Extended Abstract

Journal of Biopolymers Research

2019

Vol.3 Issue.1

Clinical, Imaging and Pathological Characteristics of Brain Implanted Polylactic Co-Glycolic Acid Polymers Conjugated with Temozolomide

Jill Hicks, Simon Platt R, Shannon Holmes P, Elizabeth Howerth, Allison Haley, Jared Kaplan M and Edward Kaplan J

Ph.D., Department of Small Animal Medicine and Surgery, University of Georgia, USA

Abstract

Definitive treatments for primary brain tumours are still sought. Slow-release local chemotherapy may provide a good effect and poly (lactide-co-glycolide) (PLGA) micro cylinders could allow this. We evaluated the neurological and histopathological consequences, and MRI visibility, of PLGA micro cylinders conjugated with Temozolomide and gadolinium implanted in normal canine brains. Eight purpose-bred beagles had cerebral implantation of micro cylinders combined with Temozolomide and gadolinium. MRI was performed following implantation and 28d later prior to necropsy and brain histopathology. All adverse events were associated with implantation and resolved. Dogs with six micro cylinders at 0 and 6.25% gadolinium had mild inflammation and all other dogs had greater brain inflammation, which increased with higher gadolinium concentrations and micro cylinder number. Micro cylinders with gadolinium were identifiable on MRI. Brain implantation of PLGA micro cylinders conjugated with gadolinium and Temozolomide is tolerated in healthy beagles. The lowest gadolinium percentage and micro cylinder number should be used if this therapy is pursued

Keywords

Local chemotherapy; Primary brain tumor; Dog; Magnetic resonance imaging; Gadolinium

INTRODUCTION

Primary brain tumours occur more commonly in dogs than any other domestic species [1] and while their incidence is only reported to range from 14-20/100,000 to up to 3% of the canine population, [2,3] the e ̊ects of brain tumours on both dogs and their families are oien devastating. Meningiomas, the most common primary brain tumour of dogs [4,5] have shown good response to more extensive surgical resection [6-8] and both conventional and stereotactic radiation therapy [9,10]. Glial tumours arise from the neuroectoderm and most notably include low-grade astrocytomas, oligodendrogliomas, and glioblastoma multiforme, representing 17%, 13% and 3% of primary canine brain tumours respectively [5,11,12]. Here tumours have less definitive information regarding their treatment and appear to be less responsive to conventional therapies overall [13]. Glioblastoma multiforme (GBM) is the most common primary malignant brain tumour in humans, and is associated with a poor long-term prognosis despite multimodal therapy [14]. Temozolomide (TMZ) is an imidazotetrazine derivative of the alkylating agent dacarbazine and has become standard of care as part of the multimodal treatment for GBM in humans [15]. Temozolomide treatment led to an improvement in median survival time in human patients with GBM undergoing standard surgical resection/debulking with post-operative radiation therapy from 12 months to 15 months, and an increase in the two-year survival rate from 10% to 27% [15]. Here have been no studies evaluating the eٮcacy of TMZ in canine patients with GBM, though systemic administration has been demonstrated as being tolerated in dogs receiving oral Temozolomide at doses of 60-100 mg/m2 once daily for five days on a 28 day cycle, with gastrointestinal and hematologic e ̊ects most common [16,17]. In general, evaluation of chemotherapy for primary canine brain tumours is very limited; a recent study evaluating the use of lomustine (CCNU) for primary intracranial tumours in dogs revealed no survival benefit [2].

Results

All dogs successfully completed all aspects of the study. Neurologic abnormalities were not present in any dogs prior to micro cylinder implantation and there were no significant physical examination abnormalities prior to the study period. Dog 4 was neurologically normal and dogs 1-3 and 6-8 had an absent menace in the right eye as their only abnormality one day following implantation. Dog 5 experienced a noticeable surgical complication; his lei lateral ventricle was entered during the initial placement of the implantation needle as evidenced by cerebrospinal fluid exiting the needle prior to its adjustment. Implantation was completed aier redirection of the implantation needle, but this dog appeared behaviourally blind in both eyes with an absent menace OU as the neurologic exam abnormalities one day following surgery. Mild scleral hemorrhage was also present in Dog 5. Otherwise, the only notable physical examination abnormalities were associated with the surgical sites in all dogs, none of which experienced complications. Dogs 1-3 and 6-8 were neurologically normal by the day seven examination following implantation and dog 5 gradually regained neurologic function over the course of the study, first regaining a menace response OS and appearing neurologically normal by the day 28 post-implantation examination.

Conclusions

Our results indicate that it would be appropriate to evaluate the potential clinical eٮcacy of Temozolomide-and gadolinium-conjugated PLGA micro cylinders as an intratumoural chemotherapy option for the treatment of primary canine brain tumours, but that the lowest concentration of gadolinium that allows for post-implantation imaging and the lowest number of micro cylinders possible for tumour coverage should be used in clinical patients.

Email: jhicks@yahoo.co.us

This work is partly presented at Joint Event on International Conference on Polymer Waste-Biopolymers & Bioplastics, October23- 25, 2019 at Frankfurt, Germany