pediatric lymphoma

170 SHOULD TEENAGERS WITH HODGKIN LYMPHOMA (HL) BE TREATED IN PEDIATRIC OR ADULT PROTOCOLS?

J. Landman-Parker 1, F. Christophie 2, C. Sebban 2, T. Leblanc 1, P. Carde 1, A. Thomas 3, M. Fellmann 4, O. Oster 1, M. Henry-Arriau 1

1Société Française des Cancers de l’Enfant (SFCE), Paris, France, 2Groupe d’Études des Lymphomes de l’Adulte (GELA), Villejuif, France, 3Lymphoma Group, EORTC, Brussels, Belgium

Aims: In France, adolescents can equally be treated in a pediatric or an adult care unit. Since treatment policy highly depends upon this choice, we found important to describe their outcome after adult or pediatric protocols and to define the most appropriate strategy.

Patients and methods: Between January 1982 and December 1998, 2,358 patients < 30 years were enrolled in 5 pediatric and 5 adult protocols. Pediatric protocols were based on ABVD, MOPP-ABVP, OPFA-COOP or VBVP and 20 Gy involved-field irradiation (IFRT) after good response to chemotherapy. Adult protocols were based on mantle or subtotal nodal irradiation alone or a combination of MOPP, ABVD, MOPP-ABVP or VBVP and mantle or IFRT. Radiation doses ranged from 35 to 40 Gy. Teenagers were treated either in pediatric or adult protocols.

Results: There were 529 children (C) aged 0 to 14, 450 teenagers (T) aged 15 to 19 and 1379 young adults (A) aged 20-29 years at diagnosis. Teenager characteristics were closer to young adults than to children. Disease extension, histological subtype and B symptoms. 70 teenagers were treated with pediatric protocols and 380 with adult protocols. After a 7-year median follow-up, the 10-year TFFS rates were 87%, 85% and 82% for C, T and A, respectively (p = 0.02), and the 10-year OS rates 93%, 89% and 91%, respectively (p = 0.02). Among teenagers, the results of pediatric and adult protocols did not statistically differ; however, the burden of therapy was clearly different. Among teenagers treated in pediatric protocols, 30% received a chemotherapy devoid of alkylating agents and anthracyclines while 51% had alkylating agents and anthracyclines. Among teenagers treated in adult protocols, all received either alkylating agents or anthracyclines of whom 57% had both alkylating agents and anthracyclines. Radiation fields and doses were also dramatically reduced in pediatric protocols.

Conclusions: The similar outcomes of teenagers treated in pediatric and adult protocols appeals to include teenagers in the less intensive protocols.

171 BURKITT LYMPHOMA AFTER SOLID ORGAN TRANSPLANTATION IN CHILDREN

S. Cohen-Gogol 1, J. Landman-Parker 1, Y. Bertrand 2, B. Necker 1, C. Schmitt 3, E. Drahokoupilova 1, M. Kyncl 3, J. Stary 1

1Institut Gustave Roussy, Villejuif, France, 2Hop Trousseau, Paris, France, 3INSERM, UMR-S754, Villejuif, France

Introduction/background: Burkitt lymphoma (BL) is said to have a worse outcome than the other post transpl lymphoproliferative diseases.

Material/methods: After enquiry into French pediatric organ transplant centers and into the Registre National des Hémopathies de l’Enfant, 13 cases of histologically proven BL, < 18 years (y) of age, were reported (1997-2007) and retrospectively analysed.

Results: 11 cases were eligible: 1 death before diagnosis (dg), 1 clinical file lost. 9 boys, 2 girls. 9 patients (pts) had liver (L) and kidney (K) transplant. Median (med) age at transpl was 14 months (m) (L), 87m (K). EBV seroconversion occurred at a med time of 9m after transpl and 23m before BL. At dg, K graft recipients had a mean clearance of 50 ml/min/sqm. 3 L graft recipients were showing chronic rejection. The med time of BL onset was 2y 9m (L), 1y 11m (K). There were 6 stages III, 1 stage IV, 4 L3 ALL. 10/11 pts had high EBV blood viral load at dg. Immunosuppressive treatment was reduced in all cases (no acute rejection observed). 3 pts received rituximab without efficacy. 10/11 pts were treated according to SFOP LMB96 or LMB2001 protocol. 3 pts underwent transplantation at T1 (1 K) but 1 pt died. Efficacy. 10/11 pts were treated according to SFOP LMB96 or LMB2001 protocol. 3 pts underwent transplantation at T1 (1 K) but 1 pt died. Efficacy. 10/11 pts were treated according to SFOP LMB96 or LMB2001 protocol. 3 pts underwent transplantation at T1 (1 K) but 1 pt died. Efficacy.

