1051

DIAGNOSTIC IMAGING IN THE FOLLOW-UP OF PATIENTS WITH BRAIN GLIOBLASTOMA (GBM) RECEIVING POSTOPERATIVE PRE-IRRADIATION CHEMOTHERAPY (CHT)

Gornish M* Loven D+ *Neuroradiology Section, +Oncology, Departments of Radiology and Beilinson Medical Center, Petah Tiqva, Israel

Serial brain CT scans performed monthly on 22 patients with GBM for evaluating pre-irradiation CHT were reviewed to detect pitfalls of interpretation. Our main observations are: (1) First postoperative studies, aimed at disclosing residual tumor, should be performed using iodinated I.V. contrast injection within 7 days of surgery. (2) Uniformity in the I.V. contrast injection (of at least 30 gr iodine) and in the examination technique, is required to ensure comparable studies. (3) Persistent areas of contrast enhancement with an atypical appearance, even in the absence of mass effect, are suspicious for active tumor and should be considered for further diagnostic imaging studies, e.g. MRI with gadopentate injection. Representative cases will be presented to illustrate these conclusions.

1052

THERAPEUTICS USE OF MAB-LABELLED LIPOSOMES CARRIERS FOR RADIOISOTOPES AND DRUG IN BRAIN TUMORS.

G.P. ROMBI* , F.COSSU* , G.MELIS* AND V.ANEDDA§

* IST.RAD.UNIVERSITA' * MED.NUCLEARE U.S.L. 21
§ LAB.CENTRALE U.S.L. 21 - CAGLIARI - ITALY

General toxicity of drugs and radioisotopes in Cancer therapy is first due to a very low specificity of cell targeting. From several years the authors have been studying the ability of liposomes as selective carriers. After studying "in vitro" the different liposome size, the liposome composition and the methods to reach an high grade of selectivity, several "in vivo" approaches have been tested in order to evaluate the tumor cell targeting. The chosen carriers were SUV liposomes (0.05 mcm.), prepared by a dialytical removal of detergent (Sodium cholate), with the following composition: Cholesterol,DPC, Sulphatides and DPE-SPDP forming complex with DTT treated (Fab')2 anti Tenascine, CEA, Ca 19.9, CA 72.4 or CA 15.3 and, in some cases, iron compounds to achieve a local circulating carriers concentration and a plasmatic perfusion slowing down after exposition to a magnetic field. Seven patients, two affected by Medulloblastoma, one affected by Astrocitoma (III°), three affected by secondary brain localisation oflung cancer and one affected by brain localisation of breast cancer, have been perfused with a multifunctional mab-labelled liposomes suspension (Fab' 200 mcg/ml with 8:1 mab-liposomes ratio). Liposomes contained 131-I (50 mCi) or antiblastic drugs (5-FU 500 mg, BCNU 200 mg, Cis-Pt 50 mg, ADM 40 mg and Fe3O4 when submitted to a magnetic field in patients with metastatic localisations), moreover, when surgery was possible , target tissue liposomes concentration was evaluated by immunohystochemical and E.M. means. As scintigraphic results shown, a very large amount of liposomes reach the target cells, trespass the E.B.B. and Iron-charged carriers permit an enhanced permanence in the primary and metastatic localisations with a satisfactory concentration on the target areas. Clinical results show 4 C.R. and 3 P.R. after 8 cycles of treatment, repeated every week. Finally the authors think that this method is one of the most promising technique for selective carrying of radioisotopes, drugs and other non-specific substances for therapy of brain tumors.

1053

RADIOIMMUNOTHERAPY OF GLIOBLASTOMA BY DIRECT INTRATUMOUR ADMINISTRATION OF RADIOLABELLED MONOCLONAL ANTIBODIES.

