**MRI ischemic and hemorrhagic lesions in arterial and venous territories characterize central nervous system intravascular lymphoma in dogs**

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**ABSTRACT**
Intravascular lymphoma (IVL) is characterized by the proliferation of large malignant lymphocytes within the lumen of blood vessels. This study aimed to describe the MRI features of confirmed central nervous system IVL in dogs and compare them with histopathological findings. For this retrospective, multi-center*,* descriptive case series, medical databases from seven veterinary centers were searched for cases of histologically confirmed IVL. Dogs were included if an MRI was performed. The MRI studies and histopathology samples were reviewed to compare the MRI changes with the histopathological findings. Twelve dogs met the inclusion criteria (12 brains and three spinal cords). Imaging of the brains revealed multifocal T2-weighted/FLAIR hyperintense and T1-weighted iso-hypointense lesions, with variable contrast enhancement; areas of abnormal diffusion both in arterial and venous territories in diffusion weighted imaging; and meningeal enhancement. On gradient echo images (GRE), the changes comprised tubular susceptibility artifacts, consistent with the “susceptibility vessel sign”, and additional variably sized/shaped intraparenchymal susceptibility artifacts. Spinal cord lesions presented as fusiform T2-weighted hyperintensities with scattered susceptibility artifacts on GRE and variable parenchymal and meningeal contrast enhancement. On histopathology, subarachnoid hemorrhages and neuroparenchymal areas of edema and necrosis, with or without hemorrhage, indicating ischemic and hemorrhagic infarctions, were found. These lesions were associated with severely dilated meningeal and parenchymal arteries and veins plugged by neoplastic lymphocytes and fibrin. Due to the unique angiocentric distribution of IVL, ischemic and hemorrhagic infarcts of variable chronicity affecting both the arterial and venous territories associated with thrombi formation can be detected on MRI.

**INTRODUCTION**
Intravascular lymphoma (IVL) is a rare form of extranodal lymphoma, characterized by predominantly intravascular proliferation of neoplastic lymphocytes, with little to no extension into adjacent parenchyma.1,2 Although a systemic disease, selective organ involvement has been recognized, with a predilection for the central nervous system (CNS).3 Small and medium-sized blood vessels are typically affected, while lymphatic vessels and large blood vessels are usually spared.2 The exclusively intravascular localization of IVL in humans is attributed to deficient extravasation of lymphoma cells, most probably due to a loss of the two adhesion molecules ICAM-1 (CD54) and beta-1 integrin (CD29).4 A similar pathogenic mechanism is only partially confirmed in dogs where neoplastic lymphocytes show marked expression of CD44, suggesting their predisposition to aggregate, but are only inconsistently expressing CD29, suggesting that CD29 might not be primarily involved in the pathogenesis of canine IVL.5 Despite the intravascular growth pattern of IVL, circulating neoplastic cells are generally not detected in the peripheral blood,2,6 except in cases with bone marrow involvement.1,7 Extravascular masses are uncommon in IVL.7 With progressive plugging of arterioles, venules, and capillaries of the CNS by malignant cells, vascular occlusion triggers thrombosis, ischemic damage, hemorrhage, and infarcts.
The clinical presentation of IVL in human patients is heterogeneous and depends on affected CNS areas. Presumptive antemortem diagnosis of CNS IVL relies heavily on magnetic resonance imaging (MRI), while the definitive diagnosis requires histological confirmation. In the last decades, multiple studies on the MRI features of human CNS IVL have been published, however, due to the rarity of the disease, the literature consist mainly of case reports and cumulative reviews.3,8-15 The most commonly reported human MRI findings are multiple brain parenchymal lesions consistent with ischemic infarcts. Nonspecific white matter lesions, T2-weighted (T2w) hyperintense lesions in the pons, meningeal enhancement, and rarely mass-like lesions and hemorrhage are other described features. No pathognomonic MRI findings have been identified, and, furthermore, neuroimaging may miss CNS involvement in up to 50% of patients with neurological symptoms.1,3,8,9,13
Only five case reports describing the MRI findings in dogs with CNS IVL have been published in the veterinary literature, and a few additional cases are included in other publications.5,16-22 Multifocal T1-weighted (T1w) iso- to hyperintense, T2w and T2w-fluid attenuated inversion recovery (FLAIR) hyperintense lesions, and variable parenchymal and meningeal enhancement are reported.5,16-19 Areas of signal void on gradient echo (GRE) images and abnormally restricted diffusion on diffusion-weighted imaging (DWI) are also described, displaying varying combinations of infarctive, hemorrhagic, and neoplastic features.18,20
This study aimed to provide a detailed description of the MRI features of histologically confirmed CNS IVL in a larger number of dogs, and compare them with the neuropathological findings to better characterize the origin of the MRI changes.