Conclusion: Post transpl BL children can be cured by intensive treatment such as SFOP LMB although infectious complications can be more frequent and severe. BL and its management seem to have little influence on the graft (direct toxicity or rejection).

172 DIAGNOSTIC EFFECTIVENESS OF FDG-PET FOR THE INITIAL STAGING OF CHILDHOOD NON-HODGKIN LYMPHOMAS

E. Kahricova 1, O. Bektalavek 2, J. Votrubova 2, D. Sumeranue 1, E. Drahokoupilova 1, M. Kyncl 3, J. Stary 1

1Pediatric Hematology and Oncology, Charles University, Prague, Czech Republic, 2Nuclear Medicine, Na Homolce Hospital, Prague, Czech Republic, 3Radiological Techniques, University Hospital Motol, Prague, Czech Republic

Introduction/background: Positron emission tomography with fluorine-18-fluorodeoxyglucose (FDG-PET) was proven useful in the management of aggressive non-Hodgkin lymphomas (NHL) adults. Experience with PET in childhood NHL is limited. The aim of our study was to assess the usefulness of PET for initial staging of childhood NHL and its impact on the therapy planning.

Material and methods: In this prospective study 36 children and adolescents (age range, 3 to 19 years) with histologically proven NHL (Burkitt’s NHL, n = 14; diffuse large B-cell lymphoma, n = 12; lymphoblastic NHL, n = 5; peripheral T-cell lymphoma, n = 5) were included. Staging was based on the Murphy classification. PET scans were compared with the results of conventional staging methods (CSMs), including ultrasound, computed tomography, magnetic resonance imaging, bone scan, and bone marrow examination; follow-up data (mean follow-up time, 3 years); and histology. A lesion- and patient-based analysis of PET and CSMs were performed.

Results: PET revealed 23 additional lymphoma manifestations (13 nodal, 10 extranodal) in 12 patients (33%), and failed to visualize bone marrow infiltration (15% lymphoma cells) in 1 patient with lymphoblastic NHL. In 1 patient with diffuse increased bone marrow FDG uptake, bone marrow examination demonstrated only benign myeloid hyperplasia. PET and CSMs indicated the same clinical stage in 29 of 36 patients (80%). Different stage was documented in 7 children. PET correctly modified stage in 5 children; in 2 patients was incorrect. Sensitivity for PET and CSM for pre-treatment staging was 96% and 86%, specificity 88% and 88%, and accuracy 94% and 86%, respectively. As a consequence of these PET findings chemotherapy plans were modified in 3/36 (8%) children.

Conclusions: PET contributed to more accurate initial staging of children with NHL. Compared with CSMs, PET was significantly superior in detection of nodal (normal sized nodes) and extra-nodal lymphoma (spleen, liver and bone) involvement. Supported by grant MZ0 CR 64203.

173 INTENSIVE CHEMOTHERAPY FOR SYSTEMIC ANAPLASTIC LARGE CELL LYMPHOMA IN CHILDREN AND ADOLESCENTS: FINAL RESULTS OF CHILDREN'S CANCER GROUP STUDY 9541

E.J. Lowry 1, P. Spostito 2, S.L. Perkins 3, T. Gross 4, J. Finlay 5, M. Abdornwiche 6

1Ped. H/O, Children’s Hospital of the King’s Daughters, Norfolk, VA, United States, 2Pathology, University of Utah Health Sciences, Salt Lake, United States, 3Ped. H/O, Nationwide Children’s Hospital, Columbus, United States, 4Ped. H/O, Children’s Hospital Los Angeles, Los Angeles, United States, 5Ped. H/O, University of Nebraska Medical Center, Omaha, United States

Background: Anaplastic large cell lymphoma (ALCL) is characterized by advanced disease (70-80% of pediatric cases) and accounts for 10-15% of childhood lymphomas. Treatment strategies for pediatric ALCL vary from short B-NHL chemotherapy to prolonged leukemia therapy. The optimal treatment strategy is unknown.

