558 ORAL

Individually modified involved field technique of the German/Austrian Pediatric Hodgkin Study (HD90): A way to reduce treatment volume without increase of relaps

K. Dieckmann, R. Pötter, J. Hofmann, U. Haverkamp, A. Drochtert, F.J. Prott, W. Wagner, G. Schellong. *Department of radiotherapy and radiobiology, University of Vienna, Austria*

Purpose: Definition of the supra- and infradiaphragmatic involved lymph node area to be irradiated within combined modality of treatment of pediatric Hodgkin's Disease (HD 90) based on clinical examination and modern sectional imaging. Comparison with the classical "involved field"- radiotherapy (1966). Analysis of the location of relaps compared with the modified treatment volume.

Material and Methods: From October 1990 to October 1995 602 patients have been enrolled in the German-Austrian multicenter pediatric HD-study with 73 centres participating. Centralized treatment planning at the study office was performed for 577/602 patients before radiotherapy was started. For each of these patients the individual spread of disease at diagnosis was documented based on the documentation forms filled in by the respective center indicating the extent of disease. A central review of chest X-ray films, Chest and abdominal CT was added. An individual proposal for the radiation field was set up and sent to the respective centre.

The radiation fields proposed were compared to the classical IF -radiotherapy for 577 patients with supra- and infradiaphragmatic disease. Location of tumor recurrence has been analysed.

Results: The individualisation of classical IF-radiotherapy led to changes in altogether 40% of the patients. Most changes were in the supradiaphragmatic involvement: 235/577 changes were volume reduction. The cases of volume enlargement referred to including the thoracic aperture. For the neck and the mediastinum typical patterns of spread resulting in modified IF-radiotherapy could be identified: upper neck: lower neck including the supraclavicular region: upper mediastinum including the thoracic aperture: upper mediastinum including bilateral hili. The proposed radiation fields were in 95% a combination of one or more of these areas. Modified involved field technique with treatment volume reduction could be realised only in a few cases of infradiaphragmatic disease.

Analysis of recurrence (n = 34; 12/96) revealed only one recurrence in a lymph node area treated by a modified radiation field.

Conclusion: Classical IF-radiotherapy can be modified based on modern sectional imaging especially for supradiaphragmatic lymph node involvement. Volume reduction do not jeopardize local control within effective combination treatment.

559 ORAL

Radiotherapy in treatment of Ewing's sarcoma of the chest wall (Askin tumors)

A. Schuck[1], Ch. Rübe[1], J. Hofmann[2], M. Paulussen[4], J. Dunst[3], H. Jürgens[4], N. Willich[1]. *Dpts. of Radiotherapy of the Universities of [1]Münster; [3]Halle; [4]Dpt. of Ped. Oncology, Münster, Germany; [2]Dpt. of Radiotherapy of the University of Vienna, Austria*

Purpose: In Askin tumors, radiotherapy is an important modality. In the CESS 81, 86 and EICESS 92 studies it is used as only local treatment or as preoperative or as postoperative irradiation, always in combination with chemotherapy. The results of radiation treatment are evaluated.

Methods: Since 1981, 146 patients with Askin tumors have been treated according to the study protocols CESS 81, CESS 86 and EICESS 92. 119 of them received irradiation as local treatment. 53% of the patients had sarcomas of the ribs, 27% of the scapula, 12% of the spine, 6% of the clavicula and 2% of the sternum. The median follow up is 38 months.

Results: The relapse free survival after 5 years was 46%. It was 66% after operation alone, 75% after preoperative, 48% after postoperative irradiation and 35% after irradiation alone. The difference between the 4 local treatment modalities was not statistically significant (p = 0.16%). Local control was best after operation alone and preoperative irradiation with 100%, it was 81% after postoperative irradiation and 79% after irradiation alone. Again the difference was not statistically significant.

Conclusion: Most patients received radiotherapy. Although there is a tendency of better local control after operation alone, this is partly due to a positive selection. Local control and survival after sole or combined radiation therapy are good.

560 ORAL

The role of radiotherapy in the combined treatment of stage I childhood rhabdomyosarcomas. Results of the german cooperative soft tissue sarcoma study (CWS) in 104 patients

B.F. Schmidt[1], M. Herbst[2], W. Alberti[3], E. Koscielniak, T.B. Pilgrim, R.K. Knietig, J. Treuner[4]. *[1]Dpt. of Radiotherapy Katharinenhospital Stuttgart; [2]Dpt. of Radiotherapy Univ. Hospital Regensburg; [3]Dpt. of Radiotherapy Univ. Hospital Hamburg; 4 Dpt. of Pediatric Oncology Olgahospital Stuttgart, Germany*

Purpose: Local radiotherapy in children is to be restricted to indications of proven efficiency due to the impending late radiation sequelae. Is radiotherapy necessary in addition to chemotherapy after initial complete tumor resection (stage I, IRS)?

