

Positive and Adverse Effects of Radiotherapy for Canine and Feline Brain Tumor

(イヌおよびネコの脳腫瘍に対する放射線治療の効果と副作用の検討)

学位論文の内容の要約

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令和元年 12 月

Cancer is the leading cause of death in cats and dogs, since companion animals are living longer by progress of veterinary medicine and improving rearing management. Treatment of canine and feline cancer usually involves surgery, chemotherapy and radiation therapy (RT) just like for human medicine. Recently, RT has been highly performed in veterinary medicine. Number of RT performed in Nippon veterinary and life science university teaching hospital was gradually increased (89 cases for 2010, 103 cases for 2012, 147 cases for 2013, 167cases for 2014 and 2015). RT is frequently performed for brain tumor. Therefore, the purpose of this study was to determine the therapeutic and/or adverse effects of RT against brain tumors.

The purpose of chapter 1 was to determine the therapeutic and/or adverse effects of RT against pituitary tumors in dogs with pituitary-dependent hypercortisolism, as monitored by frequent post-RT detailed MRI examinations, clinical signs, and changes in hormone concentrations. Nine dogs with an adreno- corticotropic hormone (ACTH)-secreting pituitary mass diagnosed by magnetic resonance imaging (MRI) underwent RT for 4 weeks (total of 48 Gy in 4 Gy fractions). Pituitary height/brain area (P/B) value, clinical signs, basal plasma ACTH concentrations, serum cortisol concentrations (pre- and post-ACTH stimulation test) and adverse effects of RT were evaluated before and post-RT.

The P/B value was significantly lower in all nine dogs post-RT. One dog lacking any neurological signs demonstrated no change in clinical signs pre and post-RT. Out of 8 dogs which exhibited neurological signs pre- RT, half of them demonstrated complete resolution of their signs, whereas the other half showed transient resolution. In all animals with recurrence of neurological signs, pituitary tumor regrowth was not observed; however, MRI revealed moderate to severe pituitary hemorrhage. Late adverse effect (bilateral otitis media) was observed in three of nine dogs post-RT. RT did not induce any significant changes in the dogs' basal plasma ACTH concentration and pre- and post-ACTH serum cortisol concentrations.

In conclusion, RT is effective to reduce pituitary size and the mass effect, but does not appear to affect blood hormone concentrations, necessitating additional medical treatment against hypercortisolism. Periodic MRI imaging post-RT enables early detection of adverse effects of RT.

The purpose of chapter 2 was determine the therapeutic and/or adverse effects of the combination therapy of RT and hydroxyurea against meningioma in dogs, as monitored by frequent post-RT detailed MRI examinations, clinical signs, and tumor size. Seven dogs of eight dogs with a meningioma diagnosed by MRI underwent RT for 4 weeks (total of 48 Gy in 4 Gy fractions). One dog of eight dogs with a meningioma diagnosed by MRI underwent RT for 6 weeks (total of 36 Gy in 6 Gy fractions). To examine the therapeutic and adverse effects of the combination therapy of RT and hydroxyurea against meningioma in dogs, MRI examinations and clinical signs were evaluated before and post-RT.

One of 4 dogs which exhibited neurological signs pre- RT, demonstrated complete resolution of her signs, whereas the other three dogs showed transient resolution. In three dogs with recurrence of neurological signs, a tumor regrowth, hemorrhage and spinal cord metastasis were observed by MRI examination. Three of 4 dogs which did not exhibit neurological signs pre- RT, showed neurological signs after RT and tumor hemorrhage was detected in two of three dogs by MRI examination . Remained one dog did not show changes in clinical sign before and after-RT.

Duration of survival day was over 500 days , and the mean survaival day was about 900 days.

In conclusion, the combination therapy of RT and hydroxyurea is effective for meningioma in dogs, since duration of survival is prolonged. However, recurrence of neurologic signs were observed related to tumor hemorrhage.

In chapter 3, a 12-year-old, castrated male cat with diabetes mellitus was diagnosed with acromegaly and examined with magnetic resonance imaging (enlarged pituitary gland, 8 mm); serum hormone concentrations were measured. After the first course of radiation therapy (4Gy, 12 fractions), insulin

administration was not required from day 420 after diagnosis. Enlarged pituitary tumor (8 mm) recurred, and insulin dosage amount of the cat was increased on day 1,065. The second course of radiation therapy (6 Gy, 4 fractions) was performed on day 1,201 and insulin administration was again discontinued. However, the cat died from lymphoma on day 1,397. Postmortem examination revealed pituitary adenoma. Most tumor cells were positive for chromogranin A, synaptophysin, and growth hormone immunohistochemistry. The pancreatic islet cells revealed diffuse hyperplasia. We achieved long-term successful management of an acromegalic cat with two courses of RT. However, a protocol for a second course of RT for feline recurrent pituitary tumor should be further discussed.

This study examined the therapeutic and adverse effects of RT against several brain tumors in dog and cat. Furthermore, periodic MRI imaging and physiological examination post-RT enables early detection of adverse effects and neurologic signs. RT against brain tumors in dog and cat is useful for extending duration of survival day and alleviating neurologic signs.