22 patients (pts) less than 20 years old with advanced malignant tumor (13 abdominal non-Hodgkin's lymphomas: NHL, 3 yolk sac tumors: YST, 3 Ewing's sarcomas: ES, 3 neuroblastomas: NB) received high dose chemotherapy (vincristine 2 mg/m^2, top dose 2 mg iv and adriamycine 60 mg/m^2 iv on day -7 and cyclophosphamide 45 mg/kg iv on days -6 to -3), total body irradiation (600 rad on day -1) and ABMT (day 0). The supportive care included reverse isolation, immunoglobulin 0,4 g/kg iv q 2 weeks, cotrimoxazole and digoxin per os and substitution of erythrocytes and thrombocytes. Granulocytes were given to febrile pts not responding to systemic antibiotic treatment. Hematopoiesis recovered in 20/21 evaluable pts within 3 - 12 weeks. In one pt a severe thrombocytopenia persisted. Disease-free survival after ABMT (number of pts and months): NHL stage III 5/7 (35+ 23+ 20+ 5+ 5+), NHL stage IV 3/6 (7+ 2+ 1+), YST 1/3 (26+) ES 0/3, NB 0/3. One patient has died due to complications of therapy. Tumor was the cause of death in all other pts. In the three surviving pts with NHL stage IV the bone marrow was treated in vitro with a monoclonal antibody (anti Y 29/55) and complement to eliminate NHL-cells before ABMT. We think that ABMT will help to improve the so far poor prognosis of pts with advanced abdominal NHL.

26.

THE EFFECTS OF HIGH DOSE POLYCHEMOTHERAPY WITH AUTOLOGOUS BONE MARROW TRANSPLANTATION (ABMT) IN 18 CHILDREN WITH RELAPSED LYMPHOMA. O. Hartmann(1), F. Pein(1), T. Philip(2), P. Biron(2), J. Lemerle(1).
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(2) Centre Léon Bérard - LYON - FRANCE.

The prognosis of the Non-Hodgkin Malignant Lymphoma in children is particularly poor after the first relapse. In an attempt to improve it, 18 children have been treated with high dose polychemotherapy plus ABMT. 11 were B lymphomas and 7 were T lymphomas. For the majority of the patients (13/18) the bone marrow has been collected and frozen during the first remission. Before using this high dose chemotherapy the relapse was treated by different conventional chemotherapies in order to use this regimen on patients with "residual disease". Among the 18 patients 2 were in second CR, 7 were in second PR, 9 had progressive disease at the time the high dose regimen was administered. This polychemotherapy was the combination of BCNU 200 mg/m2 Days 1,2,3 ; Cyclophosphamide 1600 mg/m2 Days 2, 3,4,5 ; Cytosine-Arabinoside 200 mg/m2 Days 2,3,4,5 ; 6 Thio-Guanine Days 2,3,4,5. The ABMT was performed at day 6. The results of this treatment were : C.R. 13 ; P.R. 3. Progressive Disease 2 ; In terms of survival : 5 pts (4 B Lymphomas, 1 T Lymhoma) are alive and NED et 5+, 11+, 12+, 14+, 16+ months from ABMT ; 1 pt is alive with progressive disease at 4 months from ABMT and 12 pts are dead. 9 of them of the disease.

The toxicity of this regimen was high but tolerable. 2 deaths were observed after hematological reconstitution and related to prolonged immunodepression.

These results are encouraging and the role of this treatment will be discussed depending on the "T" or "B" subtype of the lymphoma.

27.

NON RECOVERY FROM TOXIC APLASIA ASSOCIATED WITH HIGH DOSE METHOTREXATE, AFTER AUTOLOGOUS BONE MARROW GRAFT. T. Philip, P. Biron, L. Dutou, L.Holzapfel, J.B.Cotton, M.Brunat-Mentigny, Oncology Pediatric Unit. Centre Léon Bérard, Lyon, France

We report one case of severe methotrexate (MTX) toxicity who died after 27 days of extreme granulocytopenia and 16 days after autologous bone marrow graft used as a rescue for the toxic aplasia.

