The magnetic resonance (MR) imaging features of central nervous system lymphoma in eight dogs and four cats are described. Intracranial lesions affected the rostrotentorial structures in six dogs and caudotentorial structures in two cats. Lesions affected the spinal cord in two dogs and in two cats, and appeared to have both intra- and extraparenchymal components in two dogs. All lesions were hyperintense in T2-weighted images when compared to white matter, most were hypointense in T1-weighted images (7/12), and most were hyperintense in fluid-attenuated inversion recovery (FLAIR) images (5/9). When compared to grey matter, these lesions appear either isointense (5/12) or hyperintense (7/12) on T2-weighted images, half of them were hypointense in T1-weighted images (6/12), and most were isointense in FLAIR images (7/9). Lesion margins were usually indistinct in T2-weighted images (10/12) and had perilesional hyperintensity in FLAIR images (7/9). The majority of lesions (10/12) had abnormal meninges around the lesion and half (6/12) had generalized contrast enhancement. Mass effect was evident in all lesions. Although not specific, when combined with the history and neurologic signs, MR features aid presumptive diagnosis that should be confirmed by cytology or histopathology.

Key words: cats, central nervous system lymphoma, dogs, magnetic resonance imaging.

Introduction

Diagnosis of CNS lymphoma is supported by the identification of lymphoblasts in cerebrospinal fluid (CSF).\(^1,\)\(^2\) Sensitivity of this test is low; lymphoblasts are identified in only about 30% of humans with CNS lymphoma,\(^3\) although there are no comparable animal data. Therefore, presumptive ante-mortem diagnosis of CNS lymphoma in humans is based on magnetic resonance (MR) imaging to identify specific morphologic features.\(^4,\)\(^5\) There are few descriptions of MR imaging findings in animals with CNS lymphoma,\(^2,\)\(^6-9\) hence it is unclear if similar criteria could be used in veterinary patients.

Here, we describe the MR imaging findings in dogs and cats with CNS lymphoma to identify features that might aid ante-mortem diagnosis of this condition. The data have implications for clinical management of dogs and cats with CNS mass lesions.
TABLE 1. MRI Features of Canine and Feline CNS Lymphoma (The Signal Intensities are Compared to White Matter/to Grey Matter)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Canine brain (n = 6)</th>
<th>Canine spinal cord (n = 2)</th>
<th>Feline brain (n = 2)</th>
<th>Feline spinal cord (n = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1-weighted Hypointense</td>
<td>3/4</td>
<td>1/1</td>
<td>1/1</td>
<td>2/0</td>
</tr>
<tr>
<td>T1-weighted Isointense</td>
<td>2/2</td>
<td>1/1</td>
<td>1/1</td>
<td>0/1</td>
</tr>
<tr>
<td>T1-weighted Hyperintense</td>
<td>1/0</td>
<td>0/0</td>
<td>0/0</td>
<td>0/1</td>
</tr>
<tr>
<td>T2-weighted Hypointense</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>T2-weighted Isointense</td>
<td>0/4</td>
<td>0/0</td>
<td>0/1</td>
<td>0/0</td>
</tr>
<tr>
<td>T2-weighted Hyperintense</td>
<td>6/2</td>
<td>2/2</td>
<td>2/1</td>
<td>2/2</td>
</tr>
<tr>
<td>FLAIR Hypointense</td>
<td>0/0</td>
<td>–</td>
<td>0/0</td>
<td>–</td>
</tr>
<tr>
<td>FLAIR Isointense</td>
<td>2/5</td>
<td>–</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>FLAIR Hyperintense</td>
<td>4/1</td>
<td>–</td>
<td>1/1</td>
<td>–</td>
</tr>
<tr>
<td>T1-weighted+Gd Homogenous</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>T1-weighted+Gd Heterogeneous</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Perilesional hyperintensity on FLAIR Present</td>
<td>6</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Perilesional hyperintensity on FLAIR Absent</td>
<td>0</td>
<td>–</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mass effect Mild</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Mass effect Moderate</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mass effect Marked</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Localization Intraparenchymal</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Localization Extraparenchymal</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Localization Intra-extraparenchymal</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diffuse meningeal contrast enhancement Present</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Diffuse meningeal contrast enhancement Absent</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Meninges around the main lesion Abnormal</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Meninges around the main lesion Normal</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

