Imaging Findings of Primary Intracranial Histiocytic Sarcoma in a Dog

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NOTE. Internal Medicine

18F-fluorodeoxyglucose Positron Emission Tomography and Magnetic Resonance Imaging Findings of Primary Intracranial Histiocytic Sarcoma in a Dog

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(Received 25 March 2009/Accepted 21 June 2009)

ABSTRACT. A 10-year-old, neutered male, Maltese dog presented with a three week history of intention tremor, right hind limb rigidity, poor coordination, and occasional circling to the left. On magnetic resonance imaging (MRI) of the brain, a mass was identified in the right occipital lobe and cerebellum. Three weeks after the initial MRI scan, we performed an 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) of the brain. The FDG-PET demonstrated areas of hypermetabolism in the right occipital lobe, cerebellum, pons, and medulla oblongata. When the standardized uptake value was calculated, the hypermetabolic lesion was higher than the gray matter values. The anatomical location of the hypermetabolic lesion was more precisely identified by the PET-MRI fusion images. The dog was definitively diagnosed as a primary histiocytic sarcoma of the brain. This is the first report of PET findings of an intracranial histiocytic sarcoma in a dog.

KEY WORDS: canine, FDG-PET, intracranial histiocytic sarcoma, MRI.

Positron emission tomography (PET) and magnetic resonance imaging (MRI) are the most commonly used imaging tools in human medicine, based on the molecular and morphological imaging [6, 10]. In dogs, PET findings of the experimentally induced intracranial tumors have been reported, but there are no prior clinical reports on the PET features of spontaneous brain tumors [7, 13]. This case report firstly demonstrates the PET characteristics of an intracranial histiocytic sarcoma in a dog.

A 10-year-old, neutered male, Maltese dog presented with a three week history of intention tremor, right hind limb rigidity, poor coordination, and occasional circling to the left. There were no abnormal findings on physical examination. On neurological examination, the dog had mildly depressed mentation, right hind limb rigidity, and a head tilt to the left side. Postural reactions were delayed and spastic in the right limbs, and were most marked in the pelvic limbs. The cranial nerves and spinal reflexes were normal. Complete blood count and serum biochemistry profiles were within normal range.

Because a head tilt and hind limb rigidity, opposite to the side of the head tilt, were simultaneously observed, paradoxic vestibular syndrome, due to a unilateral lesion involving the vestibular portion of the cerebellum, was highly suspected. Thus, MRI of the brain was performed using a 0.2 Tesla unit (E-Scan, ESAOTE, Italy). Under general anesthesia with isoflurane, pre- and post contrast T1-weighted images (WI) (TR, 500 ms; TE, 26 ms) and T2-WI (TR, 3800 ms; TE, 90 ms) were acquired in the transverse, sagittal and dorsal planes. The mass was identified in the right occipital lobe and cerebellum. It was spherical and well defined with isointensity in T1-WI and isointensity centrally with a poorly defined, hyperintense rim around the mass in T2-WI (Fig. 1A and B). After intravenous administration of gadolinium-diethylenetriamine pentaacetic acid (Omniscan; Nycomed, Inc., Princeton, NJ) (0.1 mmol/kg body weight, IV), the mass lesion was moderately enhanced with a diameter of 15 mm (Fig. 1C). The right lateral ventricle was severely compressed by the mass (Fig. 1A-C). There were no specific abnormalities on the cerebrospinal fluid analysis.

Based on the clinical signs and MR findings, an intracranial tumor was strongly suspected. The dog was treated with 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU) (Lomustine, medac Gmbh, Hamburg, Germany) (60 mg/m², PO, q21d) and prednisolone (1 mg/kg, PO, q12h). For one week after the chemotherapy, the clinical signs were improved, however these symptoms gradually worsened over the following two weeks. Three weeks after the initial presentation, per the owner’s request, the dog was euthanized.