Methods: From 1981 to 1996 104 stage I patients (pts) were treated with a combined modality regimen according to the CWS protocol. 84 were of embryonal (RME), 20 of alveolar (RMA) histology. Radiotherapy (~45 Gy) was given in 19 pts (18%). The outcome was evaluated after a median follow up of 70 months.

Results: In continuous complete remission/alive are 87/92% of RME and 75/85% of RMA. Local/combined/systemic relapses were to be observed in 5/7/1% of RME and 5/5/15% of RMA. There were no significant differences between the irradiated and the not irradiated group. The majority of local relapses could be salvaged by second line treatment including radiotherapy or mutilating surgery.

Conclusion: Radiotherapy as an adjunct to multidrug-chemotherapy does not improve further the rather good prognosis in initially completely resected pts. This seems to be true for RME, hopefully even for RMA, but the number of RMA-cases is small. These findings are in keeping with the SIOP, IRS and Italian group data.

561 ORAL

Myeloablative therapy, stem cell rescue and gene transfer in advanced ewing tumors (AET)

St. Burdach, H. Pape, T. Kahn, B. van Kalck, W. Rüther, C. Bender-Goetze, E. Koscielniak, F. Zintl, H. Gadner, H. Jürgens. *Stem Cell Transplant Programs at Düsseldorf, Münster, München, Jena Univ. Medical Centers, Olga Hospital, Stuttgart, FRG; St. Anna Kinderspital, Wien, Austria*

Ewing Tumors (ET) are defined by expression of *ets/ews* chimeric transcription factors and early systemic spread. High dose therapy (HDT) and stem cell rescue has improved the prognosis of AET patients. The European Intergroup (EICESS) has established the following indications for HDT in AET: Patients with primary multifocal bone tumors, patients with early (≤2 y after diagnosis) or multiple relapse. As of Nov 1996, probability of EFS for these patients is 32% (n = 50, mean survival time: 52 mo). Results may be affected by histology, transplant type and immunotherapy. Classical Ewing Sarcoma: 35% EFS v.s. MPNT: 27%; autotranplants: 34% v.s. allotransplants: 20% EFS; Patients receiving IL2 post autotransplant: 62% v.s. patients without IL2: 28% EFS. In spite of improved cure rates after HDT, relapse remains a major problem occurring primarily in the lung, within the shielded region, within involved bones outside the radiation field and at the site of lesions detectable only by NMR or PET but not by conventional Tc bone scan. RT-PCR also revealed contamination of both marrow and peripheral grafts with residual ET cells. Based on the IL2 data, we have developed a tumor vaccination strategy utilizing cytokine gene transfer. To this end, we have transfected IL2 as well as other immunstimulatory cytokine genes (IL7, GM-CSF) into ET cell lines derived from transplanted patients as well as into autologous patient fibroblasts. Transgenic IL2 expression in vivo leads to induction of a unique cytokine induced killer cell population, which could not be solicitated by treatment with exogenous IL2. We conclude: HDT is efficacious in AET for prevention of relapse. Extension of involved compartment irradiation, post ransplant immunotherapy, detection of minimal residual disease and graft purging may further improve the outcome of AET patients.

562 ORAL

Desmoid tumors in children

A.I. Kovalyov. *Byelorussian State Institute for Physicians Post-Graduate Training, Minsk, Belarus*

Desmoid tumors (DT) belong to fibromatoses, and in TNM classification – to q1 fibrosarcomas. Their rate among soft tissue sarcomas is about 25%, and among all benign and malignant soft tissue tumors – 3%.

From 1960 to 1996 we followed up 64 children aged from 1 to 18 years, which is about 18.1% of all DT patients (352). There were 26 boys and 38 girls. Eleven children had abdominal desmoids (AD), 51 had extraabdominal desmoids (ED), and 2 children had a combination of AD and ED. Congenital DTs were registered in 12 children, mothers of three of them having DT in combination with diffuse polyposis of the colon. Primary DTs were in 37 children, 27 presented with recurrences, 20 of them with multiple ones. DT sites were femur (26), gluteal area (18), abdominal wall (11), shin (10), foot (8), thoracic wall (7), hand (6), neck (5), shoulder (4), lumbar area (4), perineum (2), abdominal wall and femur (2), cheek and lower jaw (2). The total number of desmoid lesions was 105. The size of DT ranged from 5 to 35 cm, its maximum weight was 3.8 kg.