and the median duration of neurologic signs for multicentric CNS lymphoma was also 30 days (range 1–30 days). Diagnosis of CNS lymphoma was based on necropsy in five dogs and two cats, and identification of lymphoblasts in CSF in three dogs and two cats. One dog with lymphoblasts in CSF also had necropsy that confirmed the previous diagnosis.

MR images were obtained with a 0.4-Tesla permanent magnet (Hitachi Aperto, Hitachi Medical Corporation, Tokyo, Japan) or a 1.5 Tesla superconducting magnet (Gyroscan NT). Transverse MR images of the brain were acquired using T1-weighted and T2-weighted sequences, and T1-weighted sequences after intravenous administration of gadoterate meglumine (gadolinium; Dotarem). Sagittal T2-weighted images were also acquired routinely. Additional transverse fluid-attenuated inversion recovery (FLAIR) images and/or dorsal plane images were also made on a patient by patient basis.

MR images were reviewed by a board-certified veterinary radiologist (C.R.L.) with reference to lesion location, signal intensity compared to both the white matter and also grey matter, degree of enhancement following intravenous administration of gadolinium, appearance of lesion margins, presence of perilesional FLAIR hyperintensity, and degree of mass effect.

Results

Two dogs with primary CNS lymphoma had lesions localized to extraparenchymal structures. Multicentric CNS lymphoma in six dogs affected only extraparenchymal structures in two, intraparenchymal structures in two, and both intra- and extraparenchymal structures in two. Lesions in two dogs were confined to the spinal cord; both affected extraparenchymal structures and were margined indistinctly from the surrounding tissue. One was considered to be primary CNS lymphoma and one multicentric CNS lymphoma.

Two cats with primary CNS lymphoma and one with multicentric CNS lymphoma had extraparenchymal lesions, and one cat with primary CNS lymphoma had an intraparenchymal lesion. Both of the cats with spinal cord lesions were considered to be primary CNS lymphoma. As in dogs, the lesions affecting the spinal cord were indistinctively margined from the surrounding tissue.

The imaging findings are summarized in Table 1 (Figs. 1–4). All lesions were hyperintense in T2-weighted images when compared to white matter, most were hypointense in T1-weighted images (7/12), and most were hyperintense in FLAIR images (5/9). When compared to grey matter, these lesions appear either isointense (5/12) or hyperintense (7/12) on T2-weighted images, half of them were hypointense in T1-weighted images (6/12), and most were isointense in FLAIR images (7/9). Lesion margins were usually indistinct in T2-weighted images (10/12) and had perilesional hyperintensity in FLAIR images (7/9).
The majority of lesions (10/12) had abnormal meninges around the lesion and half (6/12) had generalized contrast enhancement. Mass effect was evident in all lesions.

All intracranial lesions in dogs were rostroventral. Single anatomic sites were affected in three dogs, affected only meninges in two, and the frontal lobe in one. In three dogs, multiple intracranial structures were affected (a combination of temporal lobe, hippocampus, thalamus, and meninges in one; hypothalamus and meninges in one; and frontal and occipital lobe in one). The margins of the lesions were indistinct on T2-weighted images in five dogs. In one dog, there was an extension of the lesion into the masticatory muscles and retropharyngeal lymphadenopathy.

Intracranial lesions in two cats affected caudal ventral, extraparenchymal structures. One of these was considered to be primary CNS lymphoma and the other multicentric CNS lymphoma. One was affecting mainly the meninges and the other was affecting the pons and mesencephalon, the latter one was considered to be primary CNS lymphoma. The cat with multicentric CNS lymphoma had the lesion that was marginated distinctly from the surrounding tissue. The same cat had also an extension of the lesion into the nasopharynx and retropharyngeal lymphadenopathy.

