Conclusion: The results if compared with other national and international experience, demonstrate an increment in terms of 6 years OS. Only extension of disease at diagnosis, site of metastasis and surgery on primary site of disease seems to influence the outcome in terms of PFS.

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985 POSTER DISCUSSION

Potential role of MLL cleavage as a biomarker for treatment-related leukaemogenesis associated with topo 2 inhibitor therapy in children

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Purpose: Treatment-related leukaemia (TRL) is the most serious complication of effective topoisomerase 2 (topo 2) inhibitors in paediatric cancer therapy. Most TRLs are associated with rearrangement of the Mixed Lineage Leukaemia (MLL) gene, following drug-induced gene cleavage, and with a very poor outcome. Analysis of MLL cleavage may therefore be useful in assessing individual susceptibility to the genotoxic effects of topo 2 inhibitor therapy and, in predicting the risk of TRL.

Methods: 400 serial blood and marrow samples, obtained from 71 children receiving topo 2 inhibitors for primary malignancies and haemophygocytic lymphohistiocytosis (HLH), were studied. Cleavage in the breakpoint cluster region (BCR) of the MLL gene was detected using a hybridisation assay with a MLL cDNA probe and quantified by real time autoradiography. The results were correlated with clinical outcome and the adverse effects of treatment, and compared with those of 71 cord blood controls.

Results: MLL cleavage fragments (6.7 & 1.5kb) were detected in 6 bone marrow samples from 4 children with acute lymphoblastic leukaemia (ALL) and one with HLH. Only the 8.3kb germ-line MLL BCR product was found in the controls. MLL cleavage was identified at different time points after etoposide and anthracycline therapy in the 4 ALL patients, and following the last course of etoposide in the child with HLH. Cleavage fragments comprised 23-50% of the total MLL BCR signals. All 5 children experienced serious treatment related toxicity. Of these, one with T-cell ALL relapsed and died during treatment and the patient with HLH developed a TRL with MLL rearrangement post therapy.

Conclusion: MLL cleavage may provide a useful biomarker for the risk of TRL associated with topo 2 inhibitor therapy in children and warrants further investigation.

986 POSTER DISCUSSION

Paediatric Fine Needle Aspiration Cytology (FNAC) of NHL. An eleven-years study

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Introduction: Fine needle aspiration cytology (FNAC) is performed in IPOFG, for the initial diagnosis of paediatric lesions since 1987. It is particularly useful for the rapid diagnosis of non-Hodgkin lymphomas (NHL), and a final diagnosis can be achieved by using flow cytometry as a complement. In this study we reviewed the cases of NHL diagnosed by FNAC and compared its accuracy in NHL.

Materials and Methods: From a total of 1300 FNAC performed on paediatric patients between 1990 and 2000 in IPOFG, Lisboa, 387 corresponded to lymphoid lesions. FNAC diagnosis of NHL was done in 78. The other diagnoses were: reactive-188, Hodgkin's lymphoma-50, metastasis-21, inflammation-9, suspicious for malignancy-8, non-conclusive-18, unsatisfactory for diagnosis-17. In 71 of the 78 NHL smears were available for review and were reclassified using the REAL classification. Ancillary studies were performed in 59 cases: immunocytochemistry (34), flow citometry (25) and cytogenetics (5). Subsequent histology was performed in 28 cases. For the analysis we divided our cases in Burkitt's lymphoma (BL) and other types of NHL. Clinical records were available in 60 cases.

Results: NHL represented 60,9% of the lymphomas diagnosed by FNAC. The diagnosis of BL was done in 42 cases (59,1%). The other NHL were Lymphoblastic lymphoma-18, Diffuse large B cell lymphoma-7, Anaplastic large cell lymphoma, ALK+-2 and high grade NHL, NOS-2. Clinically, there was a male predominance. The median age was 6,3 yrs for BL and 7,5 yrs for the other NHL. BL cases were abdominal (31/42), nodal 8, facial 2 and 1 from the palatine tonsil. The other NHL were predominantly from superficial lymph nodes (13/29) and mediastinum (10/29). The median follow-up time was 48,6 months(1-126)for BL and 49,3 months (1-120)for other NHL. 40/60 patients are alive without disease (BL-73%;other NHL-56,5%),10 are alive with the disease (BL-16,2%; other NHL-17,4%), and 10 dead of the disease (BL-10,8%; other NHL-26,1%). FNAC morphology in conjunction with ancillary techniques rendered a final diagnosis in 85,7% and 75,9% of the BL and other NHL, respectively. The global diagnostic accuracy of NHL by FNAC was 81,7%.

Conclusion: FNAC is an accurate method to diagnose and classify paediatric NHL. The clinico-patologic features are identical to other published series from Western countries except for the higher frequency of BL. Its distinct morphologic features make BL the most accurately lymphoma diagnosed by FNAC.

987 POSTER DISCUSSION

Does pregnancy elicit clinical heart failure in anthracycline treated female survivors of childhood cancer?

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Purpose: Anthracyclines (AC) are well known for their ability to induce late clinical heart failure (CHF). In view of patient care we wished to establish guidelines allowing for safe peripartum management in AC treated survivors (ATS) of childhood cancer. Only two case reports about peripartum heart failure in ATS were found in the literature. In order to develop a strategy for additional clinical research it was decided to analyse the pregnancy histories of ATS registered in the database (PLEKsys) of our late effects outpatient clinic.

Methods: Female survivors were identified on the use of AC and on data entry on pregnancies. Data collected included treatment dates, cumulative AC doses, date of delivery, and cardiac problems before and/or after the pregnancies.

Results: Out of 35 pregnancies in 20 ATS 26 children were born. Seven abortions/miscarriages were found and the outcome of two pregnancies was unknown. The deliveries took place on average (± SD) 14 years (± 4) after AC treatment. Average dose of AC was 250 mg/m2 (± 154). Nine women received a dose of > or = 300 mg/m2 and 11 women received a dose of < 300 mg/m2. Eight out of the group of 9 women treated with a dose > or = 300 mg/m2 delivered in total 12 children. At last follow-up 1 of the 8 had developed a dilatation of the left ventricle more than three years after her second and last delivery and approximately 12 years after chemotherapy. In ATS treated with lower doses, one woman reported cardiac symptoms on several control visits both before and after the birth of her daughter. None developed peripartum cardiac problems.

Conclusions: No peripartum cardiac problems were found in ATS known at our late effects outpatient clinic. However, the numbers of ATS, pregnancies and deliveries are small. Up to 5% of AC treated patients will develop CHF 15 years after treatment (Kremer et al., JCO, 2001). The number studied in this series therefore is too small to be conclusive. Four of the women identified for this study have a wish to become pregnant at least once more. A further 67 ATS with this wish could be traced in the PLEKsys database, of which approximately 50% are using oral anticonceptive drugs. These observations and the lack of clinical evidence thus far, serve to illustrate both the urgency and the possibility for a well-developed clinical study to answer the question posed in the title