Because the PET features of spontaneous canine brain tumors have not been well known, just prior to the euthanasia, we performed an 18F-fluorodeoxyglucose (FDG)-PET of the brain, with the owner’s permission. The dog was fasted for 12 hr, to ensure a stable FDG uptake, and then...
injected with FDG (0.4 mCi/kg body weight). FDG was produced immediately before injection using the onsite cyclotron (Eclipse HP Cyclotron, CTI Molecular Imaging, TN, U.S.A.) at the Neuroscience Research Institute of Gachon University. The dog was placed on a heating pad and kept at 38°C for 1 hr in a quiet, radioprotective area; the scanning was performed at the MicroPET (Focus 120, Concorde Microsystems, TN, U.S.A.) under general anesthesia maintained with isoflurane. Metabolic imaging was performed with 1.18 mm (radial), 1.13 mm (tangential) and
1.45 mm full width at half maximum resolution at the imaging center. The scanning time was 1 hr. MicroPET images were reconstructed using the ordered subset expectation maximization algorithm with 10 iterations and a pixel size of 0.43 x 0.43 x 0.81 mm³. An objective assessment of the FDG uptake was performed by calculating standardized uptake value (SUV); this is defined as the ratio of activity in tissue divided by the decay-corrected activity injected into the patient and its weight [8]. The information from the MRI and PET were combined for MRI-PET fusion images, which were constructed by the registration procedure in the FMRIB software library (FSL 4.0, the Analysis Group, FMRIB, Oxford, UK). The hypermetabolic lesion, which had a SUV of more than 2.5, was only fused with the post contrast T1-WI to determine the exact anatomical location of the lesion.

The FDG-PET demonstrated a large area of hypermetabolism that is distributed through the right occipital lobe, cerebellum, pons, and medulla oblongata (Fig. 1D). This lesion was consistent with the abnormality identified in the conventional MRI; however, the diameter of the hypermetabolic lesion (22 mm) was larger than the enhanced lesion of T1-WI. In addition, brain stem lesions, which were not seen on the MRI, were observed. When the SUV was calculated, the hypermetabolic lesion was higher than the gray matter values (Fig. 1E). The anatomical location of the hypermetabolic lesion was more precisely identified by the PET-MRI fusion images (Fig. 1F).

At necropsy, a tan, 18 mm in diameter, nodular mass was located in the cerebellum with partial involvements of the right occipital lobe and dorsal portions of the pons and medulla oblongata (Fig. 2G). There were no gross lesions observed in other organs. Tissue specimens of the brain were fixed in 10% neutral-buffered formalin, embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin. Microscopically, the cerebellum had a poorly demarcated, infiltrating, highly-cellular mass composed of neoplastic round cells that were arranged in a solid cellular sheet. The tumor cells had round to reniform, vesicular nuclei and single or multiple prominent nucleoli. The cytoplasm was abundant and eosinophilic with distinct cytoplasm borders. Mitotic figures were common. Multinucleated cells were frequently noted (Fig. 2A). The meninges were diffusely infiltrated by similar tumor cells. Based on the morphological characteristics of the tumor cells, the differential diagnosis included astrocytoma and histiocytic sarcoma. The immunohistochemistry showed that the tumor cells were positive for CD18 and CD45 and were negative for glial fibrillary acidic protein (GFAP) (Fig. 2B). These results and the negative findings for other parts of the body were strongly suggested a primary histiocytic sarcoma of the brain.

Canine histiocytic sarcoma is rare; it has been reported to account for 2.8% of primary brain tumors in the clinical population [16]. Histiocytic sarcoma may present with either localized organ involvement or disseminated multiorgan involvement. The reported anatomical sites include lung, lymph node, liver, spleen, stomach, pancreas, mediastinum, skin, skeletal muscle, central nervous system (CNS), bone, and bone marrow [1]. Occasional involvement of the CNS has been described, but CNS involvement is considered to be unusual [5, 16, 18, 22].

The clinical course of histiocytic sarcoma has been reported to be rapid and uniformly fatal [15]. Chemotherapy has been largely unstudied; there are a few case reports of response to various chemotherapy drugs [14, 19, 20]. In previous study of CCNU, for the treatment of dogs with histiocytic sarcoma, the treatment with CCNU was reported to result in considerable improvement in approximately one half of the dogs with regard to gross disease [15]. In this case, the clinical signs were slightly improved for one week after the initial chemotherapy. However, the symptoms worsened over the following two weeks. Thus CCNU was not useful in this case.

