Poster Session II

AUTOIMMUNE

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IMMUNE EVENTS FOLLOWING IMMUNOABLATIVE THERAPY FOR THE TREATMENT OF MULTIPLE SCLEROSIS (MS)

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This report details the immunology of the first patient enrolled in the Canadian trial of immunoablative therapy with autologous stem cell transplantation (SCT) for MS. This trial tests the concept that immunoablative therapy can stop autoimmunity in MS and halt further CNS damage. Furthermore reconstitution of a naïve immune system should be functional and self-tolerant. A 31-year-old woman with secondary progressive MS underwent a CD34 selected autologous SCT after receiving Busulphan (16 mg/kg), Cyclophosphamide (200 mg/kg) and rabbit ATG (5 mg/kg). **MS Activity:** The patient is clinically stable 24 mo. post SCT with no relapses or progression of disabilities. There is sustained resolution of gadolinium activity and improved T2 metrics by MRI. Thus MS activity has been shut down. **Immune ablation:** The patient became lymphopenic. All lymphocyte subpopulations were decreased. There was loss of humoral immunity to mumps and measles at 18 mo. post SCT and lost cutaneous reactivity to candida at 6 and 12 mo. post SCT. Antigen specific in vitro T cell responses to myelin basic protein (MBP), tetanus toxoid (TT) and copaxone (GA) were reduced or abolished following SCT. There was >1000 fold reduction in recent thymic emigrants 3 mo. post SCT and a reduction in circulating naïve T cells. Thus immunoablation was achieved. **Immune reconstitution:** The patient has not developed opportunistic infections. The lymphocyte count has slowly risen during the post SCT period. Both helper and suppressor populations remain profoundly low with mainly a memory phenotype. The CD4:CD8 ratio normalized at 12 mo. post SCT. Thymic emigrants in the circulation have increased to about 10% of baseline. B cell and immunoglobulin levels are normal. Humoral immunity is polyclonal. A positive cutaneous response to candida antigen testing occurred 24 mo. post SCT. Specific in vitro T cell responses to TT following reimmunization are currently being evaluated. This preliminary data suggests that the post transplant immune system is protective and self-tolerant. The data from this patient indicates that complete immunoablation was achieved and is associated with a significant change in MS activity. The patient remains lymphopenic but is not prone to opportunistic infections. Immune reconstitution is ongoing and is NOT associated with recurrence of MS activity.

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AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR TAKAYASU'S ARTERITIS: REPORT OF THE FIRST CASE OF THE LITERATURE

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The first reports of hematopoietic stem cell transplantation (HSCT) for isolated autoimmune diseases appeared in 1996 and since then about 700 patients were transplanted. However, very few patients with vasculites were submitted to HSCT, and all patients had small or medium size arteritis (1) Fiehn Hensel, High Dose Chemotherapy with Hematopoietic Stem Cell Transplantation in Primary Vasculitis, Behcet's Disease and Sjogren Syndrome, in Burt R, Marmont A, eds, Stem Cell Transplantation for Autoimmune Diseases, Landes Bioscience, in press, 2) Marmont et al, Bone Marrow Transplantation 31, Suppl 1, S15-16, 2003). We report here the case of a 41 year old woman with Takayasu's arteritis presenting since June 1990 with constitutional symptoms, polyarthritis, myalgia, dizziness, upper and lower limb claudication and transient visual impairment. Arteriography showed irregularity and stenosis of abdmonial aorta, right and left iliac arteries, left subclavia and carotid arteries. The disease had been treated for 13 years with steroids (PO and IV) and several other immunosupressive agents (methotrexate, cyclophosphamide, chlorambucil and mycofenolate mophetil) without response. In March 2003, autologous peripheral blood hematopoietic stem cells were mobilized with cyclophosphamide (2 g/m^2) and G-CSF (10 ug/kg/d), cryopreserved and infused (3.9 million/kg) one month later after conditioning with cyclophosphamide (50 mg/kg ×4) and rabbit antithymocyte globuline (1,5 mg/kg ×3). Posttransplant complications were diarrhea, neutropenic fever and emotional liability, neutrophil engraftment occurred at D+9 and discharge was on D+16. On D+60 the symptoms had improved significantly and an angioressonance showed dramatic reduction of brachiocephalic artery stenosis and carotid arteries irregularities. This rapid improvement suggests that aggressive immunosuppression caused the observed therapeutic effect in this case but induction of tolerance and tissue repair mediated by stem cells may operate long term. This is the first case of a large size arteritis treated with HSCT and illustrate the therapeutic potential of high dose immunosuppression and cellular therapy in severe vasculitis.

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CAN THE STEM CELL MOBILIZATION TECHNIQUE INFLUENCE CD34+ CELL COLLECTION EFFICIENCY OF LEUKAPHERESIS PROCEDURES IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES?

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CD34+ cell collection efficiency (CE) reflects the proportion of CD34+ cells that is harvested during apheresis. Higher CE results in a bigger stem cell collection per procedure; reducing the number of procedures required to reach the target. 415 leukaphereses done on 201 patients (1-11 each; median 2) using Cobe Spectra cell separators over 26 months were studied to determine CD34+ cell CE. Apheresis was done for leukemia (n = 54), lymphoma (n = 130), and plasma cell dyscrasias (n = 231). Aphereses done with pre-apheresis peripheral blood CD34+ cell count (PBCD34) <0.02% were excluded to reduce variability and calculation error. Stem cells were mobilized with growth factor (GF; n = 119) or chemotherapy-GF (n = 296). 15 (n = 202) or 20 (n = 213) L blood volume was processed. The pre-apheresis WBC count was 1-93 × 10^9/L (median 20), and PBCD34 was 1-1104/mm^3 (median 19). The total number of CD34+ cells collected was 4-6531 × 10^6 (median 151); corresponding to 0.1-111.4 × 10^6 (median 2.3) per kg. There was strong correlation between PBCD34 and the number of CD34+ cells collected (r^2 = 0.80; P < 10^{-100}). CE was 7-145% (median 46). On multiple regression analysis, higher WBC (continuous variable; P < 0.0001), higher PBCD34 (continuous variable; P = 0.009), and greater blood volume processed (categoric variable; P = 0.02) resulted in lower CE. Age, sex, weight, diagnosis, year, mobilization technique, Hct, and platelets did not affect CE. PBCD34 counts were higher (median 22 vs 15; P = 0.036) in patients mobilized with chemotherapy-GF compared to GF alone despite lower WBC counts (median 16 vs 30; P < 0.0001) because of higher %PBCD34 (median 0.16% vs 0.05%; P = 0.0001). CE with WBC <20 was 7-145% (median 53%) compared to 10-132% (median 40%) with WBC 20 (P < 0.0001), suggesting that WBC <20 may be optimum for apheresis in terms of maximizing CE. Since PBCD34 increases early during WBC