Methods: The SRT program to treat pituitary adenomas was initiated in 1997. The clinical outcome of all patients treated with SRT up to 2007 were retrospectively reviewed (n = 83). Median age was 47 years (range: 14−73), with 46 males and 37 females. Twenty patients had functional and 63 had non-functional tumors. Median follow up was 42 months (range: 1−137). Two patients received SRT as their primary treatment, 38 received it postoperatively and 9 for raised hormones. Thirty-four patients received SRT for radiological progression despite prior surgery with median time to progression following surgery being 12 months (range 1−275). Before SRT, hormone replacement therapy was observed in 37% (thyroid), 35% (cortisol), and 30% (testosterone, males only). SRT dose was 50 Gy in 25 daily fractions using the GTC frame, and CT-MR fusion for planning (Radionics^{TM}). Arcs were used in 66 patients and stationary 4−6 non coplanar fields in 17. The GTV and sella contents were treated, with no expansion from CTV for PTV margin. The prescription guideline was > 95% coverage of the CTV by a minimum dose of 47.5 Gy, and maximum dose <52.5 Gy.
Results: The 3-year progression free survival rates for functional and non-functional adenomas were 94% and 92% respectively (p = 0.90). Four patients had progression (3 nonfunctional and 1 functional); among these, 2 had metastatic spread. One patient had salvage excision, 1 had radiosurgery, 1 patient required temozolamide for lepto-meningial disease and 1 required palliative radiation to treat lumbar bony metastases. Post SRT 43 patients (52%) had hypothyroidism, 35 (42%) required cortisol and 20 (24%) required testosterone. 1 patient had severe optic neuropathy. To date there were no second cancers.
Conclusion: Though with a relatively short follow up, this study suggests fractionated stereotactic radiotherapy with a narrow margin is safe and effective for the treatment of pituitary adenomas. The results compare favorably with historical outcomes achieved with conventional 2 or 3-field techniques.

8733 POSTER

Atypical meningioma: outcomes and prognostic factors

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Background: To retrospectively analyze and assess the outcomes and prognostic factors in atypical meningioma.
Methods and Materials: From April 1990 through April 2008, 45 patients with histologically confirmed atypical meningioma(WHO Grade ll) were treated with surgery and/or radiotherapy as a primary therapy at our institution. Of 45 evaluable patients, 21 patients were treated with surgery alone and 24 patients received surgery plus postoperative EBRT. Fifteen out of 21 patients who had a gross total resection(GTR) and nine out of 16 patients who had other than GTR received adjuvant EBRT. The median postoperative radiation dose was 61.2 Gy (range, 54−61.2 Gy). The median age at presentation was 52 years (range, 13−75 years) and the male:female ratio was 18:27.
Results: The 10-year cause-specific survival rate was 96.6% and 3- and 5-year progression-free survival(PFS) rates were 73.7% and 56.7%, with a median follow-up of 37.4 months (range, 6.1−217.8 months). Only one patient died from local failure and no one had distant failure. The 5-year PFS rates of patients treated with GTR only, GTR plus EBRT, other resection only, and other resection plus EBRT were 46.4%, 77.9%, 0% and 55.6%, respectively. Better PFS was significantly influenced by initial postoperative EBRT ($p = 0.025$), GTR ($p = 0.002$), male ($p = 0.033$) and Ki-67 <5% ($p = 0.002$) on univariate analysis. By multivariate analysis, postoperative EBRT, GTR, and male were associated with better outcomes.
Conclusions: In patients with atypical meningioma, postoperative radiotherapy improved progression-free survival, regardless of the extent of surgical resection. Besides adjuvant radiotherapy, GTR, male, and low Ki-67 proliferative index were independent predictors of the successful local control.

