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True Thymic Hyperplasia (TTH) After Treatment of Adult Patients (Pts) with Non-Hodgkin's Lymphoma (NHL) and Hodgkin's Disease (HD). *C. Chacon, N. Tartas, E. Domenichini, H. Pascuccelli, V. Sporn, J. Mazzucco, J. Korin, L. Barazzutti, H. Ferro, P. Busso, C. Foncuberta, G. Kusminsky, R. Chacon, J. Sanchez Avalos; Alexander Fleming Institute, Buenos Aires, Argentina; CEH, Buenos Aires, Argentina*

Although thymic enlargement has been occasionally reported after chemotherapy (CHT) in young adults with HD and NHL, systematic studies including pathologic sampling of thymic RM have not been previously performed. We report here our experience in 8 pts treated for lymphoma who had thymic enlargement within twelve months of front line CHT. Six pts with HD and 2 pts with large cell lymphoma with sclerosis (DLC w/s) showed thymic enlargement on a computed tomography scan (CT) 2 to 12 months after therapy. Seven pts showed the typical sail image in the anterior superior mediastinal space, while 1 pt showed a cystic mass. These were all adult pts, with a median age of 25 yrs old (15–38). All pts were asymptomatic and in complete remission at the time of the study. It is relevant to say that only 3 pts had initially bulky disease. In addition to the CT scans, ^{67}Ga SPECT and MRI were perfomed in the 8 pts. The enlarged thymus was ^{67}Ga negative in all 8 pts. The MRI was inconclusive in 1, false positive in 3 and negative for lymphoma in the remainder. In 4 individuals a biopsy of the thymus was performed, 3/4 fulfilled the histologic criteria of true thymic hyperplasia (TTH). In 1 pt, a muitilocular cystic thymus was excised. One patient with DLCL w/s had on the biopsy TTH plus hemorrhages and necrosis, interestingly this patient did not have bulky disease at presentation. The 8 pts are alive and in complete remission (CR) with a median follow up of 27 months (11–60). None of the pts developed other symptoms or signs of immune phenomena. TTH refers to an actual increase in thymic size, histologically has the appearance of normal thymus and should only have a minor component of adipose tissue, it is usually diagnosed with conventional radiologic studies. The results of CT scans, ^{67}Ga, MRI and histologic studies in this cohort of pts with TTH, were matched with clinical follow up. Contrarily to other reports a hyperplastic thymus has always been ^{67}Ga negative in our previous and present experience. MRI studies performed early after treatment might give false positive or inconclusive results. In conclusion we think that a residual mass in the superior anterior mediastinal space in a patient with lymphoma after treatment, might be due to TTH. These pts must not be empirically irradiated if they have a negative gallium scan.

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Presence of Activation Markers of EBV and CMV in Myelodysplasia. *S. Mundle, K. Allampallam, B. Y. Mativi, B. Dangerfield, J. Cartlidge, S. Alvi, C. Shetty, S. Dar, E. Broderick, P. Vengopal, S. A. Gregory, A. Raza; Rush Cancer Institute, Chicago, IL; Rush-Presbyterian-St Luke's Medical Ctr, Chicago, IL*

Herpes viruses have been known to establish latency in bone marrow (BM) early precursors such as a common precursor of dendritic and myeloid cells. The present studies were designed to examine if activation of these latent viruses occurs in myelodysplastic syndromes (MDS) as compared to normal marrows. Two herpes viruses, viz. Cytomegalovirus (CMV), and Epstein Barr Virus (EBV), commonly found latent in BM cells were investigated. First, BM aspirate mononuclear cells (BMMNC) from nineteen MDS patients were studied in comparison with 7 normal healthy donors. One MDS patient was studied on 2 occasions. Per FAB classification, 8 MDS cases were refractory anemia (RA), 1 RA with ringed sideroblasts (RARS), 3 RA with excess blasts (RAEB), 1 RAEB in transformation (RAEBt), 1 MDS →AML, and 5 had chronic myelomonoceytic leukemia (CMMoL). The expression of 2 m-RNA transcripts; at least one of them being indicative of virus activation, were examined for both CMV and EBV, using a reverse transcriptase polymerase chain reaction (RT-PCR). The specific primers for the Major Immediate Early Protein (IEP) and DNA Polymerase I (DNA-Pol) were selected for CMV, while for EBV, Latency related Membrane Protein 1 (LMP-1) and BZLF expression were assessed. All the MDS as well as the normal BM specimens showed the expression of latency related transcripts for the 2 viruses, IEP (Product-435bp) and LMP-1 (Product-106bp) respectively. In contrast, the expression of DNA-Pol (356bp) indicative of active CMV infection was rare both in MDS (2/19) and Normal (1/7) BMs. Int erestingly, BZLF expression (608bp), indicative of active EBV, was evident in 10/19 MDS patients studied (>50%). Comparatively, only 2/7normal BMs showed BZLF(~14%). Subsequently, long term stromal cultures were established from the BMs of MDS and normal individuals. At 75% confluency (~3–4weeks), they were overlayered with cord blood MNC (CMNC) and after coincubation for one week RTPCR assays for EBV-BZLF and CMV-DNA Pol were performed on non adherent CMNC. Of the 3 CMNC specimens tested none showed these transcripts before overlayering, nor after coincubation with normal stroma. Interestingly 1/3 CMMNC sample showed EBV-BZLF and CMV-DNA Pol m-RNA, albeit with stromal cultures from different patients. Thus, MDS stroma may be capable of activating herpes viruses and hematopoietic cells may show active herpes virus. Further studies are warranted to assess the association of herpes viruses with the pathobiology of MDS.