**MATERIALS AND METHODS**

SUBJECT DESCRIPTION AND SELECTION CRITERIA
This was amulti-center*,* retrospective, descriptive case series, conforming to the European legislation “on the protection of animals used for scientific purposes” (Directive 2010/63/EU). Medical record databases from seven Institutions (University of Tennessee, Texas A&M University, University of Liverpool, University of Glasgow, University of Montréal, Anicura Ospedale Veterinario “I Portoni Rossi”, and University of Bern) were searched for dogs with diagnosis of IVL, that were presented to the referral Institutions for investigation of neurological signs. Informed written consent for the diagnostic procedures was obtained from owners upon admission. Dogs were included if an MRI study of the brain or spinal cord was performed, and IVL was diagnosed with histopathological examination.

DATA RECORDING AND ANALYSIS

The signalment and medical information were recorded. Final decision for subject inclusion was made by three authors, two board-certified radiologists of the European College of Veterinary Diagnostic Imaging (ECVDI- CM) and American College of Veterinary Radiology (ACVR- SS), and a board-certified pathologist of the European College of Veterinary Pathology (ECVP- AO). The MRI studies and histology samples were reviewed by the same board-certified radiologists and pathologist, respectively. The same investigators compared the MRI lesions and the histology samples. All MRI examinations were assessed using a dedicated Digital Imaging and Communications in Medicine viewer program (OsiriX DICOM viewer, Pixmeo, Geneva Switzerland; workstation iMac 27-inch, macOs Catalina 10.15.7) .

*MRI*

A predefined list of MRI abnormalities was assessed and recorded in a standardized commercially available spreadsheet (Microsoft Excel 2020, Microsoft, Redmond, Wash). Images were reviewed individually, followed by consensus evaluation between the two radiologists. Features evaluated included: lesion number (focal/multifocal), neuroanatomic location and compartment, margination (poorly-/well-defined), signal intensity in T1w, T2w and T2w-FLAIR (compared to neighboring cortical or spinal gray matter, and according to the most dominant signal of the lesion), pattern of parenchymal contrast enhancement (presence/absence and homogeneous/heterogeneous), mass effect and signs of increased intracranial pressure, meningeal enhancement (presence/absence and affecting the leptomeninges or pachymeninges), presence of susceptibility artifacts, diffusion characteristics in DWI and apparent diffusion coefficient (ADC) map. In GRE imaging, two distinct patterns of susceptibility artifacts were recorded: parenchymal susceptibility artifacts and “susceptibility vessel sign” (SVS), indicating tubular areas of susceptibility artifacts corresponding to vascular thrombosis.

*Histopathology*
The diagnosis of IVL was based on prominent to occlusive growth of neoplastic lymphoid round cells in vascular lumina (veins, arteries, capillaries) of the subarachnoid space, neuroparenchyma and/or choroid plexi. For the purpose of the study, review of the neuropathology was performed on hematoxylin-eosin (H&E) stained sections, digitized H&E sections or digitized pictures of the lesions provided by the responsible pathologist. Original reports were viewed for additional information regarding multiorgan involvement, presence of extravascular masses, and immunohistochemistry results.

