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derlying disease (Mb. Gaucher). Donor examination prior to donation was as follows: hemoglobin level 110 g/L, platelet 148 × 10^9/L, WBC in normal range. Bone MR revealed typical changes for Gaucher disease. Beta glucosidase level was low (2.4 nmol/h/mg of protein) and chitotriosidase very high (60000 nmol/h/ml of plasma). There were no other signs of other diseases and we decided to proceed with HSCT. Patients were conditioned with a standard Bu + Cy regimen followed by graft versus host disease (GVHD) prevention with a combination of CSP + MTX. Marrow harvesting was complicated due to the lacking to collect sufficient number of cells and two leukaphereses were performed. After hematopoietic stem cell infusion recovery was successful and the patient was discharged form the hospital on day +35. There were no signs of acute or chronic GVHD. Complete chimerism was obtained from marrow and blood. There were no signs of Gaucher disease in bone marrow. Donor ERT was started immediately after hematopoietic stem cell donation. Recipient ERT was started 3 months after hematopoietic stem cell infusion. There were no signs of Gaucher disease in the recipient. Due to administrative reasons ERT was stopped after 2 years of treatment. Recent examinations showed that the recipient started to develop signs of Gaucher disease. ERT was introduced again in the recipient. **Conclusions:** This case report shows that hematopoietic stem cells of a donor with Gaucher disease can be successfully transplanted. Harvesting could be complicated due to the insufficient number of collected cells. Enzyme replacement therapy (ERT) can prevent the development of Gaucher disease in the recipient transplanted with Gaucher marrow.

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DONOR SPECIFIC TRANSFUSION AND EITHER METHOTREXATE OR CD154-BLOCKADE BEFORE TRANSPLANT IMPROVES RATES OF SUSTAINED ENGRAFTMENT IN DOGS CONDITIONED WITH 100 CGY TOTAL BODY IRRADIATION

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Introduction: Stable mixed chimerism can be established in dogs given a sublethal dose of 200 cGy total body irradiation (TBI) before and immunosuppression with mycophenolate mofetil (MMF) or rapamycin combined with cyclosporine (CSP) after marrow transplantation. When the TBI dose is reduced to 100 cGy, only transient engraftment is observed (11 of 11 dogs rejected their grafts). Here we asked whether stable engraftment after 100 cGy TBI could be accomplished by reducing host immune responsiveness using either the antimetabolite methotrexate (MTX) or an anti-CD154 antibody, which blocks the CD40-CD154 T-cell costimulatory pathway in conjunction with infusions of donor peripheral blood mononuclear cells (PBMC). **Methods:** One group of recipients was given iv infusions of 5×10^6 PBMC/kg from their intended DLA-identical littermate marrow donors on days −5 and −3 followed by 0.4 mg/kg MTX on days −4 and −2 (group 1). A second group received a single iv injection of 5 mg/kg anti-CD154 antibody (day −5) followed one day later by donor PBMC (combined iv/sc injections of 10^7 PBMC/kg) (group 2). Antibody dosing was based on studies of suppression of mixed leucocyte culture reactivity in vitro and in vivo pharmacokinetics. 100 cGy TBI (delivered at 7 cGy/min) was given to all dogs on day 0 followed by infusion of a median of 3.46×10^8 marrow cells/kg. Postgrafting immunosuppression consisted of MMF (10 mg/kg, BID, days 0 to 28) and CSP (15 mg/kg BID, days −1 to 35) in all dogs. **Results:** All six dogs in group 1 showed initial engraftment. Two of the six showed sustained engraftment while 4 dogs rejected their grafts at weeks 5, 8 and 10, respectively, and survived with autologous recovery. Five of six dogs in group 2 were evaluable, while one dog was too early to be evaluated. All five evaluable dogs had initial engraftment. Three of the five dogs continued to show stable mixed donor/host hematopoietic chimerism, one for >16 weeks and two for >26 weeks. Two dogs rejected their grafts, 9 and 12 weeks after transplantation, respectively, and recovered autologous hematopoiesis. **Conclusions:** Donor PBMC infusions and pretransplant host immunosuppression with either MTX or anti-CD154 antibody were partially effective in assuring sustained engraftment of DLA-identical marrow after non-myeloablative conditioning with 100 cGy TBI combined with MMF and CSP.

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SUCCESSFUL USE OF AN ANTI-TUMOR NECROSIS FACTOR-ALPHA (TNF-α) MONOCLONAL ANTIBODY (INFLIXIMAB) FOR THE TREATMENT OF CYTOMEGALOVIRUS (CMV)–INDUCED PNEUMONITIS AFTER ALLOGENEIC HAEMOPOIETIC STEM CELL TRANSPLANTATION (Allo-HSCT)