Methods: CCG-9541 used a compressed aggressive regimen T-cell lineage chemotherapy regimen consisting of a three week induction therapy (vincristine, prednisone, cyclophosphamide, daunornycin, asparaginase) followed by a three-week consolidation period (vincristine, prednisone, etoposide, 6-thioguanine, cytarabine, asparaginase, methotrexate) followed by six courses of maintenance chemotherapy at 7-week intervals (cyclophosphamide, 6-thioguanine, vincristine, prednisone, doxorubicin, asparaginase, methotrexate etoposide, cytarabine).

Results: 86 children (male 56%) with non-localized ALCL (CD30+) were treated. The majority of tumors were positive for ALK (90%) and of T lineage (83%). Extranodal disease was common (mediastinum 35%, skin 15%, lung 14%, bone 12%, liver 6%, and other viscera 17%). The 3 year EFS was 68% (95% CI of 57-78%) and the 5 year OS was 80% (95% CI of 69-87%). There were 21 relapses and 4 toxic deaths as first events. Relapse occurred early with 17 (81%) relapses occurring within 2 years of diagnosis and 12 (57%) while receiving therapy. Univariate analysis
174 CENTRAL NERVOUS SYSTEM DISEASE (CNS) IN CHILDHOOD ANAPLASTIC LARGE CELL LYMPHOMA (ALCL): EICNHL EXPERIENCE

D. Williams1, T. Mori2, A. Reiter3, M. Le Deley4, L. Brugieres5
1Paediatric Oncology, Addenbrookes Hospital, Cambridge, United Kingdom; On Behalf of EICNHL; 2Paediatric Oncology, National Center For Child Health and Development, Tokyo, Japan; 3Paediatric Oncology, Justus Liebig University, Giessen, Germany; 4Biostatistics, Institut Gustave Roussy, Villejuif, France; 5Paediatrics, Institut Gustave Roussy, Villejuif, France

Background: CNS disease is a recognized rare manifestation of ALCL.

Material and methods: CNS disease incidence, mode of presentation, other sites of disease and outcome were analysed in children enrolled in a multicentre international prospective study for childhood ALCL ALCL9, from 9 European Groups and Japan. Involvement was defined as >5 blasts/mm² in CSF with morphology consistent with ALCL, an intracerebral tumour (ICT) on imaging or unexplained cranial nerve palsy.

Results: 12 children with CNS disease from 529 (2.3%) enrolled in ALCL9 from Nov 1999 - May 2006. M:F ratio = 1, median age 10.5yrs. 3 patients had isolated CNS disease (ICNS), all with an ICT. 9 patients had other sites of disease, including mediastinal, visceral or skin in 8.7% and ICT; associated with CSF blasts in 2, and cranial nerve palsy in 4.5% had blasts in the CSF and not ICT. Treatment: ALCL9 protocol (3), high risk arm of the BEAM (4) or LMB protocol (5, 14 patients with ICT’s including 2/3 with ICNS also received cranial irradiation). RT: 10/12 achieved CR with 1st line treatment. Relapsed or progressed during 1st line treatment, median 6.5 months. The CNS was involved again in 3/6, 2 of which had an ICT and 1 had blasts as initial CNS disease. With a median follow up of 28 months, 8 are alive, 6 in CR1 and 2 in CR2. 2 died of disease and 2 of treatment related toxicity. 2 with isolated CNS disease who received RT remain in CR1. 1 with ICNS, relapsed in the CNS only, had RT as part of 2nd line treatment and remains in CR2.

Conclusions: CNS is a rare site of disease in patients with ALCL. Its presentation as isolated disease or as a site in more disseminated disease should perhaps be considered separately. In the former, radiotherapy may have role in tumour disease control. In the latter, in this cohort, CNS disease was usually seen in association with advanced stage disease.

176 COMPARISON OF FLOW CYTOMETRY AND QUANTITATIVE PCR TO MEASURE CIRCULATING TUMOR CELLS IN NPM-ALK POSITIVE ANAPLASTIC LARGE CELL LYMPHOMA

G. Damm-Welt1, J. Schiefenstein1, S. Schwalm1, W. Woesemann1
1Pediatric Hematology and Oncology, Justus-Liebig-University, Giessen, Germany

Introduction: Quantification of occult circulating tumor cells in bone marrow or blood allows identifying patients with a high risk for relapse in NPM-ALK positive anaplastic large cell lymphoma (ALCL). We compared a flow cytometric (FCM) assay with the established quantitative real time PCR for NPM-ALK for the quantification of circulating tumor cells in 21 patients with ALK positive ALCL.

