

is highly variable; however, chorioretinal involvement has been rarely described. The case: An 8 year-old girl received a cord blood transplantation in February 2005 for a relapsing acute lymphoblastic leukaemia. She was treated by ganciclovir for *cytomegalovirus* (CMV) reactivation from April to June 2005. Six months after BMT, she presented with prolonged fever, tonsillar necrosis, small pulmonary nodules and positive EBV-PCR in blood and CSF. She underwent bilateral tonsillectomy that showed polymorphic PTLD induced by EBV. She was treated with monoclonal anti-CD20 antibody infusions and a reduction in immunosuppression. Consequently, she improved and EBV-PCR became negative. Seven months after BMT, the fever recurred, associated with enlarging cervical adenopathies enlargement, pulmonary nodules and positive PCR for CMV and EBV in blood. Pathological analysis of pulmonary nodules and cervical lymph nodes biopsies confirmed PTLD. One month later, the patient complained of sudden loss of decreased vision in her left eye. The ophthalmologic examination showed a chorioretinitis and acute retinal necrosis (ARN). EBV PCR of vitreous material revealed high viral load although it was negative in blood. The pathological analysis of the retinal biopsy showed an important infiltration by lymphoproliferative cells LMP-1 positive, but negative for CD20. In situ hybridization with Eber probe confirmed the presence of EBV. Specific treatment consisted of local radiation therapy (150 Gy). Five months after, visual acuity was 6/6 in the right eye and perception of hand movement at 1 meter in the left eye.

Discussion: We report a rare event of confirmed chorioretinal PTLD induced by EBV after BMT in a child. Although rare, ocular PTLD should be part of the differential diagnosis of chorioretinitis and ARN in these patients. Diagnosis was confirmed by retinal biopsies. Positive EBV-PCR on vitreous fluid pleads in favour of the diagnosis and can be helpful, since there is not always a good correlation between viral loads in the blood and those in aqueous and vitreous humor.

49

Development of Invasive Fungal Infection and Related Mortality in Hematopoietic Stem Cell Transplant Recipients with Graft-Versus-Host Disease Receiving Posaconazole versus Fluconazole Prophylaxis

P. Chandrasekar*, W. Morais de Azevedo, S. Durrant, H. Greinix, A. Langston, J.H. Lipton, V. Reddy, D.H. Vesole, S.R. Tarantolo, N. Boparai, H. Patino, A.J. Ullmann. *Harper University Hospital, Division of Infectious Disease, Detroit, MI, USA*

Background: Invasive fungal infection (IFI) is an important cause of morbidity and mortality for hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD). Efficacy and safety of prophylaxis with posaconazole (POS) and fluconazole (FLU) were evaluated in HSCT recipients with GVHD in an international, randomized, clinical trial.

Objectives: This subanalysis evaluated IFI development and associated mortality.

Methods: Patients were randomized to receive POS oral suspension (200 mg 3× daily) or FLU encapsulated tablets (400 mg 1× daily) for up to 112 days. Primary endpoint was incidence of proven/probable IFI, determined by blinded expert panel, during the primary time period (randomization to day 112). Incidence of proven/probable IFI was also assessed during the on-treatment phase (from first to last dose plus 7 days). Deaths during the study were included in a mortality analysis. Investigators determined cause of death.

Results: 600 patients were randomized to receive POS (n=301) or FLU (n=299). During the primary time period, prophylaxis with POS resulted in fewer IFIs than with FLU (5% vs 9%, P=0.07) and significantly fewer cases of *aspergillosis* (2% vs 7%, P=0.006). During the on-treatment phase, significantly fewer IFIs and cases of *aspergillosis* developed in the POS than the FLU group (2% vs 8%, P=0.004; 1% vs 6%, P=0.001, respectively). During the primary time period, of 16 patients in the POS group in whom IFI developed, 10 (63%) died; of 27 patients in the FLU group, 18 (67%) died (table). Among patients in whom IFI did not develop during the primary time period, 66/285 (23%) in the POS group and 66/272 (24%) in the FLU group died.

Conclusions: In this study of HSCT recipients with GVHD, prophylaxis with POS resulted in fewer IFIs than did prophylaxis with FLU. Mortality rates were higher among patients in either treatment group who had IFIs than those who did not. Data suggest early intervention such as prophylaxis with POS,

which significantly reduces the incidence of breakthrough IFI, may more be effective than treatment of established IFIs.

