Long-Term Chemotherapy with Lomustine of Intracranial Meningioma Occurring in a Miniature Schnauzer

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ABSTRACT. A 14-year-old male miniature schnauzer was referred to us because it was circling to the right. A mass in the diencephalon was noted on brain magnetic resonance images. The dura was thickened with marked linear enhancement after contrast administration. Based on diagnostic image analysis, this lesion strongly suggested meningioma. The patient’s symptoms were well controlled by a combination therapy of prednisolone and lomustine (CCNU), and survived for thirteen months after diagnosis. This case was diagnosed as a meningioma based on histopathological findings. This report describes the clinical findings, imaging characteristics, and pathological features of a diencephalic and mesencephalic meningioma and long-term survival after lomustine and prednisolone therapy.

KEY WORDS: lomustine (CCNU), magnetic resonance imaging (MRI), meningioma.

NOTE

Primary brain tumors include neoplasms that arise from brain parenchymal tissue, cells comprising the outer and inner lining of the brain, and vascular elements. Intracranial neoplasia is well described in the dog, and the incidence of brain tumors in this species may approach 3.0%. It has been reported that primary central nervous system tumors arising from mesodermal origin (meningioma) are the most common intracranial tumors in dogs, followed by neuroectodermal (glial) tumors (e.g., astrocytoma and oligodendroglioma) [2, 9, 12].

Diagnosis of specific tumor types from magnetic resonance imaging (MRI) characteristics is sometimes difficult in both people and animals, and a definitive diagnosis may depend upon incisional or excisional biopsies. Brain tumors exert their pathologic effects both by directly encroaching on and/or invading brain tissue and by such secondary effects as peritumoral edema, inflammation, obstructive hydrocephalus, and hemorrhaging. Treatment of dogs and cats with primary brain tumors can be divided conceptually into supportive and definitive therapy [2].

A 14-year-old male miniature schnauzer with body weight of 5.8 kg was presented to the Veterinary Medical Teaching Hospital of Konkuk University due to a 4-week history of circling to the right and anorexia. Intermittent circling was observed first, and clinical signs worsened progressively. Neurological examination revealed continuous clock-wise circling. Cranial nerve deficits included both bilaterally decreased menace response (MR) and pupillary light reflex (PLR). Based on the neurological examination, clinical signs were likely due to a structural brain lesion. The results of complete blood count (CBC) profiles were within the reference range. Serum chemistry profiles showed increased alkaline phosphatase (581 U/L; reference range: 0 to 142 U/L) and alanine aminotransferase (82 U/L; reference range: 13 to 53 U/L).

Thus, we performed a brain MR scan (E-scan; ESAOTE, Italy) using 0.2T unit. T1- and T2-weighted images and postcontrast T1-weighted images were obtained. MR scanning confirmed a mass in diencephalon and mesencephalon that was isointense on the T1-weighted images and hyperintense on T2-weighted images (Fig. 1 and Fig. 3). This lesion was enhanced after intravenous administration of gadolinium-diethylenetriamine pentaacetic acid (Omniscan; Nycomed, Inc., Princeton, NJ) (0.1 mmol/kg body weight, intravenously [IV]), and the dura was thickened with marked linear enhancement to the same degree as the tumor (Fig. 2 and Fig. 4). The width of the mass was 16.5 mm, and its length was 14.8 mm.

Before CSF collection, we used 15% mannitol (1 g/kg CRI for 30 min; Daehan Pharm Co., Ltd., Korea) to decrease intracranial pressure and collected cerebrospinal fluid (CSF) from the cerebellomedullary cistern. The results of CSF analysis were normal. To rule out canine distemper virus infection and toxoplasmosis, canine distemper virus antigen (RT-PCR) and toxoplasma IgG/IgM (Neodin Vetlab, Seoul, Korea) were tested, and all results were negative for the CSF. In addition, bacterial and fungal cultures were performed on the CSF, and the results were all negative.

Two weeks after prednisolone (Prednisolone; Korea Pharma Co., Ltd., Korea) (1 mg/kg body weight, per os [PO] q 12 hr) administration, circling and cranial nerve deficits disappeared. However, three months later, clinical signs relapsed and worsened. Lomustine (Lomustine; medac GmbH, Hamburg, Germany) (CCNU; 60 mg/m², PO, q 6 weeks) was then administered and clinical signs improved gradually.
Three weeks after administration of lomustine, severe myelosuppression was noted on CBC profiles (WBC: 0.96 × 10^3/μl; reference range: 6–17 × 10^3/μl; PCV: 25%; reference range: 37–55%; platelets: 170 × 10^3/μl; reference range: 200–900 × 10^3/μl). Recombinant human erythropoietin (Ricomon; choongwae Pharma Corporation, Korea) (50 IU/kg body weight, subcutaneously [SC], q 48 hr) and recombinant human granulocyte-stimulating factor (Leucokain; CJ Corp., Korea) (5 μg/kg body weight, SC, q 48 hr) were administered.

