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MULTIFORM GLIOBLASTOMA COMBINED THERAPY BY RADIATION AND A-INTERFERON

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The aim of the project is the study of the combination of Radiotherapy (RT) with interferon alfa-2a (A-INF) in patients with glioblastoma multiform who had previously been submitted to various surgical treatments. All the patients have been subjected to radical RT with Co^{60} and the total tumor dose was 6000 cGy during a 6weeks period with sumultaneous starting the provision of paracetamol and A-INF in dose $9X10^6$ IU sc 3 times per week for a 6 month period. So far 20 patients have been studied who have all been subjected to the above mentioned scheme. No considerable statistical expance of survival or free of relapse interval has been observed. The study is in progress and numerical increase in the free of relapse interval, has already been observed in comparison with the patients who had formerly been liable to shere RT.

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FLOW CYTOMETRY (FCM) OF GLIOMAS (Gr.III-IV) FOR PREDICTING RESPONSE TO CHEMOTHERAPY (CHT)

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FCM was studied on deparaffinized gliomas of 35 patients (pts) who received CHT (mainly Procarbazine, Lomustine and Vincristin); 24 pts had CHT before irradiation (group I) and 11 previously irradiated pts had it at recurrence (group II). Disease was measurable by CT in 30 pts (19/24 and 11/11 respectively). Fourteen tumors showed only one population of cells, always diploid [DNA-index (DI)=1.0], and 16 also showed a second population of cells. In group I 9/19 pts had benefit from CHT [7 responded and 2 no changes (N.C) for ⩾3 months]; five of these 9 showed a second population of cells, mainly near-diploid (D.I.=1.1-1.4;). Only 2/10 pts with progressing tumors showed a second population of cells. In group II 11/11 pts benefited from CHT (6 responses and 5 N.C.); 9/11 showed a second population of cells, always aneuploid (D.I.>1.4). Our findings suggest that the appearance of a second population of cells, mainly if aneuploid, correlates with benefit from CHT.

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CENTRAL NERVOUS SYSTEM METASTASES IN WILMS' TUMOR

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Spinal cord and brain metastases in Wilms' tumor are apparently very rare. Between the years of 1973-1992 417 cases with Wilms' tumor were diagnosed, treated and followed-up as a single institution. Cerebral and spinal metastases were observed in only four cases (3 girls and one boy) during this period. Ages were between 3-8 years at the time of Wilms' tumor diagnosis. All the patients were in favorable histologic subgroups. Three patients were in stage III and one patient in stage IV according to the NWTS -III staging system. The diagnosis of metastatic disease was established by histopathological findings in two cases, the remainder were diagnosed on the basis of neuroradiologic findings. All patients were on therapy at the time of CNS metastases. Two of the patients had metastases in the brain during 15th and 48th months'periods.Two patients were treated with combinations of surgery, radiation therapy and chemotherapy One with brain involvement, one with spinal cord metastases). They died of progressive disease in the 15th and 60th months respectively. The third patient was treated with radiation and chemotherapy, and she is still alive with disease. The last patient died of the findings of cerebellar herniation at the 20th months of her follow-up. Autopsy could not be performed. Thus we do not know whether this was metastases or independent primary brain tumor, which is reported as being more common in this entity.

Key words: Wilms'tumor; brain metastasis; CNS tumors

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LEVAMISOLE ASSOCIATED ALTERATIONS OF PHAGOCYTIC ACTIVITY IN CHILDREN WITH BRAIN TUMOR

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We recently studied the phagocytic activity(PA) in 29 patients(pts)with brain tumor(BT).Eleven pts with BT aged 2-14 years received immunomodulator Levamisole(LM)2,5 mg/kg/bw for 3 consecutive days every 2 weeks for 6-12 months.Adherent granulocytes(G)and monocytes(M)were exposed to viable yeast cells for 30 min at 37°C. The number of adherent and digested particles, index ingestion(Ii),per G(x=3,39)and M(x=1,03) was higher in LM treated pts than in non-treated pts,G Ii x=2,08,M Ii x=0,99.G digestion,D% (x=8,4)and MD%(x=69%)was much better in pts that had taken LM;GD%(x=4%)and MD%(x=45,6%)in non-treated pts with BT were significantly reduced.Conclusion.We show here that the Levamisole induces functional activation of PA in the treated pts with BT.The incidence of intercurrent infection in LM treated pts was lower. Children took levamisole in this therapeutic dosage without complications during of treatment