**RESULTS**
Over a 16-year-period (October 2005-November 2021), 12 dogs were identified. The represented breeds were Rottweiler (n = 2), mixed breed (n = 2), and one each of Cocker Spaniel, Labrador Retriever, Golden Retriever, German Shepherd Dog-Lurcher, Pointer, Portuguese Water Dog, Hound Dog, and Bernese Mountain Dog; there were six male (two intact and four castrated) and six female (three intact and three spayed) dogs, with a median age of 7.25 years (range 2.5 to 12 years). Individual information on animals’ signalment, presenting complaints, neurological examination, imaged area of the CNS, and MRI findings is provided in Supplement 1.
MRI studies were performed using high-field MRI scanners; specific characteristics of the MRI machines and contrast media are listed in Supplement 2.
Ten dogs had MRI of the brain (one dog had two examinations performed three months apart), one dog of the spinal cord, and one of both (a first examination of the spinal cord, and an additional study of the spinal cord and brain four months later), resulting in a total of 12 MRI studies of the brain and three of the spinal cord. Of the brain studies, one was an immediate postmortem study.

*Imaging findings- brain*
Brain lesions were intra-axial and predominantly multifocal (10/12) (Figure 1). Well- and poorly-defined lesions often coexisted. All lesions but one were T2w hyperintense; the remaining lesion showed mixed hyper- and hypointense signal. T1w iso-hypointensity was observed in all cases. Contrast enhancement was visible and heterogenous in 6/12 cases, absent in 5/12 cases, and unavailable for the postmortem study. Leptomeningeal enhancement was detected in 10 cases, varying from focal to diffuse. In three cases, it was associated with pachymeningeal enhancement, mainly along the cerebral falx. Neither mass effect nor signs of increased intracranial pressure were detected in 7/12 cases; 3/12 cases showed mass effect with compression of the ventricular system and/or midline shift; 2/12 cases showed transtentorial herniation. DWI was performed in five cases (b-values 800-1000); all had abnormal signal, with a different combination of hyperintense lesions in DWI and corresponding low values on the ADC map (n = 4); increased signal in DWI and normal values on the ADC map (n = 4); hypointense signal in DWI and high values on the ADC map (n = 1). One case showed all three types of lesions (Figure 2), while the others showed one (n = 2) or two (n = 2). Most of the lesions were confined to the vascular territories described for arterial infarcts. One case showed a large parasagittal lesion extending along the longitudinal fissure from the olfactory to the occipital lobes (Figure 3), not conforming to the typical arterial territories, with an approximately symmetric pattern, and a predominant hyperintense signal in DWI and low values on the ADC map. A similar pattern of T2w hyperintensity and T1w hypo-isointensity was detected in three other cases, two did not have any DWI, and one showed hyperintense DWI and normal values on the ADC map. GRE sequences were available in 11 cases. Intraparenchymal susceptibility artifacts were recorded in 10/11 cases (Figure 4). Multifocal punctuate and small lesions were more common (7/10), while a single small lesion was present in 2/10 cases. A single large hemorrhagic lesion was identified in the remaining case. The SVS was recognized in seven cases, varying from a few thin lesions to widespread susceptibility artifacts along many sulci (Figure 5). Leptomeningeal enhancement was striking at the location of the SVS. Susceptibility artifacts were also detected in the choroid plexi in 6 cases (one plexus n = 4; two plexi n = 1; all plexi n = 1) (Figure 6). One dog had a follow-up MRI that showed increased number and conspicuity of the SVS, progressive involvement of the choroid plexi and meninges, and a greater number and extension of the T2w hyperintensities.

*Imaging findings- spinal cord*
The three spinal cord studies showed multifocal interrupted poorly-defined T2w hyperintense, T1w iso-hypointense, heterogeneously enhancing intramedullary lesions (Figure 7). The affected spinal cord segment was swollen, with attenuation of the cerebrospinal fluid (CSF) signal in the myelographic sequence in all cases; meningeal enhancement was detected in one case. Lesions became more widespread in the dog that had a follow-up examination. One spinal cord case had a GRE sequence performed, and pinpoint areas of susceptibility artifacts in the cord parenchyma and central canal were identified.

