

Objective: Non myeloablative conditioning regimen (NMCR) for AHSCT have been developed to reduce procedure-related toxicity. The aim of this approach is to extend indications of AHSCT to patients (pts) who are not eligible previously for high dose chemotherapy or total body irradiation. We describe infectious morbidity related to this new procedure in our unit in a retrospective study.

Results: 45 AHSCT with NMCR were performed in our unit between 1997 to 2001, 32 males, 13 females, with a median age of 48 years (range 18–62). Hematologic diagnosis were 8 AL, 12 MM, 2 CML, 5 NHL, 3 MDS, 6 Hodgkin diseases, 3 CLL, 6 solid tumors. Engraftment was observed in all pts with a median of 21 days (range 12–49) for PNN >0.5 g/l, and 18 days (range 0–201) for platelets >50 g/l. Ten pts received donor lymphocyte infusions (DLI). Nineteen pts (48.7%) presented acute GVHD: 7 without any DLI, 4 before DLI and 8 after DLI (2 grade 1, 7 grade 2, 4 grade 3 and 2 grade 4).

Nineteen pts (42%) presented 39 infections : 1 episode, $n=7$; 2 episodes, $n=7$; 3 episodes, $n=3$; 4 episodes, $n=1$; 5 episodes, $n=1$. Twenty two infections (56.5%) occurred in 13 pts during 3 months post transplant : 18 septicemia (12 Gram-negative bacilli, 5 Gram-positive cocci, one yeast), 1 septic chock without documentation, 2 cytomegalovirus (CMV) infections, 1 zoster. Only 4 of these infections occurred after engraftment (3 bacterial septicemia and 1 CMV disease). The pt with fungal septicemia died before engraftment. We observed 17 late infections (43.5%) in 11 pts : 3 septicemia, 1 septic chock without documentation, 2 CMV diseases, 6 probable invasive aspergillosis, 1 zoster, 1 *Campylobacter colitis*, 1 *Staphylococcus aureus* pneumonia, 1 EBV lymphoma and 1 enterovirus encephalitis. Overall, bacterial infections were observed in 56% of cases, viral in 20% and fungal in 18%. No infection occurred in 26 pts (58%).

Five pts with hematologic malignancy relapse presented a probable invasive aspergillosis.

Twenty eight pts died (62%), 16 in relapse, 9 (32%) with infection : 1 fungal septicemia, 1 viral encephalitis, 1 hepatitis, 6 invasive aspergillosis.

Conclusion: Most of infections observed after AHSCT with NMCR were bacterial in our experience.

Infections in hematopoietic stem cell transplant (HSCT) recipients (RC): 1994–2001

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Aim: To describe the results of our strategies of prevention and treatment of infectious episodes during the neutropenic phase in HSCT Rc.

Materials and methods : Total number of HSCT: 417; number of patients (pts): 388; mean age: 33.9 (1–70); female: 256 (61%); hematological diseases: 247 (59%), solid tumors: 168 (40%), others 2; autologous (AU)

314 (75%), allogeneic (AL) 103 (25%): related 89 (85%, haploidentical 3–2%), non-related 14 (13%): bone marrow 10, umbilical cord blood 4. Mean engraftment days: 12.8 (0–48). Weekly surveillance cultures (WSC) were done: anterior nares swab: detection (dt) of methicillin-resistant (R) *Staphylococcus sp.*, penicillin-R pneumococci and *Aspergillus sp.*, mouthwash: dt of *Candida sp.*, penicillin-R *Streptococcus sp.* and stool: dt of multidrug-R aerobic gram-negative bacilli (AGNB), vancomycin-R *Enterococcus* and *Candida sp.* Routinely selective gastrointestinal decontamination for AGNB and antifungal prophylaxis were not done. Fluconazol (FLU) was used only in pts with *non-C. krusei* colonization detected by WSC. The initial empirical treatment for neutropenia and fever was ceftazidime plus amikacin. The febrile episodes were defined according to the guidelines of the Immunocompromised Host Society (1990).

Results: 434 febrile episodes were detected: a) microbiologically defined infection 150 (34.5%): mono or polymicrobial bacteremia (B) 63, fungemia (F) 2; site of infection (SI) with B 37 and with F 3; bacterial SI without B 55 and fungal SI without F 6; b) clinically defined infection 90 (21%) and c) possible infection 194 (45%); there were 11 pts without fever. Isolated microorganisms: 121 from 105 B and F, AGNB 52 (43%) with 46 (85%) Enterobacteriaceae, gram-positive cocci 53 (44%) with 41 (77%) *Staphylococcus sp.*, others 11 (9%) and *non-C. albicans* 5 (4%). Nine pts had polymicrobial B and 7 more than one episode of B. The most frequent sites of infections with or without microbiological documentation were: urinary tract 51 (25%), lungs 48 (23%), skin and soft tissues 31 (15%), anal 25 (12%) and catheter 21 (10%). Two hundred thirty colonized pts (55%) received FLU prophylaxis and 136 pts (33%) empirical amphotericin B (desoxycholate 119, liposomal 28). Related transplant mortality was 10% (38/388), AU 8% (25/314), Al 13% (13/103) and associated with documented infection 2% (7/388).

