were performed within 14 days, $p < 0.05$). Volume reduction was dependent of both initial volume and necrosis. Statistical modelling of these data after exclusion of lesions with short follow-up resulted in a group with a median initial volume of 5.3 ccm and a median maximum reduction of 3.1 ccm. Thus, each 3 Gy-fraction thus induces a volume reduction of 0.31 ccm. To make a lesion of 5.3 ccm (corresponds to a diameter of 2.15 cm) disappear on CT scans, an equivalent dose of 56 Gy in 2 Gy-fractions is needed.
Conclusions: Because permanent local control requires sterilisation of all clonogen tumor cells incl. those no longer visible on CT after macroscopic CR, even small lesions of just over 2 cm diameter should receive more than 28 fractions of 2 Gy. If 10×3 Gy is to be given together with a sensitising agent and the aim of inducing a CR, the agent must induce killing of the remaining $0.53-0.31 = 0.22$ cm of cells, which means increasing the effect of WBRT alone by 71%.

505 POSTER

Treatment of newly diagnosed high-grade glioma with concomitant and adjuvant temozolomide and radiotherapy – UK experience

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Background: In the UK the current management of high-grade gliomas is maximal surgical debulking followed by radiotherapy. It has been shown that the addition of temozolomide (TMZ) to radiotherapy significantly increases median survival (14.6 vs 12.1 months (Stupp et al, 2005 N Engl J Med 352 (10): 1036–8). Our centre has considerable experience with TMZ and has treated patients with a similar regimen. This study aims to confirm whether these results are replicated in practice in the UK.
Material and methods: We retrospectively reviewed 102 patients treated for high-grade gliomas with radiotherapy ± TMZ between 1998 and 2003. A search of our radiotherapy database and patient records was undertaken. Patients who were diagnosed with high-grade glioma and who did not receive radiotherapy or who only received a palliative dose were excluded from the study. Radiotherapy was administered to a dose of 60–65 Gy in 30–37 fractions over 6 weeks. TMZ was administered orally at a dose of 75 mg/m^2 daily for 6 weeks durig radiotherapy, followed by adjuvant TMZ for 6 cycles on days 1–5 of a 28-day cycle (150–200 mg/m^2/day).
Results: 102 patients (71 male, 31 female) with high grade gliomas were planned for treatment with radical radiotherapy (mean age = 52.6 years, range 21–72). 84 patients had glioblastoma multiforme (GBM), 18 had WHO grade III tumours. 53 patients underwent surgical debulking. 51 patients (50%) received concurrent TMZ and radiotherapy followed by adjuvant TMZ (median number of cycles = 3). 48 patients (47%) initially received radiotherapy alone but 10 of these received chemotherapy on disease progression. 3 patients died before treatment started. The choice of treatment options was partly historical (availability of TMZ) and partly the preference of the treating consultant. There were no identifiable patient factors influencing the decision for radiotherapy alone or combined treatment. Only 2 cases had grade III/IV haematological toxicity during concurrent treatment. Patients treated with concurrent TMZ and radiotherapy had a significantly better median survival by log-rank comparison of 12.5 months compared with 9 months for those treated with just radiotherapy ($p = 0.029$).
Conclusion: The addition of TMZ to the standard treatment of radiotherapy for high grade gliomas gives improved overall survival. This study shows that the published Phase III results can be replicated in everyday practice and that the regimen is both practical and effective.

506 POSTER

Shiga-like toxin inhibits cell viability and induce apoptosis in human glioma cells

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Tumour growth is due to an imbalance between cell proliferation and cell death. Increasing apoptosis (programmed cell death) is the most important mechanism for tumour cell death and tumour mass reduction during treatment with cytostatic drugs and irradiation. We therefore aimed at identifying mechanisms for induction of apoptosis by shiga-like toxin and to study its potential use for increasing the efficacy of tumour treatment. Shiga-like toxins have low adverse effects and are only cytotoxic to eukaryotic cells that express its cell surface receptor CD77. CD77 is over-expressed by several solid tumours such as breast carcinoma, ovarian carcinoma, and brain tumours.
We found that two glioma cell lines (U343 and SF767) that over-expressed CD77 also were sensitive for 0.001–5 ng/mL shiga-like toxin in a fluorometric cytotoxicity assay after 72 h incubation whereas other non-CD77-expressing cells were not. The cytotoxicity of the toxin was due to apoptosis as demonstrated by TUNEL staining after 48 h incubation using flow cytometry. 2 μmol/L of the CD77-receptor analogue PPMP (1-phenyl-2-hexadecanoyl-3-morpholino-1-propanol) eradicated CD77 expression after 3 and 6 days incubation and also completely inhibited shiga-like toxin cytotoxicity and apoptosis in both cell lines.
Our results suggest that shiga-like toxin may be used as a potent cytotoxic drug in the treatment of CD77-overexpressing tumours.