P.Riva*, A.Arista+, C.Sturiale+, G.Franceschi*, A.Spinelli *, N.Riva*
*Nuclear Med. Dept.;+ Neurosurgery Dept. "M.Bufalini" Hospital Cesena ITALY

22 patients with recurrent glioblastoma (21 brain and 1 spinal cord) following the failure of surgery, radiotherapy and chemotherapy, underwent intratumour radioimmunotherapy . The BC-2 and BC-4 (SORIN-BIOMEDICA, Italy) monoclonal antibodies (MAbs) were employed. They are two murine IgG1 recognizing different epitopes on the molecule of tenascin (TN). This antigen is expressed in very large amount in the stroma of glioblastoma but not in normal brain ,so leading to a strong tumour targeting. The isotope utilized was I-131. The radiolabelled antibodies were injected directly in the tumour mass by means either of a removable catheter stereotaxically inserted into the lesion or of an indwelling catheter placed in the site of disease during the operation. The patients were admitted to the protocol provided previous immunohistochemistry study carried out on the fresh tumour specimen has demonstrated the presence of tenascin.In addition they underwent a quantitative immunoscintigraphy, by administering intratumorally a tracer dose in order to calculate the dosimetry data and forecast the effectivenes of RIT.For therapeutical applcations escalating doses were given ranging between mCi 15 (MBq 555) to 57 (2140). In many cases the RIT was repeated two (7 pt.), three (4pt.) or four (3 pt.) times in order to maximize tumor irradiation. Both the systemic and brain toxicity resulted absent while the HAMA production following the intralesional MAbs administration occurred only in few cases.The median survival of our group is,at present, 16 months. The objective response consisted of 4 CR (median duration 18 months) and 4 PR (median 11 months). So response rate was 36.3%. Conversely 7 SD (median 11 months) and 8 PD (median 4 months) were observed.

1054

SUPRATENTORIAL MALIGNANT GLIOMAS. LONG TERM RESULTS AFTER COMBINED TREATMENT.

Asensio C, Castillo I, Esquivias J, Massare E, García Puche JL, Pedraza V.
DEPARTMENT OF RADIATION ONCOLOGY. UNIVERSITY HOSPITAL. GRANADA. SPAIN.

The records of 191 patients with supratentorial malignant gliomas long followed after treatment were reviewed in order to insight on the biological behaviour of these tumors, define the patterns of relapse and survival at long term and separate prognostic subgroups. Patients were divided in three categories: ASTROCYTOMA/OLIGODENDROGLIOMA (A-O/28%), ANAPLASTIC ASTROCYTOMA (AAF/20%) and GLIOBLASTOMA MULTIFORME (GM/52%). Necrosis was the determinant distinctive factor between GM and AAF and mitotic numbers, nuclear atipia, cellular pleomorphism and endothelial proliferation were used for differentiating A/O from AAF. After subtotal or apparently radical surgery, moderate Dose/Volume for A/O patients and high Dose/Volume for AAF/GM patients were used as standard RT schedules. The minimum tumor dose at the enhanced CT areas was 50 Gy and "boosts" ranging from 5 to 15 Gy were given to different "clinical target volumes" in A/O, AAF and GM patients. The maximum isoeffect dose ($TD \times N^{-0.44} \times T^{-0.06}$) raised to 1061 neurets. Results obtained are the following: 1) Late relapses were observed only in A/O patients; 2) 82%/95% of relapses in AAF/GM patients were observed within 3 years after treatment; 3) probability of survival (life-table method) at 2, 5 and 10 years raised to 40%, 15% and 3% for A/O, AAF and GM patients, respectively; 4) radical surgery but not RT dose and volume improved the probability of survival in A/O patients; 5) a positive but not statistically significant effect on survival was demonstrated for RT dose and volume in AAF/GM patients; 6) Age turned out to be an important prognostic factor in all kind of patients. The above results let to think that higher doses can improve the survival in A/O patients and that the principle high Dose/Volume in AAF/GM patients needs to be revised.

1055

TUMOR EXPOSURE TO FOTEMUSTINE IN MALIGNANT GLIOMAS. THE HIGHER THE BETTER ?