Christophe was a 15 years old boy with a Murphy stage IV NHML Burkitt type. Treatment was the French Cooperative LMB 80 in which high dose MTX is used extensively. The drug was well tolerated with no emesis at all. MTX enzymatic dosage at 36 hours was normal and the patient was discharged. The boy came back on day 7 with clinical (Hyperthermia, Toxidermia, continuous diahrrea and abdominal pain) and biological (extreme leucothrombocytopenia, increased BUN and creatinine) signs evocating MTX toxicity. 11 days after the beginning of the extreme granulocytopenia 5 out of the 8 bad prognosis factors of this accident were present. Autologous bone marrow graft was then decided. 1.3 10^8 nucleated cells per kg and 21.10^4 GMCFU c/kg were reinjected. Despite intensive supportive care Aspergillus infection occured and the boy finally died 16 days after ABMG and on day 27 of the aplasia. No sign at all of bone marrow activity was found on WBC, and postmortem bone marrow smears and biopsy.

In conclusion ABMG has not been usefull as a supportive care in this case. One can assumed that an immunological mechanism destroyed first the patient bone marrow cells and secondly the reinjected stem cells. Plasmapheresis just before ABMG could be discussed for future cases.

28.

HAEMOPOIETIC STEM CELLS IN NON CRYOPRESERVED AUTOLOGOUS BONE MARROW TRANSPLANT. J.Ninane, M.J.Latour, G.Cornu, M.Symann, Cliniques Universitaires St Luc & Ludwig Institute for Cancer Research, UCL, 1200 Brussels, Belgium.

Six children aged 18 months to 4 years were given a high dose Melphalan (150-180mg/m^2) as a late intensification for solid tumours in complete or good partial remission. High dose melphalan was followed by an autologous bone marrow transplant (ABMT) kept at 4°C, infused 12 to 24 hours later.

Granulocyte-macrophage progenitor cell (CFUc) and erythroid progenitor cells (BFU-E, CFU-E) were assayed upon bone marrow harvesting and bone marrow reinfusion in order to test haemopoeitic stem cell viability. Furthermore the number of CFUc/kg reinfused was compared to the number of days necessary to obtain an absolute neutrophil count of 0.5.10^9/L. The number of bone marow haemopoietic progenitors recovered was higher than 74 % for CFU-c, higher than 61 % for BFU-E and higher than 83 % for CFU-E. The number of CFUc reinfused per kg varied from 20.10^3 to 22.5 .10^4; there was no direct correlation between the number of CFUc reinfused and the number of days to recover 0.5.10^9 neutrophils/L.

For this small series of patients we conclude that most of cryopreserved bone marrow stem cells are viable for up to 24 hours at 4°C. There seems to be no direct correlation between the number of CFUc reinfused per kg weight and the number of days to recover 0.5.10^9 neutrophils/L.

29.

ROLE OF ^{192}IRIDIUM AFTER-LOADING CURIETHERAPY IN THE TREATMENT OF PEDIATRIC MALIGNANCIES
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- Fifty-three children were treated by Iridium after-loading curietherapy as local treatment,in combination with chemotherapy in forty-seven patients.
- The most common sitesof the primary tumorWERE pelvic-perineal (55 %) and cervico-facial (40 %).
- The pathologic diagnosis was rhabdomyosarcoma in 72 %, yolk sac tumor in 12 %, undifferentiated embryonal sarcoma in 2 cases, malignant mesenchymoma in 2 cases, clear cell carcinoma in 2 cases, fibrosarcoma 1 case, salivary gland epithelioma 1 case.
- Curietherapy was used in 45 previously untreated patients : local control was obtained in 40/45 cases, the two year survival was 82 %.

  For 11 previously treated patients local control was obtained in 9/11 cases, the two year survival was 54 %.

  7 children of 29(at greater than 3 year follow up) HAD sequellae.
- Our results make a strong argument for an important place of ^{192}I afterloading curietherapy in the treatment of pediatric malignancies. However, a rigorous technique and appropriate dosimetry are absolutely necessary in order to obtain maximum local control, with hopefully a lower incidence of sequellae.
