

85.

OCULAR LEUKEMIA (GRANULOCYTIC SARCOMA) IN TURKISH CHILDREN WITH AMML: AN ULTRASTRUCTURAL ANALYSIS. A.Cavdar, K.Kiliçturay, S.Gözdagöglu, E.Babacan, A.Arcasoy, U.Ertem, Department of Pediatrics (Pediatrics Oncology and Hematology Research Unit (TUBITAK) Medical School of Ankara University and Gülhane Military Academy.

Our earlier report indicated a high frequency of AMML with ocular manifestations in Turkish children. This report is to describe ultrastructural studies in 12 cases out of 23 orbital leukemia (AMML). The striking features of ocular manifestations were orbital tumor, exophthalmos, chemosis and proptosis. Bone marrow (BM) from 12 patients and orbital tumor from 3 cases were ultrastructurally analysed by electron microscope (Zeiss EM-9). The blast cells in our series of leukemia demonstrated several ultrastructural features described for AMML and AMoL in the literature. Interestingly, intracytoplasmic virus like particles (VLP) measuring 75 - 100nm resembling type C-RNA structures were observed in 3 BM and one eye sample. Evidence of budding, in favor of C-RNA viruses have also been observed occasionally in our cases. GS₃ antigen from the orbital tumor as an expression of type C virus has been previously demonstrated. Furthermore a reverse transcriptase (RT) with similar biochemical and immunological properties to that known type-C viral RT, has been isolated recently from the orbital tissue. In the light of these two findings, existence of VLP observed in this study may be interpreted in favor of C-type RNA viral structures.

86.

THE SIGNIFICANCE OF CHROMOSOMAL FINDINGS IN MYELOID LEUKEMIA OF CHILDHOOD. O.A. Haas, H.Gadner, E. Nacheva, P.Fischer, W. Schmid W. Schmidmeier

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Although myeloid leukemia has been observed in every age group, it occurs rarely during childhood. Within the last three years cytogenetic studies have been performed on eleven patients with myeloid leukemia in the St. Anna's Children Hospital, using the banding technique. The results of these studies have been compared to clinical and haematological findings. Five patients suffered from chronic myeloid leukemia (CML), and six from an acute myeloid leukemia (AML). The Philadelphia-Chromosome (Ph¹), which is characteristic of the adult form of CML, was also found in four children. Clonal evolution of the chromosomal abnormal cell population occurred in five patients. These changes resembled karyotyp patterns seen in acute phases of CML in adult patients. AML patients with an abnormal karyotype in their leukemic cells survived significantly shorter than those patients with a normal karyotype. In conclusion, cytogenetic analysis has shown to be a valuable method in improving diagnosis and characterization of myeloid leukemias in childhood.

87.

ANTHRACYCLINES IN CHILDHOOD CANCER. C.T.C. Tan for the Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, New York 10021

Daunorubicin (DNR) has an established role in the treatment of acute leukemia; its analogue, doxorubicin (DX) has in addition antitumor effect in a broad spectrum of childhood solid tumors. Both DNR and DX are cardiotoxic; prior cardiac radiation increases the incidence of cardiomyopathy. New anthracycline molecules are being studied for compounds with a broader antitumor spectrum or a more favorable therapeutic index than either DNR or DX. In transplanted murine tumors the activity of new anthracycline derivatives shows: 4-demethoxydaunorubicin (4DMDR) has higher potency and antileukemic effect and reduced cardiotoxicity than DNR. 4-demethoxydoxorubicin has higher potency and antileukemic effect with

equal activity in solid tumors but markedly reduced cardiotoxicity than DX, and both are active orally. 4'deoxydoxorubicin has higher potency, equal antitumor activity with marked reduced cardiotoxicity than DX. Currently we are studying 4DMDR; to date 9 acute leukemia and 4 solid tumor previously treated children have been entered. Total prior anthracycline doses were <270mg/m² and the ECHO cardiograms were normal. Solid tumor patients received 10,15 or 20mg/m² while leukemia children received 10,15,20 or 30mg/m² intravenously (IV) in three equally divided daily doses every 3 weeks. 3 of 9 children with leukemia have achieved marrow remissions for 1 and 8+ weeks. Myelosuppression is the dose-limiting toxicity. Other side effects have been mild including oral ulcers and transient elevation of liver enzymes. Cardiomyopathy has not been observed to date. The IV maximum tolerated dose (MTD) in leukemia may be 30mg/m². Oral 4DMDR is being studied in adults. As soon as the IV MTD is confirmed we will study oral trials of 4DMDR in children.