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Several pro-inflammatory cytokines have been shown to play a fundamental role in the genesis and perpetuation of adaptive immune responses. Recent investigations into the biological relevance of such cytokines in systemic inflammatory responses have demonstrated a protective role for them during the early phase of infection. However, the activity of inflammatory cytokines after the pathogenic challenge has been resolved has also been shown to represent a deleterious, often lethal, role in which unspecific inflammatory reactions (but not the infectious agent) overwhelm the body. Recently, a monoclonal antibody capable of blocking the effects of TNF-α (infliximab) has been proven capable of modulating systemic inflammatory responses. Here we describe the successful treatment of adult respiratory distress syndrome caused by CMV with infliximab in a recipient of allo-HSCT. The patient involved was a 35 year old male that received an HLA-compatible unrelated peripheral blood HSCT for chronic myelogenous leukemia in June 2001. The patient was subjected to myeloablative conditioning (fractionated total body irradiation + cyclophosphamide) and received cyclosporin A and methotrexate for GvHD prophylaxis. On day +34 the patient complained of chest pain and developed dyspnea, fever and chills; CT scan revealed the presence of bilateral diffuse micronodular interstitial infiltrates. Lung biopsy and culture demonstrated the presence of inclusion bodies suggestive of CMV infection while the presence of other bacterial, viral and fungal agents was ruled out. Qualitative CMV-specific PCR subsequently confirmed the diagnosis at titers of 313.8 pg/mL. The patient received IV immunoglobulins + ganciclovir therapy and supportive care. By day +45 the patient continued with fever and showed worsening lung edema (became polypneic, attained less than 75% blood-oxygen saturations in spite of non-invasive mechanical ventilatory support and developed hypoxic encephalopathy). On day +48 the patient received the first of two 200 mg doses of infliximab. By day +50 the patient was feverless, had less dyspnea and achieved blood oxygen saturations above 90% at ambient air and without mechanical ventilatory support. Both physical examination and chest x-rays revealed a dramatic clinical improvement by day +53. Here we discuss a therapeutical role for TNF-α blocking monoclonal antibody (infliximab) in the management of post-infectious pathogen-induced systemic inflammatory responses.

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ALLOTRANSPLANTATION WITH REDUCED INTENSITY CONDITIONING THAT INCLUDES ALEMTUZUMAB LESSENS TRANSPLANT-RELATED MORTALITY AND INCIDENCE OF RELAPSE IN PATIENTS WITH HIGH-RISK MYELOID DISEASES

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Patients with high risk myeloid disease can be transplanted with reduced intensity conditioning regimens that maximize remission duration while minimizing transplant-related mortality. Incidence of survival, relapse, tempo of engraftment and incidence of grades I-II and III-IV acute GVHD were evaluated. Three conditioning regimens have been utilized: fludarabine 30 mg/m^2 × 5 days, melphalan 140 mg/m^2 × 1 day in all groups and alemtuzumab 20 mg/d × 5 days (group 1), × 3 days (group 2) and × 2 days (group 3). Fifteen patients (median age 48, range 24-58 years) were in the study. Twelve patients had AML, two had CML and one had MDS. Six patients were in CR at time of transplant and nine had relapsed or refractory disease. Patients were consecutively assigned to group 1 (seven patients), group 2 (five patients) and group 3

(three patients). Stem cell sources included BM (four patients), PBPC (10 patients) and one cord blood transplant; related (6 patients) and unrelated (9 patients). Match grade was 6/6 for 13 transplants, 5/6 for one and 4/6 for the cord blood. GVHD prophylaxis was standard dose cyclosporine or tacrolimus and MMF, tapering after day 60. Median follow-up was seven months (range 1.5-30 months). There were no WBC engraftment failures. Neutrophil (ANC >500/dl) engraftment occurred at a median of 13 days (range 10-48 days). Three patients had grade I-II acute GVHD and one had chronic GVHD. One had grade III acute GVHD. Relapse occurred in three patients and they received DLI immunotherapy. Twelve patients survived to day 100 (80%). Four were alive at one year and four others who are still alive have not reached the one year mark. Four of the seven patients died with residual/relapsing disease (26%) and three died with treatment related toxicity (20%). Eight of 15 patients remain in follow-up. We conclude that the application of fludarabine, melphalan and alemtuzumab conditioning regimens has been successful in these high risk patients, with a low incidence of acute GVHD (27%), no engraftment failures and a low incidence (20%) of relapsed disease.

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INFECTION-RELATED MORTALITY AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FROM HLA-MATCHED RELATED AND UNRELATED DONORS