Patients with IFIs	POS (n=16)	FLU (n=27)
Total deaths, n (%)	10 (63)	18 (67)
Cause of death, n (%)		
Progression of IFI	2 (13)	6 (22)
HSCT/GVHD	2 (13)	6 (22)
Adverse events	6 ^a (38)	5 ^b (19)
Unknown	0	1 (4)

^aIncludes: intracranial hemorrhage, brain stem herniation, bacterial sepsis, cardiopulmonary arrest, disseminated *varicella zoster*, upper gastrointestinal bleed.

^bIncludes: diffuse alveolar hemorrhage, cardiac and respiratory failure, *cytomegalovirus* pneumonia, respiratory insufficiency.

50

Risk Factors for Adenoviral Disease in Pediatric Allogeneic Stem Cell Transplant Recipients

E.J. Anderson^{1*}, K. Thormann¹, M. Kletzel¹, J.A. Guzman-Cottrill², X. Zheng¹, B.Z. Katz¹.

¹Children's Memorial Hospital, Chicago, IL, USA, ²Oregon Health and Science University, Portland, OR, USA

Background: Risk factors for *adenovirus* (ADV) infection following allogeneic stem cell transplantation (ASCT) from retrospective studies include graft versus host disease (GVHD), T-cell depleted grafts, lymphopenia, retransplantation, total body irradiation, use of multiple immunosuppressives, and mismatched or unrelated donors.

Objectives: To perform a case-control study to ascertain risk factors for ADV infection in pediatric ASCT patients (pts).

Methods: We prospectively studied 40 children from 9/8/03 to 12/1/05 for ADV infection for up to 1 year (y) following ASCT. The week prior to ASCT, a throat swab, urine, and stool were sent for viral culture, and plasma was sent for ADV PCR. The same specimens were obtained weekly for the first 100 days (d), then monthly until 1 y after ASCT. We defined ADV infection as: (1) a positive ADV PCR, (2) >2 positive ADV cultures from separate sites, or (3) 1 positive culture plus clinical evidence of ADV. 1 ADV infected pt was matched with 2 non-infected pts for gender and survival to at least 21 d after the index case developed ADV. Risk factors were then compared.

Results: 6 (15%) of the 40 ASCT pts developed ADV infection. Median age of case pts was 1.4y, while that of control pts was 9.3y. 2 of 6 case pts received anti-thymocyte globulin (ATG) post-transplant as opposed to 0 of 2 matched

controls. 2 of 6 case pts underwent previous ASCT compared with 1 of 12 controls. Case pts recovered their lymphocyte counts to 200/mm³ a median of 18.5 d following transplant while control pts were 14 d. Matched related transplants occurred in only 1 of 6 case pts but in 6 of 12 control pts. There were no differences between case and control pts regarding ethnicity, diagnosis leading to transplant, pretreatment conditioning, episodes of GVHD, or treatment with ganciclovir.

Conclusions: Younger age, receipt of ATG post-transplant, and a longer time to lymphocyte recovery appeared to be risk factors for developing ADV infection. GVHD, total body irradiation, and conditioning regimen were not. Receipt of a transplant from a completely matched related donor appeared protective.

51

Factors Influencing CMV Seropositivity in Stem Cell Transplant (SCT) Patients and Donors

P. Ljungman*, R. Brand. Karolinska University Hospital, Stockholm, Sweden

Background: CMV remains an important factor for outcome of allogeneic stem cell transplantation (SCT). The serological status of both donors and recipients are important factors for transplant outcome.

Objective: Our aim was use the registry of the European Group for Blood and Marrow Transplantation to study trends over time as well as analyzing the effects of age, gender, and country on the donor and recipient CMV serostatus.

Patients & Methods: 40,311 patients and 23,048 donors were selected from the registry database. The patients were transplanted 1985–2004. Logistic regression models were constructed predicting seropositivity using as covariates year of SCT, age, gender, and country for both patients and donors separately.

Results: Females had a higher likelihood to be seropositive than males both among patients (OR 1.22; 1.15–1.30; $p < 0.001$) and donors (OR 1.23; 1.13–1.34; $p < 0.001$). The risk to be seropositive increased by age (patients OR 1.19/decade; 1.17–1.21; $p < 0.001$; donors OR 1.24/decade; 1.22–1.27; $p < 0.001$) but decreased by calendar year (patients OR 0.98/year, 0.97–0.99; $p < 0.001$; donors 0.98/year; 0.97–0.98; $p = 0.001$). There were major differences between different countries with the BENELUX countries having the lowest and Italy the highest probabilities to be seropositive for both patients and donors.