105 DTs in 61 children were subjected to surgical treatment, 3 patients were administered no surgery. After surgical treatment relapses occurred in 60% of the cases. After combined modality treatment they occurred two times rarer and after a longer period of time. Remote results are known in all the patients: 14 persons are alive for 3–5 years, 6 – for 6–10 years, 18 – for 11–15 years, 13 – for 16–20 years after the first operation. Of all the children, only one girl has an inoperable tumor. The rest are healthy. In none of the cases malignization of DT, conversion into fibrosarcoma or metastasizing were observed. In one girl a spontaneous regression of DT recurrence was registered at the beginning of menses and subsequent two childbirths. The mother and children are healthy.

563 ORAL

Nasopharyngeal carcinomas of childhood

M. Serin, H.Ş Erkal, A. Çakmak. *Department of Radiation Oncology, Ankara University Faculty of Medicine, Turkey*

Aim: This study reviews the authors' experience, from 1980 through 1995, in management and outcome of 56 children with nasopharyngeal carcinomas.

Methods: There were 23 females and 33 males, their ages ranging from 7 to 19 years (median, 16 years). Twelve children had WHO type 1, 4 had type 2 and 40 had type 3 carcinomas. Six children were at Stage II, 9 at Stage III and 41 at Stage IV (TNM-AJC). Sixteen children had T4 tumors and 18 had bilateral nodal involvement. External beam radiation therapy consisted of 50 to 70 Gy (median, 64 Gy) to primary tumor and 50 to 74 Gy (median, 66 Gy) to involved nodes, delivered in 1.8 to 2 Gy daily fractions. Fourteen children with T1–3 tumors received 1 to 3 (median, 2) fractions, each of 5 Gy, of HDR intracavitary brachytherapy boost. Thirteen children received neoadjuvant, 4 neoadjuvant and adjuvant and 7 concurrent chemotherapy.

Results: Follow-up ranged from 0.3 to 16.8 years (mean, 9.6 years). Complete primary tumoral response was achieved in 49 out of 55 and complete nodal tumoral response in 39 out of 40 evaluable children. Overall survival (OS) and disease-free survival (DFS) were 52.6% and 48.3% respectively, at 5 years and 52.6% and 48.3%, respectively, at 10 years. There were 6 primary, 3 nodal and 2 primary and nodal tumoral failures among children exhibiting complete response. There were 11 systemic failures among all children. In univariate analysis: T-stage and bilateral nodal involvement were significant prognostic factors for OS and T-stage. N-stage and bilateral nodal involvement for DFS. In multivariate analysis; age. T-stage. N-stage and addition of chemotherapy were significant prognostic factors for OS and T-stage, N-stage, and addition of chemotherapy for DFS. Two children died of adjuvant chemotherapy-related toxicity. Of 23 children with longer than 5 years of follow-up, 12 had mild neck atrophy, 3 shortening of clavicles, 2 trismus, 1 hypothyroidism and almost all xerostomia and dental caries.

Conclusion: Although radiation therapy alone is effective in achieving primary and nodal tumoral control, it should be accompanied with chemotherapy in attempt to improve OS and DFS.

564 POSTER

Specificities and optimization of peripheral blood stem cell collection in children: Treatment for malignancies can be mobilization

Ph. Brault[1], P.S. Beaussier[2], C. Bayle[2], V. Lapierre[2], F. Beaujean[1], J. Antonini[2], E. Benhamou[2], D. Valteau-Couanet[2], O. Hartmann[2]. *[1]GIP Sud Est Francilien; [2]Institut Gustave Roussy, 94805 Villejuif, France*

Autologous peripheral blood stem cells (PBSC) is currently used to support high dose chemotherapy for children with solid tumors. However the volume of extracorporel blood loss required by leukapheresis and the veinous access could limit the procedure in small children.

Patients: Between 06/88 and 08/96, 136 children (median age: 96 months, median weight: 16 kg) with solid (n = 126) or hematologic malignancy (n = 10) underwent 141 stem cell mobilization episodes with hematopoietic growth factor (HGF) alone (86 first pts) or in combination with cytotoxic chemotherapy (CT) (different regimen prescribed for the malignancy, 50 pts). To optimize the PBSC collection, we have monitored the number of CD34+ cells in blood.