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PRELIMINARY PHASE II TRIAL OF OXALIPLATIN (L-OHP) IN MALIGNANT ASTROCYTOMAS

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L-OHP is a platinum compound active in several experimental tumors devoid of renal and hematologic toxicities as demonstrated by phase I studies.
From 1/90 to 2/93, 14 patients (pt) bearing a grade 3 or 4 astrocytomas according to Daumas-Duport classification, were included in a phase II trial using a 130 mg/m^2 6 hours IV infusion of L-OHP every 3 weeks. Metoclopramide was used as antiemetic treatment. Patients were treated until progression. Major inclusion criteria were : pt WHO PS ≥ 2. unpreviously treated by chemotherapy with an inoperable histologically proven grade 3 or 4 measurable malignant astrocytoma and normal haematological, renal and hepatic functions. Toxicity was evaluated by cycle (cy) according to WHO scale and tumor response was assessed every 2 cy up to Levin criteria.
Patients characteristics were as following : male/female ratio = 1.8 ; mean age = 48,5 years (23-64) ; median PS = 1,8 (0-2). Tumor histology was : astrocytomas grade 4 = 10, astrocytomas grade 3 = 4.
Thirty three cy of L-OHP were performed, mean = 2,3 cy (1-6). 29 cy were evaluable for toxicity. Main toxicities were nausea and vomiting : 16 cy grade 0-2, 12 cy grade 3, 2 cy grade 4, fever : 2 cy grade 2, diarrhea : 1 cy grade 3, skin toxicity rash : 1 cy grade 2, isolated elevated ALAT (grade 1) (5 cy, 4 pt : one with a history of alcoholic consumption, 1 with high ALAT before treatment). Grade 1-2 reversible dysesthesias were experienced by 3 pt (7 cy) and grade 3 reversible dysesthesias in 1 pt (1 cy).
3/14 patients were not eligible for response, 1/14 is too early. No major or complete response was observed. We found only 1 pt with durable stable disease (18 months), 2 others had a short duration stabilisation (15 weeks, 18 weeks).
In conclusion, major antitumoral activity in malignant astrocytomas has not been observed in the current preliminary evaluation of L-OHP, given at the present dose schedule. The absence of major side effects suggests that there is still the possibility of L-OHP dose intensification.

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LATE SEQUELAE FOLLOWING TREATMENT OF CHILDHOOD BRAIN TUMORS

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The aim of this study was to assess objectively the quality of life of patients treated for childhood brain tumors and to determine risk factors for development late sequelae. The study included 70 long-term survivors being disease free 2.2-12,5 years. Me=5,5 years (seller and parasellar tumors excluded. The median age at evaluation was 14.6 years and the time of diagnosis 9.2 years. All patients received cranial irradiation (CR), 39 also received spinal irradiation (CSR) and 42 chemotherapy (Oncovin, CCNU). Moderate or severe functional deficits were present in 13 patients (19.5%), more commonly among those treated before II years of age. The other 57 patients (81.5%) had no or mild defisits compatibile with active life. Twenty percent of patients was found to have short stature and 27% had retardation in sittingheight after radiotherapy. There was statistically significant difference between group with CR and CSR). Growth hormone deficiency (GHD) was detected in 60% of patients, but all of them had no short stature. Also 30% of children whith growth impairment had no GHD. Statistically, spinal irradiation had prominent effect on growth and the younger the child is when given irradiation the greater the subsequent sceletal disproportion. The GHD had no clear relationsheep to the age of the child at the time of treatment, but risk for GHD was significatly higher in patients receiving cranial doses > 30 Gy. Thyroid dysfunction was found in 22.85% of total group and prymary hypothyroidism was evident in 12 of 39 patients (30.76%) treated with CSR. All, but one had subelinical dysfunction. The effects of spinal doses > 35 Gy on development of primary hypothyroidism were statistically proved. Two second intracranial neoplasms were diagnosed (for an incidence of 2.8%).

Key words: childhood, brain tumor