Discussion

CNS lymphoma is the most common tumor affecting the spinal cord and the second most common intracranial tumor in cats.\textsuperscript{10,11} In dogs, CNS lymphoma is the third most common secondary intracranial tumor and accounted for...
only 4% of all primary intracranial tumors.\textsuperscript{2,12} Despite the relatively high frequency of CNS lymphoma in necropsy studies, there are few published descriptions of MR imaging signs associated with CNS lymphoma. In the present series of eight canine and four feline patients, all lesions were hyperintense on T2-weighted images compared to white matter and when compared to white matter then all but one lesion were either isointense (5/12) or hyperintense (7/12) on T2-weighted images. All lesions had contrast enhancement on T1-weighted images, and the majority had perilesional hyperintensity in FLAIR images, and were localized to extraparenchymal structures. During the period of this study, more patients with CNS lymphoma may have been missed or not confirmed due to the lack of cytologic or histologic confirmation as previously reported in feline patients.\textsuperscript{7,13}

There was no apparent breed predisposition among the population of cats and dogs in this study, although Rottweilers have been reported to be overrepresented.\textsuperscript{12} The mean age of dogs with CNS lymphoma was reported to be 7.4 years\textsuperscript{2,12} and the median age of cats was 4.2 years.\textsuperscript{11} The median age of affected dogs and cats in the present study was similar to these values. In this study, males were more numerous than females (ratio 1.7:1), which is comparable to the male to female ratio in humans with CNS lymphoma, which is reported to be 1.2–1.7:1.\textsuperscript{14}

Lymphoma affected a wide range of structures within and adjacent to the CNS, as has been described previously.\textsuperscript{5} On the basis of MR images, a primary CNS lymphoma in one dog was described as intraparenchymal;\textsuperscript{2} others have been extraparenchymal and multicentric lymphomas.\textsuperscript{6,9,15} The MR features of CNS lymphoma were described in five cats with intracranial, extraparenchymal masses; however, it was not specified if these lesions represented primary CNS lymphoma or multicentric lymphoma.\textsuperscript{7} In the present study, the location and MR features of primary CNS lymphoma were similar to multicentric lymphoma. Two dogs and two cats with primary CNS lymphoma were considered to have lesions localized to extraparenchymal structures. In contrast, almost 100% of primary CNS lymphoma in humans affect intraparenchymal structures,\textsuperscript{16} although a rare form of primary CNS lymphoma called primary dural lymphoma is typically extraparenchymal.\textsuperscript{17}

A postmortem examination was performed in one dog and one cat with primary CNS lymphoma. The remaining patients with primary CNS lymphoma had a diagnostic work-up performed ante-mortem during which no other sites of lymphoma were detected; however, it is possible that these could have been classified incorrectly as primary CNS lymphoma, which would explain the extraparenchymal localization. Four dogs and one cat with multicentric lymphoma in the present study had extraparenchymal or combined intra- and extraparenchymal localization, which is comparable to humans, in whom the majority of metastatic lymphomas are extraparenchymal.\textsuperscript{16}