MRI is the principal imaging modality used for staging and follow-up in veterinary patients with CNS tumors [16]. However the MR features of primary histiocytic sarcoma of the brain have not been well reported [17]. The MRI findings, in one dog with the disease, were a multilobulated margin with a distinct border, hypointense in T1-WI and hypointense in T2-WI [16]. In this case, isointensity in T1-WI and an isointense center with a poorly defined, hyperintense rim in T2-WI were identified by the MRI. Peritumor tissue often has increased water content due to vasogenic edema, which may be related to the high-intensity signal on the T2-WI. Following the intravenous injection of a contrast agent, the lesion was rapidly and uniformly enhanced in T1-WI. This finding demonstrates the high vascularity and loss of integrity of the blood-brain barrier in areas affected by the histiocytic sarcoma. The peripheral edema of a mass lesion and the pattern of homogenous enhancement are useful for the differentiation of intracranial tumors from a granuloma or abscess that present with a hyperintense signal in T2-WI.

PET has emerged as a significant molecular imaging technique in the field of nuclear medicine [9]. Numerous new radioactive labeled compounds, ligands and probes, have been developed for the application to PET [6]. Among them, FDG is primarily used in clinical PET studies, most frequently for cancer related clinical diagnosis and management [8]. FDG-PET imaging reflects the elevated glucose consumption by tumor cells, and is used clinically for initial staging, post treatment follow-up and detection of suspected recurrence of neoplasms [9].

In this case, the FDG-PET demonstrated enhanced tracer uptake in the right occipital lobe, cerebellum, pons, and medulla oblongata. The ipsilateral postural reaction deficits may have been related to secondary brainstem involvement by compression or invasion of the cerebellar lesion. The lesion size was larger than the enhanced lesion in T1-WI and the brain stem lesions were clearly noted. Generally, the altered metabolism, such as that seen with a malignancy, precedes changes in anatomic structure. Because metabolic changes are the focus of PET scanning, its sensitivity and
specificity for neoplasms are higher, in most applications, than are imaging techniques that focus on anatomic structures such as computed tomography (CT) and MRI [2]. In this case, PET was performed three weeks after the MR examination. Thus we cannot be certain whether the differences between the MRI and PET were due to metabolic changes preceding the anatomic changes or growth and expansion of the tumor.

Increased intratumor glucose consumption correlates with the tumor grade, cell density and biological aggressiveness. Generally in humans, low-grade tumors have metabolic activity similar to white matter and higher-grade tumors, similar to gray matter [10]. In this case, the SUV of the tumor mass was higher than it was for the gray matter. The malignancy was clearly identified on the histopathological examination. Thus metabolic evaluation with FDG-PET may be useful to assess grades of canine histiocytic sarcoma.

High FDG uptake is also seen in various human brain tumors, such as gliomas, primitive neuroectodermal tumors, medulloblastoma, and malignant lymphoma [9, 10]. Because FDG uptake levels have not been well evaluated in dogs, we could not compare the PET findings of this case with different types of canine brain tumors.

Although FDG is very effective for detecting and monitoring many types of tumors, FDG uptake is neither highly specific to dividing cells nor highly correlated with the growth rate of all tumors [7]. In addition, uptake may be increased in areas of granulomatous inflammation or in normal gray matter of the brain. Tumor cell proliferation has been identified with specific indicators such as fluorodeoxyglucose and 2'-fluoro-5-methyl-1-β-D-arabinofuranosyluracil, as well as FDG with human cancers [6, 7]. The use of these markers may be useful in veterinary medicine.

PET images rarely provide accurate anatomical information due to the limits of resolution of this imaging [7]. In human medicine, PET-CT fusion systems have been developed to complement the poor spatial resolution of PET; however, soft tissue contrast in CT is less than in MRI. Therefore, a PET-MRI fusion system has been developed [6]. In this case, off-line image fusion of PET and MRI was performed using a spatial registration algorithm; this approach helped identify the anatomical location of the PET lesion. In the future, the PET-MRI fusion system can be used for the diagnosis of cancer in animals.

Recently, PET has been increasingly used in veterinary medicine [2–4, 11, 12, 21]. There are, however, no prior clinical reports of the PET features of spontaneously occurring canine brain tumors; pilot studies used experimentally induced intracranial tumor models [7, 13]. This case report described the clinical findings, MRI and PET imaging characteristics and histopathological findings of a confirmed case of intracranial histiocytic sarcoma in a dog. We showed how PET imaging can be applied for the evaluation of a canine brain tumor. Further investigations are needed for conformation and the development of guidelines for the use of PET in veterinary medicine.

ACKNOWLEDGMENTS. This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government (MEST) (R11–2002–103) and Bio R&D program through the Korea Science and Engineering Foundation funded by the Ministry of Education, Science and Technology (M10530010001–06N3001–00110).

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