*Necroscopy/histopathology*
The interval between the MRI examination and euthanasia/death was 0-32 days.
The diagnosis of IVL was achieved through complete necroscopy in nine dogs, where the disease was confirmed to be multiorganic; through neuropathologic examination of the CNS in two dogs; and through examination of a removed splenic mass in one dog. Three dogs had extravascular masses, two in the kidneys and one in the spleen. No dogs were reported to have leukemia. Comparison between the MRI features and neuropathology are reported in Table 1. Immunohistochemistry was performed in eight dogs; seven showed a T-cell immunophenotype and one was negative for B- and T-cell markers.

**DISCUSSION**

In this group of dogs with CNS IVL, multifocal, poorly and well-marginated, T2w and FLAIR hyperintense, T1w iso-hypointense lesions, with variable parenchymal and meningeal enhancement, were commonly detected in the brain and spinal cord. DWI of the brain identified ischemic lesions and infarcts at varying stages of evolution. Intraparenchymal hemorrhages and SVS in GRE contributed to this complex imaging pattern. The heterogenous imaging characteristics of CNS IVL are the consequence of concomitant ischemic, hemorrhagic and necrotic lesions of varying chronicity, that correspond to the diffuse and variable nature of vascular involvement, leading to consecutive occlusion of vessels.

No pathognomonic neuro-radiologic findings of IVL are recognized in humans, and false negative MRI results are reported in patients with neurological symptoms.1,3,8,9,13 In our cohort of dogs, only one case was initially reported to be within normal limits on MRI. After review of the histologically affected areas, subtle abnormal intensity of the cingulate gyri with mild meningeal enhancement was identified, indicating early ischemic damage. All the other dogs showed multiple lesions on MRI, reflecting a delay in presentation compared to human medicine due to the difficulty in detecting subtle neurological deficits in dogs.

Multifocal lesions dominated over focal ones, revealing the tendency of neoplastic cells to sequentially occlude multiple vessels. The progressive vascular occlusion was confirmed by the more widespread and confluent appearance of lesions in the two follow-up examinations. Focal lesions might represent an earlier stage of the disease.

T2w/FLAIR hyperintense lesions were found in the CNS of affected dogs, in agreement with previous reports.16-19 They corresponded histologically with edema, necrosis, malacia, and gliosis as sequelae of ischemia.

Cerebrovascular involvement of both arteries and veins was identified histologically in most dogs, and MRI features linked to the type of vessels predominantly affected. Some lesions showed hyperintense signal on DWI with corresponding low values on the ADC map, indicating restricted diffusion, typically associated with cytotoxic edema in acute ischemic infarcts. Other lesions had hyperintense DWI signal with normal values on the ADC map (“pseudonormalization”), corresponding to concomitant cytotoxic and vasogenic edema in subacute infarcts. Some lesions were hypointense in DWI with high values on the ADC map, revealing unrestricted diffusion associated with vasogenic edema and tissue cavitation in chronic infarcts.
Some ischemic lesions did not fit with the typical arterial territories, had heterogeneous restricted diffusion, and showed a marked extension, encompassing bilaterally and almost symmetrically the parasagittal gray matter along the longitudinal fissure. On histopathology, venous infarcts due to occlusion of the venous sinus with neoplastic cells and fibrin were confirmed. This type of lesion closely resembled that obtained in an experimental model of ligation of the dorsal sagittal sinus.23 MRI features of cerebral venous infarction have not been reported before in veterinary medicine.22 Guidelines in human medicine for diagnosing venous infarction include: infarction not conforming to a major arterial vascular territory, crossing the typical arterial boundaries, or extending over more than one arterial distribution; presence of multiple isolated lesions; involvement of subcortical regions with sparing of the cortex, or cortical-subcortical topography; often hemorrhagic component; proximity to a venous sinus.24-28 The retrograde venous pressure caused by thrombosis severely reduces the cerebral blood flow through a vicious cycle of increased intracranial pressure, blood-brain barrier disruption with edema and hemorrhage, and reduced CSF drainage, leading to neuroparenchymal ischemia and necrosis.23,26,29,30 The restricted diffusion in acute venous thrombosis suggests that cytotoxic edema is mainly responsible for the MRI changes, and that vasogenic edema follows but is not the primary pathological event.23,31 The unpaired anatomy of the dorsal sagittal sinus implies symmetry of the lesions, however asymmetric lesions topographically distant from the occlusion site are also reported in humans, reflecting variable collateral venous circulation.25,26,32 Human venous infarcts are typically localized in the parietal-occipital region and corpus callosum, areas rarely affected in arterial infarcts.27 Areas of overlapping venous and arterial territories can be found in the thalamus and basal nuclei. An unusual bilateral symmetric lesion in the thalamus was identified in one dog, associated with parasagittal lesions along the longitudinal fissure. Unfortunately, diagnosis of IVL was achieved from a splenic mass in this dog, and thrombosis of the internal cerebral vein as underlying etiopathogenesis can only be speculation.