In the present study, all lesions were hyperintense in T2-weighted images compared to white matter, most were hypointense in T1-weighted images (7/12), and most were hyperintense in FLAIR images (5/9). When the lesions were compared to the grey matter then all but one lesion were isointense or hyperintense in T2-weighted images (6/12), and most were isointense in FLAIR images (7/9). Lesion margins were usually indistinct in T2-weighted images (10/12) and had perilesional hyperintensity in FLAIR images (7/9). The majority of lesions (10/12) had abnormal meninges around the lesion and half (6/12) had generalized contrast enhancement. Mass effect was evident in all lesions. Similar characteristic MR features were described recently in a dog with metastatic cutaneous lymphoma.\textsuperscript{9} In people, lesions of CNS lymphoma are iso/hypointense compared to white matter in T1-weighted images in 99% of patients and iso/hyperintense in T2-weighted images in 96% of patients.\textsuperscript{5} Similarly, in the present study most of the lesion were hypointense in T1-weighted images (7/12) and all of the lesions were hyperintense in T2-weighted images when compared to white matter. Contrast enhancement is a consistent feature of CNS lymphoma in people.\textsuperscript{4,5,16} Meningeal enhancement is a feature associated with CNS lymphoma.\textsuperscript{18} Focal meningeal contrast enhancement in people can occur in primary dural lymphoma,\textsuperscript{17} although
generalized meningeal contrast enhancement along cortical sulci or the surface of the spinal cord, which is a feature associated with leptomeningeal metastases of lymphoma, is more common. FLAIR imaging has been recommended to maximize sensitivity of MR for infiltrative intraparenchymal lesions although in the present series more lesions were evident in T2-weighted images than in FLAIR images.

Differential diagnosis of CNS lymphoma, includes noninfectious inflammatory conditions, infectious diseases, and other CNS tumors. With noninfectious inflammatory and infectious CNS diseases, MR lesions were usually multifocal, hyperintense on T2-weighted images, and did not enhance uniformly after gadolinium administration. Meningiomas can have a dural tail, but this is not pathognomonic for meningiomas. The CNS lymphomas in this study did not have peripheral contrast enhancement in T1-weighted images after gadolinium administration, indistinct margins, and perilesional hyperintense edema. Pituitary tumors usually have marked contrast enhancement and may contain cystic or hemorrhagic areas. Lymphoma lesions in this study had mass effect, produced perilesional edema and also enhanced after contrast medium administration, similar to pituitary tumors. None of them however originated from the sellar region and or had intratumoral cystic or hemorrhagic areas.

Intracranial histiocytic sarcomas do not have specific MR imaging features and can be localized either extraparenchymal. The extraparenchymal histiocytic sarcomas can be mistaken for meningiomas because of the localization and the presence of a dural tail, but can also have a diffuse pattern that can mimic diffuse tumors or inflammatory lesions. Contrast enhancement is variable in histiocytic sarcoma, and can vary from homogenous to heterogenous. CNS lymphomas can have similar MR imaging features to those of intracranial histiocytic sarcomas in dogs, hence this tumor is an important differential diagnosis.

Pituitary tumors arise always from the area of the sellar region. If these tumors are large, they affect surrounding brain tissue by direct compression and can produce perilesional edema. Pituitary tumors usually have marked contrast enhancement and may contain cystic or hemorrhagic areas.

CNS lymphoma lesions in the present study did not have peripheral contrast enhancement. Other metastatic CNS tumors can appear as single or multiple lesions of the meninges or brain parenchyma and may appear iso/hypointense on T1-weighted images and hyperintense on T2-weighted images. Metastatic tumors can be associated with brain parenchyma or meninges with associated edema and peripheral contrast enhancement. CNS lymphoma lesions in the present study did not have peripheral contrast enhancement. It is however, important to perform a thorough diagnostic work up to exclude tumors arising in other organs that could give rise to metastases with MR features similar to those of CNS lymphomas. Use of additional MR sequences, such as diffusion-weighted (DW) imaging and apparent diffusion coefficient (ADC) imaging, may also aid diagnosis. CNS lymphomas are highly cellular tumors in which water diffusion is often restricted, making them appear hyperintense in DW images and hypointense in ADC images.

CNS lymphoma should be considered in dogs and cats in which a mass affecting the CNS is hyperintense on T2-weighted images when compared to white matter or either isointense or hyperintense in T2-weighted images when compared to grey matter, with strong homogenous contrast enhancement in T1-weighted images after gadolinium administration, indistinct margins, and perilesional hyperintensity in FLAIR images. However, these MR features are suggestive of CNS lymphoma, are not diagnostic.
REFERENCES