8734 POSTER

Oncolytic virotherapy of malignant glioma in an animal model using parvovirus H-1 (H-1PV)

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The current standard of care for malignant gliomas is surgical resection and radiotherapy followed by extended adjuvant treatment with the alkylating agent temozolomide. Regrettably, this standard treatment paradigm has only a modest effect on patient survival. Resistance to radiation and chemotherapy remains an obstacle to the treatment of brain tumours. We have demonstrated that rodent H-1 Parvovirus (H-1PV) wild type, replicating efficiently in glioma cells, may overcome the limitations of conventional therapies by its oncolytic activity. This hypothesis is supported by findings on the sensitivity to the killing effect of the virus. Normal (non-tumor) cells were found to be unsensitive to the oncolytic effect of H-1PV. In vivo, H-1PV was tested for its efficacy and safety in treatment of a rat glioma in an animal model. A single stereotactic intratumoural injection of wild-type H-1PV was sufficient for remission of intracranial gliomas (established from RG2 cells in Wistar rats) without any damage of normal brain tissue or other organs. Similarly, intravenous injection of H-1PV led to complete cure of the brain tumours with no side effects. Furthemore, tumors derived from human glioma cells in immunodeficient rats could also been shown to be sensitive to H-1PV. The contribution of immunological factors to the oncolytic activity of H-1PV is currently under investigation.
These results are the basis of a planned clinical trials on H-1PV virotherapy.

8735 POSTER

Selection of candidate genes involved in glioma pathogenesis using bioinformatics tools

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Human malignant gliomas are the most frequent form of brain tumours. They are commonly resistant to chemotherapeutic and radiotherapeutic treatments and their diffuse or infiltrative nature prevents surgical cure. The discovery during the last decade of molecular and epigenetic alterations have proven prognostically useful, but few advances have been made in the understanding of the complex mechanisms of tumour pathogenesis.
The present work deals with the selection of candidate genes potentially involved in the origin or progression of astrocytoma, the most frequent diffuse glioma. Our working hypothesis is that low and high grade astrocytoma should show differences in the expression of genes involved in biological functions that participate in tumour pathogenesis. In order to identify those functions, we used the bioinformatics tool “Gene Set Enrichment Analysis (GSEA)” to compare the following microarray experiments available in public databases: GSE4290, GSE3185, GSE1993, GSE2223 (from GEO database) and E-MEXP-597 (from ArrayExpress database). Results were obtained in terms of Gene Ontology (GO) categories (Biological process, Metabolic process and Cellular Component). Next, we selected the GSEA high scoring genes (“core enrichment”) associated to high grade (54 genes) and low grade (55 genes) tumours, in at least four of the experiments. Results were verified by the comparison of both gene lists using Fatigo+, a functional profiling method. In general, differentially expressed functions (GO hierarchy level 3) were (a) Biological process: “Cellular metabolic process”, “Macromolecule metabolic process” and “Primary metabolic process”; (b) Molecular functions: “Ion transporter activity”, “Nucleic acid binding” and “Hidrolase activity”; (c) Cellular component: “Membrane bound organelle”. We observed that specific high grade tumours share common functions with low grade tumours. This is consistent with the hypothesis that secondary tumours are generated by the evolution of low grade tumours, while primary tumours arise de novo.
Results of differential expression experiments using low and high grade tumour samples for two of the identified genes are presented.

8736 POSTER

Correlation between immunoreactivity of monocarboxylate transporter 1 in malignant glioma and tumor response to continuous intrathecal infusion of sodium butyrate

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Background: It has been suggested that the monocarboxylate transporter 1 (MCT1), which is part of the monocarboxylate transporter family, plays a major role in the uptake of butyrate. MCT1 in glial limiting membranes may play a role in equilibrating monocarboxylates between the brain cortex and the cerebrospinal fluid (CSF). Moreover, MCT1 immunoreactivity was strongest in high-grade glial neoplasma. However, sodium butyrate (NaB) is expected to be clinically useful because of its biological effects on cellular proliferation, differentiation, apoptosis and invasive metastasis. Therefore, NaB administered via the CSF enters the brain by abundant MCT1 in the glial limiting membrane, and then is distributed in the brain, where NaB is associated with MCT1 in the tumor itself. Thus, abundant MCT1 expression not only by tumor cells but also by the glial limiting membrane and ependym is supposed to facilitate a positive treatment effect of continuous intrathecal administration (CIA) of NaB for malignant glioma (MG).