Variably sized, from punctate to centimetric, intraparenchymal lesions with susceptibility artifacts were identified in GRE sequences, corresponding to the paramagnetic effect of heme products. Histologically, hemorrhagic transformation of ischemic infarcts, hemorrhagic component of venous infarcts, or pure intraparenchymal hemorrhage were observed.
Hemorrhagic transformation as a sequela of ischemic infarct is caused by reperfusion.21,33,34 Depending on the damage of the blood-brain barrier, this ranges from petechial hemorrhages to large parenchymal hematomas with mass effect.33,34 Venous infarction is more frequently accompanied by hemorrhage because of venous stasis and rupture of the blood-brain barrier.27,30,32 In such cases, blood is intermixed with edematous brain tissue. Intraparenchymal hemorrhage may also occur following vessel disruption, leading to a primary haematoma without an ischemic component.
Tubular areas of susceptibility artifacts deepening from the meningeal surface into the parenchyma following the sulci, and to a lesser extent present purely intraparenchymal, were recorded. These lesions were analogous to the SVS described in human cardioembolic ischemic stroke: the paramagnetic properties of the acute thrombus, similarly to those reported for intracerebral hemorrhages, are responsible for the signal loss encompassing the vessel lumen, and of its apparent enlargement due to blooming in GRE images.35-37 The human definition of SVS is limited to arterial thrombi, but in this study the term encompassed tumor thrombosis and stagnating blood in arteries, capillaries and veins. Subarachnoid hemorrhage was also diagnosed histologically, and probably contributed to some of the SVS identified on MRI. The likely etiopathogenetic mechanism is rupture of the subarachnoid veins due to hypertension, or inflammatory response to venous thrombosis causing increased vascular permeability and extravasation of blood into the subarachnoid space.SVS appearance depends on the age, size and type of thrombus.37 Since it is the erythrocyte content that causes the susceptibility artifact, it would seem reasonable that it should be more pronounced in case of red thrombi which are rich in fibrin and erythrocytes, formed in low-pressure venous systems as the result of activation of the coagulation cascade, compared to white thrombi, composed of platelet aggregates and formed in areas of high shear stress such as the arterial system. However, the artifact was identified in both vessel types. Fibrin thrombosis dominated histologically. The degree of blood stasis probably influences the thrombus composition, causing additional thrombosis with numerous enmeshed red blood cells independent of the original thrombus type. 37,38

Susceptibility artifacts in one or multiple choroid plexi were seen; histologically, the lumina of the choroid plexus vessels were plugged by neoplastic cells. The appearance differed from the recently reported MRI appearance of choroid plexus involvement in cases of secondary lymphoma, characterized by diffuse enlargement and multifocal nodularity.39

Parenchymal enhancement was variable and heterogeneous, likely reflecting a variable degree of blood-brain barrier disruption. Meningeal enhancement was common, and was related to infiltration of the meningeal vessels.