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88.

THE VALUE OF IFOSFAMIDE IN PREVIOUSLY TREATED CHILDREN WITH SOLID TUMOURS. A PILOT STUDY. J.de Kraker, P.A.Voûte, Werkgroep Kindertumoren, Emma Kinderziekenhuis and Netherlands Cancer Institute, Spinozastraat 51, 1018 HJ Amsterdam, The Netherlands.

Fifteen patients who had recurrent disease after treatment with the usual chemotherapy regimens were studied to determine the effect of Ifosfamide. Ifosfamide (Holoxan) was given in a dose of 80 mg/kg/day for 4 days with Vincristine (VCR) 2 mg/m² on day one every three weeks in 5 children. Eight patients received 3000 mg/m²/day for two days with VCR 1.5 mg/m², day one every three weeks. Among these patients were 3 Ewingsarcoma (E.S.), 2 osteosarcoma (O.S.), 1 adrenal carcinoma (A.C.), 1 melanomasarcoma (M.S.), 3 rhabdomyosarcoma (RMS), 1 vaginal clear cell carcinoma (Cl.ca.), 1 pancreatic carcinoma (P.ca.), 1 synoviosarcoma (Sy.sa.), 1 liver metastasis of a Wilms' tumour (W.T.) and 1 malignant schwannoma (Ma.S.). Nearly all these children had been treated before with varied combinations of chemotherapy which consisted of Adriamycin, Actinomycin D, VCR, but also Cyclofosfamide. The mean age was 10 years (2-18 yrs) and mean duration of treatment before the Ifosfamide was started 2 years (3 months - 6 yrs). Toxicity was moderate. Vomiting, bone marrow toxicity and haematuria were seen but were never a reason to withdraw the drug.

Results: complete remission was obtained in 4 cases (2 O.S., 1 RMS, 1 W.T.). Partial response (> 50% tumour shrinkage) 2 cases (RMS, O.S.), improvement (< 50% tumour shrinkage) 3 cases (A.C., M.S., RMS). Stable disease one patient (Ma.S.). Progressive disease in 5 patients. Of these 5 patients 4 were treated with the four day regimen.

Conclusion: Ifosfamide seems to be an active drug in childhood cancer and it should be studied further.

89.

THE USE OF INTRAARTERIAL CIS-DIAMMINEDICHLOROPLATINUM IN PEDIATRIC TUMORS: A PRELIMINARY REPORT. V.C.Canale, S.Tumolo, E. Grigoletto. Division of Radiotherapy and Medical Oncology, Ospedale Civile, 33170 Pordenone (Italy).

Intraarterial chemotherapy (IAC) in the pediatric age range has been used sporadically in the treatment of hepatic tumors and bone tumors of the extremities. In our Institution IAC with Cis-Diamminedichloroplatinum (CDDP) has been employed in 25 consecutive untreated adult patients (pts) with head and neck tumors. Either a 5 or a 10 day course of CDDP 20 mg. every 24 hours by continuous infusion was delivered to the 25 pts. Renal, gastrointestinal, hematologic and otologic toxicity was encountered in 57.5%, 20%, 53.5% and 0% respectively of the evaluable pts and was usually mild, easily manageable and reversible in all cases. Objective remissions were observed in 67% of the evaluable pts, with 4 clinical complete remissions. Subsequent surgery was feasible in 9 pts, radiotherapy in 12 pts and chemotherapy in 1 pt. These encouraging results prompted the use of this modality in the treatment of an 11 year old male with recurrent Ewing's sarcoma of the right ilium and massive infiltration of the adjacent soft tissue. A 10 day continuous 24 hour infusion of 20 mg. CDDP via the right femoral-iliac artery produced a prompt reduction in the tumor mass after one course of therapy. No systemic side effects or thrombotic complications were encountered.