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Encouraging Improvement in Cytopenias of Patients with Myelodysplastic Syndromes (MDS) with Thalidomide. *A. Raza, L. Lisak, C. Anderews, L. Little, F. Zorat, V. Shetty, S. Alvi, S. Mundle, K. Allampallam, M. duRant, M. Ekbal, M. Muzammil; Rush Cancer Institute, Chicago, IL; Rush-Presbyterian-St Luke's Medical Ctr, Chicago, Il*

MDS patients present with variable cytopenias even though their bone marrows (BM) are generally hypercellular. Excessive cytokine-induced apoptosis of hematopoietic cells in the marrows has been proposed as a possible mechanism to explain the paucity of cells in the periphery. Tumor necrosis factor (TNF-α) is a pro-inflammatory cytokine which has been found in excessive amounts in MDS marrows. In addition, recent studies demonstrate excessive neo-angiogenesis in MDS marrows as well. TNF-α is a potent inducer of neo-angiogenesis via upregulation of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (b-FGF). A strategy for improving ineffective hematopoiesis in MDS would be directed at suppressing TNF-α and neo-angiogenesis. Thalidomide is active at both levels. We have treated 61 MDS patients with 100–400 mg thalidomide po h.s. for 12 weeks. Of these, 22 had refractory anemia (RA), 13 had RA with ringed sideroblasts (RARS), 19 had RA with excess blasts (RAEB), 4 had RAEB in transformation and 3 had CMMoL. Of 61 patients, 11 are off study, 25 are too early and 25 are evaluable for response, 17/25 are responding while 8/25 are not. Three have a trilineage, 4 bilineage and 10 monolineage responses. Most dramatic improvements are noted in erythroid series in that long-term transfusion dependent patients are becoming transfusion-independent. Responses can take up to 12 weeks to become apparent. Most patients tolerated the drug well in low doses (200 mg hs). We conclude that thalidomide in low doses given for prolonged periods to MDS patients can produce excellent palliation and deserves to be tested in a larger series of patients either alone or in combination with chemotherapy or anti-cytokine therapy.

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Outcome of Patients with Multiple Myeloma (MM) Receiving High-Dose Chemotherapy (HDC) and Hematopoietic Stem Cell Transplantation (HSCT). *Z. Nahleh, K. Zimmerman, I. Tabbara; George Washington Univ Sch of Medicine, BMT Program, Washington, DC*

Between 8/93 and 6/99, 14 patients with MM received HDC and HSCT. The preparative regimen consisted of either high-dose melphalan (200 mg/m^2) in 6 patients or cyclophosphamide (120 mg/kg) and busulfan (16 mg/kg) in 8 patients. Half of the patients were male and the other half were females. The median time from diagnosis to transplant was 906 days (range 180-3600). The mean number of prior chemotherapy regimens was 2 (range 1–4). Four patients (28.5%) had stage I, 2 patients (14.2%) had stage II and 8 patients (57.1%) had stage III. IgG monoclonal spike was present in 10 patients, IgA monoclonal spike in 1 patient and 3 patients had light chain disease. At the time of transplant, 2 patients (14.2%) had refractory disease to VAD chemotherapy, 8 patients (57.1%) had achieved a PR and 4 patients (28.5%) were in CR. Following HDC and HSCT, 12 patients (85.7%) were in CR and 2 patients (14.2%) were in PR (1 patient had refractory disease and the other one was in PR.) The median progression-free survival (PFS) was 24.8 months (range 6–72 months.) Two patients died while in CR at 180 and 865 days post transplant from myocardial infarction and pneumonia respectively. Among patients who received Bu/Cy, the median time to ANC>500 was 11.5 days (9–18) and median time to platelet >20,000 was 14.4 days (7–38) as compared to 13 days (5–28) and 13.5 days (5–30) respectively for patients who received high-dose melphalan. The three patients who developed major toxicities (1 VOD and 2 hemorrhagic cystitis) received Bu/Cy. There was no treatment-related mortality. These data suggest that HDC and HSCT in MM is well tolerated with minimal toxicity and is associated with long-term PFS. In addition, high-dose melphalan is associated with less toxicity than Bu/Cy with comparable outcome.