Mass effect and signs of increased intracranial pressure were not common features in the brain studies, likely reflecting the dispersed infiltration pattern of the neoplastic cells with negligible mass effect.
A peculiar feature of IVL is its intravascular growth, with neither extranodal/nodal masses nor leukemia. A minimal extravascular component of IVL has been occasionally described,1,4,40 which is consistent with the observation of lymphoma cells in the subarachnoid space in our case series. Extravascular involvement with single or multiple masses observed in the CNS or in other organs, mainly in the abdomen, are sometimes reported.7,8,13 No dog in our study had solid CNS masses, but three cases had abdominal masses.
The World Health Organization classifies human IVL as a specific subtype of diffuse large B-cell lymphoma, even if rare forms with T-cell or natural killer phenotype are described.4,6 In the present study, eight dogs had immunohistochemistry performed, and interestingly seven cases exhibited a T-cell immunophenotype, and one was negative for B- and T-cell markers, while no B-cell immunophenotype was recorded. In previous veterinary case reports, all three phenotypes have been described.5,7,16-18,40

Limitations of this study mainly reflect its retrospective and multi-institutional nature. Image acquisition protocols and equipment were not standardized, and some cases had limited MRI sequences, missing DWI and GRE sequences. A time interval of up to 32 days elapsed between the MRI and histopathologic examinations, possibly causing some mismatch in the lesion comparison. Some lesions identified on MRI could not be retrospectively confirmed in histopathology because only digitalized tissue slides were available, but not the original CNS tissue. Lastly, only a small number of confirmed cases were retrospectively found, despite the collection of data from seven Institutions.

Even if the MRI lesions cannot be considered pathognomonic, intravascular lymphoma should be suspected in cases of coexisting infarctive and hemorrhagic lesions, highlighting the importance of including DWI and GRE sequences.Relapsing vascular occlusion by neoplastic cells cause lesions of variable chronicity. Tumor thrombi in arteries and veins can be visualized as tubular susceptibility artifacts in GRE sequences, resembling the human SVS. Infarcts that are atypical in their location, extending beyond the boundaries of an arterial territory, should raise the suspicion for cerebral venous sinus thrombosis.

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**Category 1**

(a) Conception and Design: Mattei, Oevermann, Specchi

(b) Acquisition of Data: Mattei, Oevermann, Schweizer, Guevar, Maddox, Fleming, Ricci, Rosati, Biserni, Griffin, Rupp, Gutierrez-Quintana, Masseau, Newkirk, Hecht, Specchi

(c) Analysis and Interpretation of Data: Mattei, Oevermann, Specchi

**Category 2**

(a) Drafting the Article: Mattei, Specchi

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**Category 3**

(a) Final Approval of the Completed Article: Mattei, Oevermann, Schweizer, Guevar, Maddox, Fleming, Ricci, Rosati, Biserni, Griffin, Rupp, Gutierrez-Quintana, Masseau, Newkirk, Hecht, Specchi

**Category 4**

(a) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Mattei, Oevermann, Schweizer, Guevar, Maddox, Fleming, Ricci, Rosati, Biserni, Griffin, Rupp, Gutierrez-Quintana, Masseau, Newkirk, Hecht, Specchi