Conclusions: (1) The use of FLU was avoided in 45% of the pts, with the benefit of decreasing toxicity and costs. (2) All fungemias were by *non-C. albicans*, probably due to the previous overuse of FLU. (3) The same empirical antibiotic treatment has been used from the beginning of the program without emergence of R strains. (4) Mortality associated to documented infection was low, supporting our strategies of prevention and treatment.

Outbreak of *Pseudomonas aeruginosa* via multiple organ transplantation from a common donor

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Background: Transmission of bacterial infections from a donor to multiple recipients may occur in the setting of

donor bacteremia. We describe a novel mechanism for transmission through direct contamination of a thoracic vascular graft that was removed at the time of organ retrieval. The use of a contaminated innominate artery jump graft for pancreas transplantation resulted in vascular anastomotic infection in multiple recipients from a non-bacteremic donor colonized with *Pseudomonas aeruginosa*.

Methods: Patient data was collected by chart review from the donor and the kidney, kidney-pancreas, heart, lung and liver recipients at 4 separate transplant centers. Isolates of *P. aeruginosa* were tested for relatedness by molecular typing using pulsed-field gel electrophoresis (PFGE).

Results: The donor was a previously healthy 25 year old man who died of a closed head injury. He was intubated for 24h prior to organ retrieval. The donor's routine tracheal suction cultures were positive for *P. aeruginosa* but all blood cultures were negative. Organs were retrieved for lung, liver, kidney-pancreas, kidney, and heart transplantation. The donor trachea was transected and the intrathoracic organs were removed first. A second transplant team retrieved the innominate artery graft, which was in close proximity to the open end of the donor trachea, and the intra-abdominal organs. The kidney-pancreas recipient had *Pseudomonas* bacteremia and rupture of the anastomosis between the innominate artery and native iliac artery 48h post-transplant; the pancreas was subsequently lost. The renal transplant recipient lost his graft from a renal artery anastomotic rupture 9 days after transplant. The liver transplant recipient died from a ruptured mycotic aneurysm of the hepatic artery associated with *P. aeruginosa* bacteremia. The lung transplant recipient developed *P. aeruginosa* pneumonia but no endovascular infection. The heart recipient had an uncomplicated post-operative course. All 5 *Pseudomonas* isolates had the same antibiogram and were found to be identical by molecular typing using PFGE.

Conclusion: We conclude that donors may transmit bacterial infections to multiple recipients by mechanisms other than donor bacteremia. This highlights the importance of obtaining donor cultures from multiple sites. In this outbreak, the spillage of tracheal secretions from the transected trachea directly contaminated the innominate artery graft, which resulted in cross-contamination of the intraabdominal organs. Although donor tracheal cultures are commonly positive, careful consideration should be given to antimicrobial treatment of recipients when a Gram-negative organism is isolated.

Selective fluconazole (flu) prophylaxis (p) in hematopoietic stem cell transplant(hsct) recipients (r)

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Aim: To evaluate our strategy of FLU P only in HSCT R with non-*Candida krusei* colonization (COL).

Materials and Methods: A prospective cohort study from July 1996 to December 2001; 289 consecutive HSCT R were included to detect *Candida* spp from oropharynx and stool (high risk pts) by weekly surveillance cultures, taken from the beginning of chemotherapy until neutropenia was resolved and were plated onto selective Chrom-agar plates. Only the pts with non-*C. krusei* COL received FLU 200 mg/day until engraftment or empirical amphotericin B initiation; pts undergoing antifungal prophylaxis or treatment at the time of inclusion were excluded. Demographic characteristics were: n pts: 289, mean age: 33.8 (0-70), female: 169 (58%), hematological diseases: 197 (68%), solid tumors: 89 (32%), others: 3 (1%), autologous (AU): 203 (70%), allogeneic (AL): 86 (30%), mean engraftment days: 12.8 (3-48).

Results: There were no differences in the frequency of MD IFI in the compared populations

- *C. albicans* was the most frequent species isolated in COL pts and caused 2 IFI
- *Candida krusei* was isolated in 6 (3.4%) COL pts, 3 selected during FLU P
- Two *C. krusei* caused 2 (1.4%) IFI and were isolated after 9 and 14 days of FLU P
- There was one mortality related to MD IFI

Conclusions: (1) There were significantly more neutropenia days and empirical amphotericin B usage in COL population. (2) FLU P only in non-*Candida krusei* COL pts was safe and cost-effective, avoiding toxicity and emergence of resistant strains.

Risk factors for CMV retinitis after allogeneic blood stem cell transplantation

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We performed a survey to elicit risk factors for CMV retinitis (CMVR) after blood stem cell transplantation (SCT). A total of 24 cases have been reported from 13 EBMT centres. In the risk factor analysis, 18 patients were included. A control group of 2467 patients was selected who were transplanted at the contributing centres during the study period who had a follow up time of more than one month. The median time from transplantation to diagnosis of CMVR was 160 days