507 POSTER

A role of herpesviruses in brain tumor development?

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Background: Malignant gliomas are the most common primary brain tumors in humans and are generally rapidly fatal despite current therapies. Except for hereditary predisposition and high dose ionizing radiation, risk factors such as occupational, environmental or medical factors are controversially discussed. In addition, a role of viruses is suspected. Recently, Cobbs et al. (Cancer Res 2002, 62:3347–50) reported that of 27 gliomas tested, all expressed multiple gene products of HCMV in contrast to brain tissues from patients with meningioma, stroke, Alzheimer's and other brain diseases suggesting that HCMV might play an active role in glioma pathogenesis. Earlier sero-epidemiological case-control studies reported an inverse correlation of glioma cases with serum antibodies against varicella-zoster virus (VZV), Epstein-Barr virus (EBV) and herpes simplex virus (HSV). HCMV antibodies were slightly more frequently observed in glioma cases than in population controls (Wrensch et al., Am J Epidemiol 2001, 154: 161–5). The present study was conducted to evaluate the role of previous herpesvirus infections in brain tumor development by (i) assessing the prevalence of HCMV gene products and/or nucleic acids in primary brain tumor tissues and corresponding blood samples, and also (ii) analyzing the sero-prevalence of anti-HCMV, anti-VZV, anti-EBV and anti-HSV IgM and IgG antibodies in patients with primary brain tumors.
Material and methods: Of 95 patients with primary brain tumors (gliomas, meningiomas, acoustic neurinomas, and medulloblastomas) biopsies from tumor tissues and blood samples were analyzed by a variety of nested PCRs for the presence of HCMV DNA, and sections of tumor tissues were analyzed by immunohistochemistry to detect HCMV-specific proteins. Furthermore, patients' sera were tested by ELISA for IgG and IgM antibodies to HCMV, VZV, EBV, and HSV, and compared to published prevalences.
Results: HCMV DNA was not detected, neither in the brain tumor tissues nor in the corresponding blood samples. Similarly, immunohistochemistry did not reveal any HCMV-specific proteins. Patients' sera were all were negative for IgM antibodies against the herpesviruses. IgG seroprevalences did not differ from published reference data in the German population.
Conclusion: The present study could not confirm the hypothesis that HCMV or other herpesviruses may play a role in glioma pathogenesis.

508 POSTER

Dexamethasone inhibit anti-cancer agent/radiation-induced apoptosis in C6 glioma cells

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Background: Dexamethasone, a synthetic glucocorticoid, is reported to induce partial resistance to anticancer drugs in glioma cells by transcriptional activation of Bcl-xL gene. In the present study, we investigated the upstream regulator of Bcl-xL gene which is activated by dexamethasone. And the effect of dexamethasone on radiation was also evaluated.
Methods and materials: For the induction of apoptosis in C6 glioma cells, 2 μM of camptothecin was added to the culture medium and up to 10 Gy of radiation irradiated onto cells. Western blot were performed to evaluate the effects of dexamethasone on Bcl-xL. Electrophoretic Mobility Shift Assay (EMSA) was conducted to assess DNA-binding activity of Stat5. To identify physical interaction between Stat5 and glucocorticoid receptor, Co-immunoprecipitation was performed. Cell viability was quantified by clonogenic assay and MTT assay. Apoptotic cell death was confirmed by a colorimetric caspase-3 assay with CaspACE™ (Promega), and DNA breakage by Cell death detection ELISA kit(Roche) or DAPI staining.
Results: Camptothecin alone increased caspase-3 activity up to 15.9 pmol pNA/μg/hour, in contrast to 3.5 pNA/μg/hour in untreated control cells. Increased caspase-3 activity by camptothecin was not seen in cells