Cerebrospinal Fluid Research

Poster presentation

A porcine model of hydrocephalus induced by gamma knife irradiation

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Background

The Leksell Gamma Knife® has been used for several decades as a relatively non-invasive, highly effective and precise therapeutic tool for brain disorders ranging from tumors to vascular malformations. It has a very benign side effect profile. To date many animal hydrocephalus models have been surgically or chemically invasive. Our exploratory model uses gamma knife to induce a lesion with the aim of increasing CSF outflow resistance at the cerebral aqueduct.

Materials and methods

A 3 month old female domestic pig (Sus domestica) was housed with an age- and sex-matched pig serving as a non-radiated control. Anesthesia was induced with tiletamine/zolazepam and xylazine and maintained with isoflurane. After securing a modified human stereotactic head frame to the pig, the coordinates of the cerebral aqueduct were determined by MRI. A single maximum dose of 200 Gy was delivered to the aqueductal lumen using the 4 mm collimators of a Leksell Gamma Knife® Model C. MRI studies with gadolinium were performed at 4, 8 and 12 weeks post-radiosurgery. At 12 weeks, the brains of both animals were extracted for gross and microscopic analysis.

Results

Marked enlargement of the third and lateral ventricles, most pronounced in the posterior horns of the lateral ventricles, was visible on imaging through 12 weeks (Evans ratio >0.3, FOHR >0.5). Lesional edema, visualized with fluid-attenuated inversion-recovery MRI (FLAIR), was maximal at 4 weeks and decreased through 12 weeks. Minimal contrast enhancement was visible at 4 and 8 weeks and resolved by 12 weeks. Subependymal FLAIR hyperintensity lining the lateral ventricles was present at 4 weeks. On dissection, the aqueductal lumen of the irradiated pig was smaller than the control's. The transverse and especially rostro-caudal dimensions of the lateral ventricles were noticeably greater. The only clinical abnormalities were gaze palsy consistent with the site of the edema, a compensatory head tilt and a slight gait disturbance. Weight gain, grooming and behavior were comparable to the control.

Conclusion

The striking ventriculomegaly, restricted lesion and benign clinical course indicate that our non-life threatening porcine hydrocephalus model is promising. The early periventricular FLAIR hyperintensity is consistent with increased resistance to CSF outflow. The minimal contrast enhancement indicates a temporary limited breakdown of the BBB. The persistent hydrocephalus at twelve weeks

despite the near resolution of the MRI abnormalities suggests potential for a long-term model with physiologic similarity to human late-onset aqueductal stenosis and applications in the development of therapeutic devices.

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