Canine glioblastoma model

A study established normative data for a model exploiting dogs with naturally occurring glioma, which can be used to test novel therapies prior to translation to human trials. Further work will focus on the effects of different therapies, including chemotherapy, radiation therapy, and immunotherapy [1].

The need for a large animal tumor model in experimental neuro-oncology led Salcman et al. to re-evaluate and to modify the transplantable canine glioma of Wodinsky and Walker. Successive passages of the original tumor brei were made in purebred beagles, from beagle to mongrel, and between various mongrel strains until an intracerebral injection of 0.1 cc on Days, 1 to 3 of life produced a 93% incidence of tumor take in all breeds. The mean survival was 13.5 +/- 1.9 days after injection (range, 10 to 19 days) in 10 litters. The tumor was invariably fatal and possessed many of the histological characteristics of human glioblastoma (i.e., capillary proliferation, pseudopallisading, frequent mitotic figures, and multinucleated giant cells). The animals were large enough to be scanned on the Pfizer 450 scanner, and the tumors were visualized in vivo as typical “ring” lesions after the injection of the contrast agent. Intravital staining with Evans blue outlined the areas of contrast enhancement observed in the same tumors by computed tomography. The apparent defect in the blood-brain barrier could be explained in part by the absence of endothelial tight junctions on electron microscopy. Stability in the histology and activity of the tumor could be demonstrated after more than 14 months of storage at -70 degrees C. The transplantable canine glioma model has many advantages including low cost, reproducible morphology, a short survival time, and relative safety for the investigator. The large size of the animal preparation allows the use of complex surgical instrumentation and radiographic study, as well as a repeated sampling of cerebrospinal and other fluids [2].

The canine glioblastoma cell line J3T1 was subcutaneously injected into a 6-week-old female BALB/c nude mice to obtain tumour fragments. Tumour fragments were implanted into adult male mongrel dog brains through surgery. Multiparametric MRI was performed with conventional MRI, diffusion-weighted imaging, and dynamic susceptibility contrast-enhanced perfusion-weighted imaging at one week and two weeks after surgery in a total of 15 surgical success cases. The presence of tumour cells, the necrotic area fraction, and the microvessel density (MVD) of the tumour on the histologic specimen were assessed. Tumour volume, diffusion, and perfusion parameters were compared at each time point using Wilcoxon signed-rank tests, and the differences between tumour and normal parenchyma were compared using unpaired t-tests. Spearman correlation analysis was performed between the imaging and histologic parameters.

All animals showed a peripheral enhancing lesion on MRI and confirmed the presence of a tumour through histologic analysis (92.3%). The normalized perfusion values did not show significant decreases through at least 2 weeks after the surgery ($P > 0.05$). There was greater cerebral blood volume and flow in the Glioblastoma than in the normal-appearing white matter (1.46 ± 0.25 vs. 1.13 ± 0.16 and 1.30 ± 0.22 vs. 1.02 ± 0.14; $P < 0.001$ and $P < 0.001$, respectively). The MVD in the histologic specimens was correlated with the cerebral blood volume in the Glioblastoma tissue ($r = 0.850$, $P = 0.004$).

The results suggest that the canine Glioblastoma model showed perfusion imaging characteristics

similar to those of humans, and it might have the potential as a model to assess novel technical developments for glioblastoma treatment [3].

In 2016 a study showed that canine gliomas form a range of immunohistochemical patterns that are similar to those described for human gliomas. The in-vitro sphere assay was used to analyze the expansion and differentiation potential of glioma cells taken from the periphery and center of canine tumors. Samples from the subventricular zone (SVZ) and contralateral parenchyma were used as positive and negative controls, respectively. The expansion potential for all of these samples was low and cells from only three cultures were expanded for six passages. These three cultures were derived from high-grade gliomas and the cells had been cryopreserved. Most of the cells obtained from the center of the tumors formed spheres and were expanded, in contrast to samples taken from the periphery of the tumors. Spheres were also formed and expanded from two areas of apparently unaffected brain parenchyma. The neurogenic SVZ contralateral samples also contained progenitor proliferating cells, since all of them were expanded for three to five passages. Differentiation analysis showed that all cultured spheres were multipotential and able to differentiate towards both neurons and glial cells. Spontaneously arising canine gliomas might therefore constitute an animal model for further characterization of these tumours [4].

1)
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