Methods: The FCM assay is based on the simultaneous detection of intracellular ALK, and surface CD30-expression of ALCL cells. Its sensitivity had been shown to reach 10⁻⁵ in cell dilution experiments. 25 bone marrow (BM) or peripheral blood (PB) samples from 21 patients with an ALK positive ALCL could be analyzed by both methods. The samples were obtained either initially or at relapse diagnosis. Control PB and BM samples were available from healthy controls (PB) and seven patients with other hematological malignancies (BM).

Results: No ALK- and CD30-double positive cells were detected in the control samples. The results of the FCM assay and quantitative PCR for NPM-ALK correlated in all samples from 20 of the 21 ALCL patients. Only one patient showed a discrepancy: a high NPM-ALK-copumber could be detected in PB and BM but no CD30 and ALK expressing cells by FCM. The sensitivity of the quantitative real time PCR exceeded the one of FCM by at least one log.

Conclusion: FCM with antibodies against ALK and CD30 can sensitively and specifically detect circulating ALCL cells in BM and PB. The results correlate well with those of quantitative real time PCR for NPM-ALK. However, it needs to be tested in a larger cohort of patients whether its sensitivity suffices to substitute quantitative PCR.
179 A COMPARISON OF PEDIATRIC T-CELL LYMPHOMATOUS LYMPHOMA AND T-CELL LYMPHOBLASTIC LEUKEMIA FOCUSED ON LOSS OF HETEROZYGOSITY OF RELEVANT CHROMOSOMAL REGIONS

B. Burkhardt1, D. Krüger1, A. Morevicke1, W. Klapper2, F. Greene2, M. Schrappe3, A. Peifer4
1Children's Hospital, University Hospital Schleswig-Holstein, Campus Kiel, Germany
2Pediatric Hematology Oncology, Justus Liebig University, Giessen, Germany
3Hematopathology and lymph node registry, University Hospital Schleswig-Holstein, Campus Kiel, Germany

Introduction: Typical chromosomal deletions have long been identified in pediatric T-cell lymphoblastic leukemia (T-ALL). However, for T-cell lymphoblastic lymphoma (T-LBL) molecular and cytogenetic data are scarce.

Methods: The study focused on the frequency, the association with clinical characteristics and the prognostic impact of Loss-of-heterozygosity (LOH) in 114 T-LBL patients (pts) and 125 T-ALL pts treated according to ALL-BFM treatment strategies. LOH in the DNA of malignant cells indicates alterations of DNA with possible functional deletion. A set of 45 markers were analyzed in the following chromosomal regions of functional relevance: chromosome 6q using 25 markers (m), chrom.7q (4 m), 9p (5 m.), 11q (5 m.), 12p (5 m.) and 17p (1 marker in m/3).

Results: In 114 T-LBL pts a total of 4634 markers and in 125 T-ALL pts a total of 5724 markers were analyzed successfully. In T-LBL, 19% of pts were positive for LOH at 6q, 4% for LOH at 7q, 48% for LPH at 9p, 5% for LOH at 11q, 6% for LOH at 12p and 4% for LOH at 17p in the gene of interest. In T-ALL, 12% of pts were positive for LOH at 6q, 2% for LOH at 7q, 51% for LOH at 9p, 2% for LOH at 11q, 7% for LOH at 12p and 1% for LOH at 17p. Regarding clinical characteristics, LOH at 6q was not associated with specific patients’ characteristics. LOH at 9p was associated with male gender in T-ALL and T-LBL. However, LOH in the Induction phase of LNH97 124, 27 and 18 episodes of hematologic, hepatic and gastrointestinal toxicity were observed in 86/101 evaluable patients.

Conclusion: Changes adopted in protocol AIEOP LNH97 improved survival and caused an overall reduction of hematologic, hepatic and gastrointestinal toxicity in the most intensive portion of the treatment.

180 HODGKIN’S DISEASE IN DEVELOPING COUNTRIES: OUTCOME WITH CHEMOTHERAPY ALONE

S.D. Joshi1, K. Kapoor2
1PH, Public Health Office Malakhet PHC-3, Malakheti, Nepal
2Oncology, All India Institute of Medical Sciences, NewDelhi, India

Background: To assess the efficacy of chemotherapy alone, using four cycles of COPP alternating with four cycles of ABVD in all stages of childhood Hodgkin’s disease (HD).

Procedure: Reports, Between January 1996 and February 2006, 148 previously untreated patients were investigated, treated, and analyzed for remission and survival.

