin and a piperacillin/tazobactam. In the case of febrile neutropenia, the most urgent issue is antibacterial therapy, based on an empirical broad-spectrum antibiotherapy. The protocol applied in our haematology department relies on a dual empirical antibiotherapy according to the Infectious Diseases Society of America (piperacillin/tazobactam and amikacin) for 3 days [5]. The combination with aminoglycoside is not recommended by the European Conference on Infection in Leukemia unless septic shock or pneumonia occurs [6]. In the case of persistent fever, antibacterial therapy relies on ceftazidime and vancomycin and amikacin. This first-line treatment regimen is maintained if effective and/or if the isolated bacterial species is sensitive to this combination. If a resistant GNB is isolated, the spectrum is enlarged to include third-generation cephalosporins (3GC) or even imipenem in the case of ESBL (extended-spectrum betalactamase-producing enterobacteria), which hydrolyze 3GC. If a GPC is isolated, vancomycin is given. This antibiotic can be added at an early stage in the case of an MRSA-carrier patient. Finally, the addition of an antifungal drug (amphotericin B) can become necessary if a fungal infection is isolated or suspected.

Results

Patient profiles, frequency and distribution of species

Over an 8-year period, 1413 patients were hospitalized in our haematology department. Of these, 829 had neutropenia with <1000 neutrophils/mm^3 (grade 3 according to the WHO classification [7]). Among these 1413 patients, 737 had at least one grade 4 neutropenic episode (<500 neutrophils/mm^3). During this period, 6412 blood culture samples (an anaerobic bottle followed by an aerobic bottle) were performed and 723 positive blood culture isolates were identified (i.e. 11.3% of the blood culture samples were positive). During this period, 89 patients underwent an allogeneic BMT. The frequency and distribution of species are presented in Table 1. The most important result of this study is the variation of the epidemiology of bacteraemia: the GPC represent 18.7% (n = 135) of the isolates, and the GNB represent 70.8% (n = 512). The dynamics of the results (Fig. 1) provide a perfect illustration of the variability of these data. The four most commonly isolated species were *Escherichia coli* (18.5%, n = 134), *Pseudomonas aeruginosa* (14.8%, n = 107), *Stenotrophomonas maltophilia* (6.2%, n = 45) and *Staphylococcus epidermidis* (5.4%, n = 39). The GPC isolates consisted mainly of *S. epidermidis* (28.9%), *Sthaphylococcus aureus* (23%, n = 31) and *Enterococcus* sp. (17.8%, n = 24), of which 55% were *E. faecalis* (n = 13). The enterobacteriaceae isolates consisted mainly of *E. coli* (51.7%) and bacteria from the *Klebsiella-Enterobacter-Serratia* (KES) group (40.9%, n = 106). The non-fermenting GNB (NF-GNB) were dominated by *P. aeruginosa* (42.3%, of which 35% were of serotype 6), *S. maltophilia* (17.8%) and *Acinetobacter* sp. (16.6%, n = 42), of which 64.3% were *Acinetobacter baumannii* (n = 27). The NF-GNB represented 49.4% of the GNB (n = 253/512 GNB). Among the other NF-GNB, mainly *Pseudomonas* non-*aeruginosa* (7.5%, n = 19), in particular *Pseudomonas fluo-*