The patient’s symptoms were well-controlled for thirteen months by supportive therapy (prednisolone) and chemotherapy (lomustine). Ultimately, the patient was euthanized due to worsening neurologic dysfunction including tetraparesis and cranial nerve deficit. A necropsy was performed and a mass in diencephalons and mesencephalon was observed. Microscopically, this mass was composed of pleomorphic cells arranged into syncytia, sheets or streams or whorls, and these patterns were delineated by fine and thin intervening fibrous septae (Fig. 5).

Histopathological findings ultimately diagnosed the tumor as a syncytial type intracranial meningioma.

Brain tumors can affect any breed and either sex in dogs. However, middle-aged to older animals are more likely to develop brain tumors than younger (less than 5 years of age) animals. The median age of dogs diagnosed with a brain tumor is 9.45 years (range: 0.25–16 years) [9, 12]. The mean age of dogs with meningioma is 11.1 years, and for every one year increase in age, there is a 40% increased risk of meningioma [12].

The histories and presenting clinical signs of patients with tumors are variable and reflect the location, size, and secondary effects of the neoplasm. In dogs with meningioma, the most common presenting clinical sign of dysfunction is seizure, followed by mentation change, vestibular syndrome, and circling [9, 12]. With the exception of seizure activity, the onset of clinical signs of neurologic dysfunction is often insidious over weeks to months, especially with meningiomas. In one study [12], meningiomas were
LONG-TERM CHEMOTHERAPY OF INTRACRANIAL MENINGIOMA

86% less likely to be located within the diencephalons than other sites. However, meningioma occurred in the diencephalon and mesencephalon in this case. Thus, this lesion was not easy to access by surgical intervention. In addition, the client declined radiation therapy due to the expense of the treatment.

In general, brain tumors should be highly suspected in elderly dogs with progressive signs of brain dysfunction. However, definitive diagnosis of a brain tumor requires a tissue sample from the neoplasm, although a confident tentative diagnosis can often be attained by imaging the brain tumor. Before pursuing advanced imaging, however, a complete blood count and serum biochemistry panel should be conducted. Thoracic radiographs should also be obtained to help rule out the possibility of metastatic neoplasia. Recently, computed tomography (CT) and MRI have become commonly used for diagnosis of brain tumors. Specific types of brain tumors may vary in appearance using these imaging modalities. However, some typical features distinguish meningiomas from gliomas. According to reports described previously [2, 4, 11, 19], meningiomas tend to have a broad-based, extra-axial attachment, exhibit distinct tumor margins, and have contrast-enhanced signs (dural tail sign). These findings were also observed in this case.

Several reports [1, 4, 11, 19] describe the dural tail sign associated with meningiomas and occasionally with other lesions in veterinary medicine. Dural tail sign has been observed in 40–60% of meningiomas, and has occasionally been observed in other diseases.

In general, treatment of dogs and cats with primary brain tumors is composed of supportive and definitive therapy. Supportive therapy consists initially of an anti-inflammatory regimen of oral prednisolone, which can be increased or decreased depending on patient response. Prednisolone therapy is believed to exert its beneficial therapeutic effects by decreasing intracranial pressure as a result of relieving tumor associated edema and decreasing CSF production. Generally, the prognosis for brain tumor patients treated with supportive therapy alone is poor. Survival times for dogs with brain tumors that are treated only symptomatically with corticosteroids and/or anticonvulsants are poor, with the reported median survival time being 59 to 81 days from diagnosis [3]. Another study [5] reported a median of 0.2 months with no therapy or symptomatic therapy only.

Definitive therapy may consist of surgical removal, chemotherapy, radiation therapy, or a combination of two or more methods. The prognosis for treatment of canine meningioma is guarded. In recent reports of canine intracranial meningioma, the median post-operative survival time was 7 months [2, 5, 18]. Radiation therapy for canine meningioma as the sole therapy resulted in median survival times between 5 and 9 months, and dogs that underwent tumor resection followed by radiation therapy had a median survival time of 16.5 months (range: 3 to 58 months) [2, 5, 16, 18].

Surgical removal was not performed in this case due to the size and location of the mass. Furthermore, radiation therapy was not performed due to refusal of the client. Thus, chemotherapy was initiated. There are limited reports of chemotherapeutic attempts to treat meningiomas in dogs. Recently, hydroxyurea has been shown to be an effective chemotherapeutic agent against meningiomas [7]. However, we used lomustine chemotherapeutic agent due to lack of a definitive diagnosis for intracranial meningioma.

This patient with intracranial meningioma survived for 13 months with only a combination chemotherapy of CCNU and prednisolone.

In conclusion, this report describes the clinical findings, imaging characteristics, and pathologic features of a diencephalic and mesencephalic meningioma and long-term survival after lomustine plus prednisolone therapy.

REFERENCES

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