Bloodstream infections (BSI) are important cause of morbidity and mortality and major complications in patients transplanted with hematopoietic stem cells (HSCT). Knowledge of local microbiological epidemiology is essential for optimal management of infections following HSCT. BSI are the most common serious infectious complications of HSCT, occurring in 13-60% of these patients and with mortality rates ranging from 10 to 27%. Understanding characteristic timing of BSI occurrence in specific patient populations enables their anticipation and early detection. On the other hand, knowing the epidemiology and sensitivity patterns of causative microorganisms is the main prerequisite for determining suitable empirical therapy. Aims of this study were to evaluate incidence, timing and etiology of BSI in patients treated with HSCT in a single institution.

PATIENTS AND METHODS

126 consecutive HSCT, performed between January 2005 and October 2008 in the Department of Hematology at University Hospital Merkur, were included in this retrospective study. Data collected from patients' medical records included following variables: patients' age, sex, underlying disorders, blood culture dates and isolates. Records were reviewed during 1 year post-transplantation period unless death occurred before that. All HSCT patients received oral antimicrobial prophylaxis with ciprofloxacin and antifungal prophylaxis with fluconazole from the beginning of conditioning therapy until engraftment or until fever, when empirical intravenous antimicrobials were started. Allogeneic transplanted patients received antiviral prophylaxis with acyclovir and Pneumocystis jiroveci prophylaxis with trimethoprim sulfamethoxazole from engraftment until the end of immunosuppressive treatment and immunologic recovery. Immunosuppressive treatment for acute GVHD prophylaxis in these patients included intravenous cyclosporine and methotrexate therapy followed by oral cyclosporine for 100 days after HSCT unless acute GVHD developed.

RESULTS

36 BSI were identified at a median of 8 (range 1-256, SD 85) days post HSCT. The majority of BSI were observed in the first month following HSCT (Fig 1), mostly (69.4% of all BSI) during the first 2 weeks. A total of 12 different bacterial species were identified (Table 2). Gram-negative microorganisms were the most frequently isolated pathogens (52.8% of BSI). The single most frequently isolated Gram-negative microorganism isolated was *P. aeruginosa*, accounting for 25% of all BSI and 45% of all Gram-negative BSI. Altogether, *P. aeruginosa* was isolated in 9 patients. Multidrug resistance (MDR) was defined as resistance to at least one of the following antibiotic groups: penicillins, cephalosporins, carbapenems, aminoglycosides and quinolones. Four of these nine isolates were multidrug resistant, including resistance to carbapenems. All isolates were sensitive to colistin. Gram-positive pathogens were responsible for 36.1% of BSI. *S. epidermidis* was the most frequently isolated Gram-positive microorganisms (22.2% of all BSI, 61.5% of all Gram-positive BSI). All cases of coagulase-negative staphylococci bacteremias were catheter related. Anaerobic bacteria were isolated 14.6% BSI. Fungi were represented 2.8% of all BSI. A trend towards higher incidence of fungemia in allogeneic HSCT patients was observed ($\chi^2$, p<0.05).

CONCLUSIONS

BSI were a frequent complication of HSCT, with highest incidence during chemotherapy induced mucosal damage and neutropenia. Despite fluoroquinolone prophylaxis, more Gram-negative than Gram-positive BSI were identified. Broad use of antimicrobial prophylaxis over the years has significantly contributed to the rising problem of infections caused by resistant microorganisms. Among Gram-negative pathogens *Pseudomonas aeruginosa* can be especially difficult to treat owing to the intrinsic resistance of this pathogen to many antibiotics and a growing problem of acquired multiple antibiotic resistance. *S. epidermidis* is the most frequently isolated Gram-positive isolate from blood and was the most difficult to treat organism, with 44% isolates being resistant to carbapenems. Empirical therapy in these immunosuppressed patients should inevitably include agents with strong antipseudomonal activity. Treatment of BSI caused by *P. aeruginosa* remains a challenge due to the multiple resistance of this pathogen in our institution.

REFERENCES