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Infection is a major cause of transplant-related morbidity and mortality after allogeneic hematopoietic cell transplantation (HCT). To clarify the importance of management of infectious complications after allogeneic HCT, we retrospectively reviewed the medical records of 185 adult patients with hematologic malignancies who underwent allogeneic HCT at our center between 2000 and 2004. The diagnoses included acute myeloid leukemia or myelodysplastic syndrome (n = 87), chronic myelogenous leukemia (n = 20), acute lymphoblastic leukemia (n = 20), lymphoma (n = 55), and other hematologic malignancies (n = 3). The conditioning regimen for conventional stem cell transplantation (CST) was cyclophosphamide plus 12 Gy total body irradiation (TBI) (n = 60) or busulfan (n = 44), and that for reduced-intensity stem cell transplantation (RIST) was fludarabine plus busulfan with (n = 18) or without (n = 61) 4 Gy TBI. One-hundred-nine patients received G-CSF-mobilized peripheral blood stem cells from an HLA-matched relative (R-PBSCT; CST 48, RIST 61) and 76 patients received bone marrow from an HLA-matched unrelated volunteer (U-BMT; CST 58, RIST 18). The median age of the patients in the RIST group was older than that of the CST group (54 years vs 38 years). Neutrophil engraftment was faster in the R-PBSCT group than that in the U-BMT group (median; day 11 vs day 18) regardless of conditioning regimens. The cumulative incidences of grades II to IV acute graft-versus-host disease (GVHD) in the R-PBSCT and U-BMT groups were 46% and 49%, respectively. Within 1 year of transplant, 11 (10%) of the 109 patients who underwent R-PBPCT and 25 (33%) of the 76 patients who underwent U-BMT died of non-relapse causes. Non-relapse mortality within 1 year after CST and RIST were 23% and 15%, respectively. Among the 36 patients who died of non-relapse causes, 17 (47%) had grades III to IV acute GVHD and 13 (36%) had infectious complications. In conclusion, our study showed that U-BMT was associated with an increased risk of infection-related mortality. Future study should focus on better management of infectious complications and GVHD after HCT from an unrelated donor.

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ALLOGENEIC STEM CELL TRANSPLANTATION IN INFANTS. A SINGLE INSTITUTION EXPERIENCE

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Allogeneic stem cell transplantation (ASCT) is the treatment of choice for a variety of hematologic and non hematologic diseases. The ASCT have special implications when the patient involved is an infant. We analyzed the results of ASCT in infants in our institution. From 1997 to 2004 every infant who was treated with an ASCT in our hospital was included. A total of 6 infants were treated with an ASCT, 3 males and 3 females. One patient had acute lymphoblastic leukemia (ALL), one osteopetrosis (OP) who underwent 2 ASCT, one severe combined immunodeficiency syndrome (SCIDS) and 3 hemophagocytic lymphohistiocytosis (HL). In one patient the bone marrow was the source of stem cells, in 3 patients it was peripheral blood, and in 2 patients the stem cells were obtained from unrelated cord blood (one underwent 2 cord blood ASCT). Four patients had a related matched stem cell transplant, and two patients had an unrelated mismatched cord blood transplant with 5/6 matches. Reduced intensity conditioning regimen was used in 5 ASCT, myeloablative in the patient with HL done in 1997, and none in the patient with SCIDS. Only the 2 ASCT achieved in the infant with OP did not engraft. Graft versus host disease (GVHD) was present in 2 of the other 4 patients. Grade IV acute GVHD due to severe GI affectation in one infant with HL who underwent cord blood transplantation occurred and hepatic chronic GVHD in the HL patient transplanted in 1997 whose haematopoietic stem cell source was the bone marrow. Five patients are alive. The girl who did not engraft after two ASCT has osteopetrosis activity. Four patients: a girl with ALL, 2 boys with HL and a boy with SCIDS are disease free survivors without GVHD 25, 16, 101, and 53 months after ASCT. A girl with HL died due to sepsis and severe GI GVHD day +35 after transplant. In conclusion, we found in this small number of patients that 5 out of 6 patients are alive and 4 are disease free after a median of 48 months. We believe that haematopoietic stem cell transplantation, specially using reduced intensity conditioning regimen, can be safely used with good results in the pediatric population.

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CHIMERISM AND T CELL RECEPTOR REPERTOIRE ANALYSIS AFTER UNRELATED CORD BLOOD TRANSPLANTATION WITH A REDUCED-INTENSITY CONDITIONING REGIMEN FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA

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A 65-year-old Japanese male was diagnosed in October 2002 as having multiple myeloma with Bence Jones kappa type, clinical stage IIIA. His disease status reached partial remission after vincristine, Adriamycin and dexamethasone (VAD) therapy. Thereafter, he received tandem transplantation, consisting of high-dose chemotherapy with autologous stem cell transplantation (ASCT), followed by unrelated cord blood transplantation (CBT) with a reduced-intensity conditioning regimen, from which a graft-versus-host myeloma effect was anticipated. CBT with a reduced-intensity conditioning regimen was performed in August 2003. HLA mismatch between the patient and the CB donor was present at two loci (B and DR). The conditioning regimen consisted of fludarabine, busulfan and total body irradiation (TBI). A total nucleated CB cell dose of 2.45×10^7/kg body weight was infused on day 0. Graft-versus-host disease (GVHD) prophylaxis had been planned with cyclosporine A and short-term methotrexate. Neutrophil engraftment ($>0.5 \times 10^9$/L) was obtained on day 46. We analyzed in detail the chimerism status of PB subsets to predict graft rejection. Although his white blood cell count (WBC) was 0.2×10^9/L on day 27, showing nearly complete donor chimerism. He developed cytomegalovirus antigenemia, bacteremia, grade II acute GVHD involving skin and liver, varicella-zoster virus infection, septic shock, hemorrhagic cystitis due to adenovirus, and acute hepatitis B virus infection after CBT. We retrospectively analyzed T cell receptor (TCR) repertoire diversity and found that TCR repertoire diversity decreased continuously after CBT. Therefore, low TCR repertoire diversity appears to be associated with various infections due to immunodeficiency.