Results: There were 134 boys and 14 girls with a median age of 8 years, 75% were less than 10 years old. 63.5% had advanced stage III-IV disease. 8 symptoms were present in 54% of cases, bulky mediastinal mass in 18 cases (12.2%), spleen and bone marrow involvement in 22 (14.9%) and four cases (2.7%), respectively. Mixed cellularity (MC) subtype was found in 80%. Response to treatment was evaluated in 135 patients: complete remission (CR) was achieved in 121 patients (90.8%), partial remission (PR) was achieved in 5 patients due to progression (11.4%), and three (2.3%) died on therapy. Four patients with mediastinal residual disease were given additional involved field radiotherapy. Out of 111 patients analyzable, four (4.5%) had relapsed 6-30 months after completing chemotherapy, and were treated with additional cycles of ABVD and low-dose involved field radiotherapy. The 5-year actuarial overall survival (OS) and event-free survival (EFS) are 91.5 and 87.9%, respectively.

Conclusion: Chemotherapy alone after alternating COPP/ABVD, without additional radiotherapy, provides high rates of durable remission and is an effective therapy in childhood HD in developing countries, even in case of large mediastinal mass and peripheral or abdominal bulky disease.

181 A PILOT STUDY OF MYELOABLATIVE (MA) AUTOLOGOUS STEM CELL (AUTO SCT) FOLLOWED BY REDUCED INTENSITY ALLOGENIC TRANSPLANTATION (RI ALCOST) IN CHILDREN WITH POOR RISK HODGKIN’S DISEASE (HD) AND NON-HODGKIN’S LYMPHOMA (NHL)

P. Satwani1, B. Bradley2, L. Harrison3, B. Tallman3, L. Baldinger3, J. Garnvin3, D. George4, M. Bhatia1,5,6, J. Kurtzberg3, M. S. Cairo
1Pediatrics, Medicine & Pathology, Columbia University, New York, United States
2Pediatrics, Columbia University, New York, United States
3Duke University, North Carolina, United States

Background: AlloSCT may benefit patients with poor risk HD and NHL by providing a graft vs. lymphoma effect. In relapse/refractory (RR) HD pts, Majhail et al (Blood 2016) reported OS of 9%–37% post MA Auto SCT. Similarly, outcome for children with poor risk NHL remains dismal (Bradley/Cairo, BMJ 2008). Carella et al (JCO 2008) demonstrated the success of MA AutoSCT followed by RI AlloSCT in adults with R/R lymphoma. We investigated the feasibility of MA AutoSCT followed by RI AlloSCT in children with poor risk HD (Induction failure, early relapse ≤1yr), late relapse (stage III-IV), 2nd or 3rd relapse and NHL (induction failure, 1st, 2nd or 3rd PR and 2nd or 3rd CR) (estimated 30% OS).

Methods: MA conditioning prior to AutoSCT was CTX 1500 mg/m2 x 4 d, BCNU 100 mg/m2 x 4 d, VP-16 800 mg/m2 x 5 d. AlloSCT conditioning was Fludarabine 30 mg/m2 x 5 d, Busulfan 3.2 mg/kg x 2 d, and R-ATG 2 mg/kg x 4 d (MUD). CD34+ NBLs received rituximab and HD pts received involved field radiotherapy prior to RI AlloSCT.

Results: Seventeen pts: 9 NHL, 8 HD, median age 15yrs, median F/U: 37 (198-252) d. 2 did not proceed (parental withdrawal) to RI AlloSCT and one patient died before RI AlloSCT. Donors: 2 MBD, 3 MUD, 9 UCB. Median time to RI AlloSCT after MA Auto SCT was 115d (95-219). Engraftment was achieved at a median of 20d for PMN and 33d for platelets. Donor chimerism reached 2% in 11/12 all eligible pts by d100. Toxicities were grade 3 (5) hematoma (n=1), (3-4) infection (n=8), (4) pulmonary fibrosis (n=1), (4) hearing loss (n=1), (4) neurotoxicity (n=1). GvHD: grade II-III aGVHD (4/14), cGvHD (3/14). Five pts are alive and NED post RI AlloSCT. Five pts died: 2 NRM and 3 relapsed. The probability of OS at 1yr is 66%.

Conclusions: MA AutoSCT followed by RI AlloSCT is feasible and well tolerated in children with poor risk HD and NHL. A larger study with longer follow up is required to determine if this approach will reduce relapse, long term toxicity and/or improve survival compared to MA AutoSCT alone.