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TABLE 1 Comparison between the MRI features and neuropathology findings

|  |  |
| --- | --- |
| **MRI features**  | **Neuropathology** |
| T2w/FLAIR hyperintense, T1w iso-hypointense multifocal lesions | Areas of edema, necrosis, and gliosis  |
| Meningeal enhancement | Infiltration of arachnoid vessels and subarachnoid space by neoplastic cells |
| Abnormal DWI/ADC map signal in arterial and venous territories | Ischemic (arterial) and venous infarcts due to vascular occlusion with neoplastic cells and fibrin |
| Intraparenchymal lesions with susceptibility artifacts in GRE | Intraparenchymal hemorrhages in infarcted areas |
| Susceptibility vessel signs | Severe dilation of arteries and veins (parenchymal, meningeal) and occlusion with either neoplastic cells, fibrin or both; subarachnoid hemorrhage |
| Choroid plexus susceptibility artifact | Dilation of choroid plexus vessels and occlusion with neoplastic cells; hemorrhage and infiltration of neoplastic cells in the interstitium of the choroid plexus  |
| Parenchymal enhancement | Blood-brain barrier disruption and infiltration by neutrophils and macrophages secondary to necrosis |

**FIGURE LEGEND**

Figure 1: Transverse T2w (A), T1w (B, E), T1w/C (C, F), and T2w FLAIR (D) sequences of the brain of cases 10 (A-C) and 1 (D-F). (A-C) There are multifocal poorly-defined T2w hyperintense, T1w hypointense, heterogeneously enhancing lesions, and associated meningeal enhancement along the falx. (D-F) There is a focal T2w FLAIR hyperintense, T1w isointense left hippocampal lesion, with no contrast enhancement.

[A: TR = 5453 ms, TE = 105 ms, ST = 3.5 mm; B and C: TR = 930 ms, TE = 11 ms, ST = 3.5 mm; D: TR = 9000 ms, TE = 78 ms, inversion time = 2500 ms, ST = 4.5 mm; E and F: TR = 555 ms, TE = 12 ms, ST = 4.5 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness

Figure 2: Transverse T2w (A, E), DWI (B, F), exponential ADC map (C, G) (eADC, which removes the T2-shine through effect), and ADC map (D, H) of the brain of case 8 at the caudate nuclei (A-D) and occipital lobes (E-H).

(A-D) There is a parasagittal (asterisks) T2w hyperintense lesion, with hyperintense DWI signal, high values on the eADC map, and low values on the ADC map, indicating restricted diffusion (acute infarct). In the left thalamus (arrows) there is a focal T2w and DWI hyperintense lesion, with low values on the eADC map, and high values on the ADC map, indicative of unrestricted diffusion, suggestive of chronicity.

(E-H) There is a left occipital T2w and DWI hyperintense lesion. The dorsal part of the lesion (arrowheads) has normal values on the eADC and ADC maps, indicating ”pseudonormalization” (subacute infarct). The ventral part of the lesion (dashed arrows) has low values on the eADC map and high values on the ADC map, indicating chronicity.
[A and E: TR = 4416 ms, TE = 94 ms, ST = 4 mm; B and F: TR = 8500 ms, TE = 104 ms, ST = 4 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness

Figure 3: (A-B) Dorsal and sagittal T2w brain images of case 8 showing an extensive bilateral asymmetric hyperintensity along the entire longitudinal cerebral fissure.

(C-E) Transverse T2w, T2\*w and T1w FLAIR/C at the caudate nuclei, confirming the bilateral T2w hyperintensity (C), with susceptibility artifacts (D) and strong meningeal enhancement (E).
(F) Histopathologic examination of the same dog shows hemorrhagic infarction of the cingulate and marginal gyri (arrows). (G) Higher magnification of the boxed area in (F), showing marked distension of medium- and large-sized subarachnoid arteries and veins (largest artery and vein are labeled with A and V, respectively). (H) Distension and occlusion of a subarachnoid vein with neoplastic cells and fibrin (labeled N and F, respectively) from case 11.