Results: 380 leukapheresis were performed with a median number of 3 per pt before 1996, and 2 in 1996 with a significant ($p = 0.05$) higher median of total CD34+ cells harvested ($8.99.10^6$ vs $6.74.10^6$ CD34+/kg). 80% of children had central lines for the PBSC harvest. We observed 45 clinical problems (hypocalcemia, hypovolemia, shock, and minor events: tiredness, isolated or in combination). 68% of pts were transfused at least once time with RBC and 8% required platelet support before the procedure. There is no difference between HGF alone and CT + HGF in term of mobilization failure. A significant correlation between the number of blood CD34+ cells (the day before and day of collection) and the leukapheresis product was found ($r = 0.59$ and 0.8 respectively). All the pts with $>1.10^6$ CD34+/kg in leukapheresis product had more than 11200 CD34+ cells/ml in blood. **In conclusion:** PBSC harvest required strategic care, especially for children who weight less than 10 kg. We have observed that most CT regimen used in pediatric malignancies can mobilize PBSC. The monitoring of daily blood CD34+ level at the end of aplasia is useful to select the best day to begin leukapheresis in order to optimize the number of collections.

565 POSTER

Thyroid cancer in childhood – Value of total thyroidektomy

Th. Hoelting, Ch. Herfarth. *Department of Surgery, University of Heidelberg, Germany*

The prognosis of children with thyroid cancer is good despite frequent local invasion or metastases. The value of thyroidectomy is controverse.

Methods: Between 1970–1996, 20 children aged 4–16 years underwent surgery for thyroid cancer (papillary: n = 15; follicular: n = 3; medullary: n = 2). Clinical and pathologic findings, therapy and outcome were analyzed. Median follow-up was 7.5 years (1–25 y).

Results: 4 children had extrathyroidal tumor invasion (20%), 5 other had multifocal intrathyroidal tumor spread (25%). Cervical lymph node metastases were found in 9 (45%), distant metastases in 4 children (20%). All underwent total thyroidectomy, 4 as completion procedure. Radioiodine therapy was performed in 16 children (80%). Surgical complications included 1 vocal cord paralysis and 2 temporary hypocalcemias.

Cervical lymph node recurrences developed in 4 children. All were cured by surgical and radioiodine therapy. One girl died after 4 years from multiple metastases of a medullary thyroid carcinoma. All other are alive and free of disease.

Conclusions: Our surgical approach for thyroid cancer in children is total thyroidectomy with selective lymph node dissection. Indications are (1) a high frequency of multifocal and/or metastatic disease and (2) a smaller dosis of postoperative radioiodine.

566 POSTER

Evaluation of minimal and residual disease (MRD) in Ewing's tumors (ET) at diagnosis and during treatment

C. Fagnou[1], J. Michon[1], O. Oberlin[2], M. Peter[1], M. Brunat-Mentigny[3], P. Chastagnier[4], G. Leverger[5], J.M. Zucker[1], H. Magdelenat[1], O. Delattre[1]. *For the SFOP (Société Française d'Oncologie Pédiatrique); [1]Institut Curie, Paris; [2]Institut Gustave-Roussy, Villejuif; [3]Centre Leon Bérard, Lyon; [4]CHU de Brabois, Nancy; [5]CHU Trousseau, Paris, France*

Purpose: As Ewing's cells express specific chimaeric transcripts as a result of the t(11;22)(q24;q12) chromosome translocation or of its variant t(21;22), the reverse transcriptase-polymerase chain reaction (RT PCR) technique can detect MRD.

Material and Methods: Using a one tube nested PCR amplification procedure, blood and/or bone marrow (BM) from 113 patients with ET were evaluated for the presence of tumor cells at various times before and during treatment.

Results: At diagnosis, 16/62 patients had circulating tumor cells. The spontaneous occurrence of these circulating cells before biopsy could be established in some cases, but in other the detection might be related to the mobilisation of cells linked to the tumor sampling. The presence of circulating tumor cells was not correlated with the size of the primary tumors nor with the presence of metastasis. Ewing cells infiltrating BM were detected in 13/41 patients. The presence of RT-PCR positive BM was most frequently observed in patients with metastasis (8/17 vs 5/24), but, half of the patients (9/17) having lung or bone metastasis did not had RT-PCR positive BM.