M. FRENAY (1), P. BIRON (2), M. POISSON (3), B. GIROUX (4)
(1) Centre Antoine Lacassagne, NICE - (2) Centre Léon Bérard, LYON - (3) Hôpital Pitié Salpétrière, PARIS, - (4) I.R.I.Servier, COURBEVOIE, FRANCE

Two modalities of chemotherapy (C.T.) with Fotemustine (FT) were investigated in malignant gliomas (MG) in order to increase drug concentration at the tumor site and are compared to conventional intravenously CT. Either, **high dose (HD)** following by bone marrow rescue (BMR) or **intraarterial route (IA)** by carotid/vertebral arteries (a). Dose effect (DE) relationship was explored with adverse effects (AE) according to WHO criteria and activity assessed with the rate of partial response at CT Scan. HD : 26 evaluable pts with newly diagnosed glioblastoma (GM) in 15, anaplastic astrocytoma (AA) in 6 and other primary tumors (PT) in 5, received FT 500 to 1 000 mg/m² and BMR. 92,6 % and 96,3 % of grade 3-4 for leucopenia and thrombopenia respectively were observed (nadir 16 and 17 days). Hepatic toxicity was noted in 48 %. Other AE was epigastric pain at 800, 900 and 1 000 mg/m². Maximum tolerated dose (MTD) was 900 mg/m². Response rate (RR) at days 28 was 23 % and overall survival (OS) was 43 weeks. IA : 30 pts with GM in 22, AA in 6 and other PT in 2, received FT from 100 to 200 mg by carotid a. and 80 mg by vertebral a. every 6 wks using infraophtalmic modality. AE were loss of vision in 5 cases and encephalopathy in 2. MTD was 150 mg by carotid a.. No toxicity in the vertebral territory has been observed. RR in biopsed or partially removed tumors (26 / 30) was 36 % (10/26). Results (HD + IA) were compared with **conventionnal therapy** FT, 100 mg/m²/w, 3 wks in 63 pts with recurrent MG. RR was 22 % and OS 40 wks. Haematological toxicity was mild. **In conclusion**, HD seems have a comparable activity to the conventionnal therapy but associated with high levels of toxicities well controled by the BMR. IA seems to be more active compared with conventionnal therapy but ocular and cerebral toxicities are limiting factors to develop this modality excepted using other strategies of IA infusion (infraophtalmic route, low dose of FT) Conventionnal therapy with FT is active with a good tolerance and may be recommanded in outpatient basis.

1056

CARBOPLATIN AND VM26 DURING RADIOTHERAPY IN HIGH GRADE GLIOMAS.

Brandes A., Zampieri P., Rigon A., Amistà P., Scelzi E., Zorat P.L., Paccagnella A., Berti F., Padoan A., Rotilio A., Fiorentino M.V.; G.I.T.N.O, ULSS 21. PADOVA.

PATIENTS CHARACTERISTICS: from April 1991 21 pts were elegible for the study: 14 males and 7 females, median age 49 (23-70) median Karnofsky Performance Status (KPS) 70;8 anaplastic astrocytomas and 13 glioblastomas,

ELEGIBILITY: Karnofsky Status ≥50, histological diagnosis, age from 18 to 70.

STUDY DESIGN: patients (pts) received BCNU 150/m2 i.v. 9 days after surgery. Thirty days later, radiotherapy 1.8-2 Gy/ day for 5 days a week on limited fields is started up to 60 Gy with simultaneous chemotherapy with Carboplatin 200 mg/m2 on day 1-22-43 and VM26 50mg/m2 days 1-2-3-22-23-24-43-44-45. BCNU 150 mg/m2 is repeated for 2 cycles after 30 and 70 days from the end of the radio-chemotherapy course.

TOXICITY: (WHO): hematological G1: 5 pts, G2: 1 pt, G3: 1 pt, neurological: G3 in 1 pt. Dose reduction: BCNU given at 75%: 3 cycles (cys); at 50%: 3 cys; CBCDA at 75%: 6 cys, at 50%: 4 cys.

RESULTS: 21 pts completed chemo-radiation and 8 PR (38%) and 10 N.C.(47%) were obtained. Global MST was 59 wks: 55 wks for GB and 70 for AA. TTP was 37.4 wks: 55.8 for AA and 30 wks for GB ,respectively. At 18 months 60% of AA are alive and 23% of GB.

CONCLUSIONS: 1) early chemotherapy + concurrent chemoradiotherapy are feasible and well tolerated; 2) the response rate and stabilization rate are promising; 3) up to now only two patients have died.