[A: TR = 4250 ms, TE = 96 ms, ST = 3 mm; B: TR = 3400 ms, TE = 96 ms, ST = 4 mm; C: TR = 4416 ms, TE = 94 ms, ST = 4 mm; D: TR = 650 ms, TE = 20 ms, ST = 4 mm; E: TR = 2350 ms, TE = 25 ms, inversion time = 1013 ms, ST = 4 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness

Figure 4: Transverse T2\*w brain images (A-C) showing a large space-occupying (A-asterisk, case 7), a focal small (B- arrow, case 5), and multiple punctate (C- dashed arrows, case 6) lesions with susceptibility artifacts. On histopathology, intraparenchymal hemorrhage was found. In A there are also rounded and tubular lesions with susceptibility artifacts, representing microbleeds and SVS.

(D-F) Transverse DWI (D), ADC map (E), and Flow Sensitive Black Blood Imaging (F) brain images of case 9 showing an area of restricted diffusion, hyperintense in DWI with corresponding low values on the ADC map, indicative of acute ischemic infarct, associated with susceptibility artifacts, representing a hemorrhagic component.

[A: TR = 477 ms, TE = 12 ms, ST= 4 mm; B: TR = 708 ms, TE = 23 ms, ST = 4 mm; C: TR = 708 ms, TE = 23 ms, ST = 4 mm; D: TR = 4288 ms, TE = 94 ms, ST = 3 mm; F: TR = 44 ms, TE = 35 ms, ST = 1 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness

Figure 5: Transverse T2\*w (A, C), T1w/C (B), T1w FLAIR/C (D, F), and Blood Oxygenation Level Dependent (E) images of the brain of cases 10 (A, B), 6 (C, D) and 4 (E, F), displaying tubular areas of susceptibility artifacts (black arrows) along the sulci, representing the susceptibility vessel sign, with associated leptomeningeal enhancement (white arrows).
(G, H) Histopathology reveals severe dilation and occlusion of multiple subarachnoid arteries and veins due to intravascular presence of neoplastic cells and/or fibrin (case 11).

[A: TR = 806 ms, TE = 17 ms, ST = 3.5 mm; B: TR = 930 ms, TE = 11 ms, ST = 3.5 mm; C: TR = 708 ms, TE = 23 ms, ST = 4 mm; D: TR = 2021 ms, TE = 20 ms, inversion time = 750 ms, ST = 4 mm; E: TR = 28 ms, TE = 40 ms, ST = 1 mm; F: TR = 2378 ms, TE = 20 ms, inversion time = 750 ms, ST = 4 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness

Figure 6: Transverse T1w FLAIR/C (A, C) and Blood Oxygenation Level Dependent (B, D) brain images of case 4 showing enlargement (white arrows) and susceptibility artifacts (black arrows) of the choroid plexi of the right lateral (A, B) and 4th (C, D) ventricles.
(E, F) Histopathology of case 4 (E) and 9 (F) shows marked dilation of small- and medium-sized vessels due to presence of numerous neoplastic cells (VN) and distension of the choroid plexus interstitium (IN) due to infiltration with neoplastic cells, hemorrhage (H) and edema.

[A and C: TR = 2378 ms, TE = 20 ms, inversion time = 750 ms, ST = 4 mm; B and D: TR = 28 ms, TE = 40 ms, ST = 1 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness

Figure 7: Sagittal T2w images of the thoracic (A) and lumbar (D) spinal cord of case 11, demonstrating multifocal interrupted fusiform hyperintensities. In the transverse T2\*w sequence (B- reference line in A), speckled susceptibility artifacts are seen (arrows). Microscopically (C), susceptibility artifacts correspond to engorged vessels and hemorrhages, while T2w hyperintensities shown in A and D correspond to hemorrhagic myelomalacia. The transverse T1w/C (E- cranial reference line in D) and subtraction (F- caudal reference line in D) images show meningeal (dashed arrow) and patchy parenchymal (arrowhead) enhancement.

[A and D: TR = 2500 ms, TE = 100 ms, ST = 4.5 mm; B: TR = 989 ms, TE = 13 ms, ST = 4 mm; E and F: TR =532 ms, TE = 7.5 ms, ST = 4 mm]. Abbreviations: TR, Time of Repetition; TE: Time of Echo; ST, Slice Thickness