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Imaging Diagnosis – Magnetic Resonance Imaging Of Diffuse Leptomeningeal Oligodendrogliomatosis In A Dog With "Dural Tail Sign"

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Key words: leptomeningeal oligodendrogliomatosis, dural tail, dog

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Presented the poster in the ACVP (American College of Veterinary Pathologists) meeting in 2014 in Atlanta.

Abstract

A case of diffuse leptomeningeal oligodendrogliomatosis affecting the brain and spinal cord of a dog is presented. A 7.5 year old, male neutered Staffordshire bull terrier presented for evaluation of a chronic history of tetraparesis and seizures, with a multifocal neuroanatomical localization was determined. Extra-axial intradural lesions with an atypical presentation of a dural tail sign were seen on magnetic resonance imaging (MRI). Histologically, the lesions were consistent with a leptomeningeal oligodendrogliomatosis. To the authors' knowledge a dural tail sign has not previously

been reported as an MRI characteristic of diffuse leptomeningeal oligodendrogliomatosis in dogs.

Signalment, history and clinical findings:

A 7.5 year old, male neutered Staffordshire bull terrier presented for evaluation of tetraparesis. Tail paresis was detected 1 year prior to presentation but further investigation was not performed at the time. Nine months prior to presentation the patient began having seizures, which were treated with anticonvulsant therapy (Phenobarbital, 60mg PO BID). Six months prior to presentation the patient developed an abnormal thoracic limb gait. Over the following six months the signs progressed to dribbling urine, and occasional collapse in the pelvic limbs when walking. On presentation the dog was quiet but alert and responsive with an ambulatory tetraparesis and proprioceptive ataxia. Postural reactions were reduced in all four limbs but worse on the right side. Spinal reflexes were reduced in some limbs, with an absent withdrawal of the left thoracic limb and reduced flexion of the tarsus of the right pelvic limb. Perineal reflex and tail tone were reduced. Decreased menace response and positional ventral strabismus of the left eye was present. The neuroanatomic localization was determined to be multifocal based on these findings.

Imaging, diagnosis and outcome:

Magnetic resonance (MR) images of the brain and the spinal cord were acquired using a 1.5 Tesla magnet (Magnetom Essenza, Siemens, Camberley, United Kingdom) with head and spine coils. The protocol included T2-weighted (T2w) and T1-weighted (T1w)

turbo spin echo sequences, T2 –weighted FLAIR (T2-FLAIR), T2 *-weighted gradient recalled echo (GRE), and T1w images after manual intravenous administration of gadoterate meglumine (0.1 mmol/kg of gadopentetate dimeglumine, Magnevist; Bayer HealthCare Pharmaceuticals, United Kingdom). Post – contrast T1w images were obtained immediately after injection in sagittal, transverse and dorsal planes.

Within the calvarium, an irregular, predominantly left sided, parasagittal lesion was found extending along the skull base, around the pituitary gland and optic chiasm, and into the brainstem. In comparison to gray matter, the lesion was homogeneously hyperintense on T2w images, while on T2-FLAIR images it had mildly increased intensity. On T1w images the lesion was mildly hypointense to normal gray matter, and on post-contrast images it showed marked homogeneous enhancement. Post-contrast images revealed thickening of the adjacent meninges consistent with a “dural tail sign” extending caudal and lateral to the lesion (Fig. 1A & Fig. 1B). No evidence of susceptibility artifact on GRE images was detected. On T2w and GRE images in the region of the cerebral arterial circle well-defined, macroscopically normal, intralesional blood vessels could be appreciated. Extension of the lesion ventral to the rostral area of the brainstem (to the level of the colliculi) was present bilaterally, although this finding was more prominent on the left than on the right side at level of the foramen magnum. A large, fluid-filled, irregular cystic structure was visible dorsorostral to the cerebellum, causing caudal displacement of the lamina quadrigemina, marked compression and slight herniation of the cerebellum through the foramen magnum. Severe dilation of the ventricular system and of the olfactory recesses were also noted. There was a reduced amount of cerebrospinal fluid in the sulci, compression of the third ventricle and

compression/distortion of the interthalamic adhesion. Mentioned above findings are suggestive of increased intracranial pressure.

The intracranial lesion continued through the foramen magnum to merge with the lesion within the cervical vertebral canal. At the level of the second cervical vertebra (C2) the lesion had a thickened, solid appearance and then became cavitated cranially. This lesion extended continuously along the entire vertebral canal as an irregular intradural lesion ventral to the cord. At the level of L5-S1, the lesion could be seen invading nearly the entire height of the spinal canal and extending caudally, mainly along the ventral aspect of the vertebral canal. (Fig. 2). The spinal cord lesion was T2w hyperintense, T1w isointense and showed marked, fairly homogeneous contrast enhancement with similar intensity characteristics as the intracranial lesion. Throughout the length of the spinal cord, but most marked in the cranial cervical spine there was marked dilation of the central canal, consistent with syringohydromyelia.

The imaging diagnosis was an intradural - extramedullary diffuse infiltrative disease. Taking in consideration duration of the clinical signs, differential diagnoses included meningiomatosis, less likely lymphoma, carcinomatosis or histiocytic sarcoma. Infectious diseases was considered less likely as a differential diagnosis because patient did not have travel abroad history. The presence of an arachnoid diverticulum rostral to the cerebellum, hydrocephalus, and syringohydromyelia were also consistent with increased cerebrospinal fluid pressure. Due to the poor prognosis, the patient was

euthanized immediately after imaging. A cerebrospinal fluid (CSF) sample was not obtained.

On gross examination, a grey, gelatinous, extra-axial lesion was diffusely expanding the meningeal space along the entire spinal cord, causing severe compression. The process extended to the ventro-lateral aspect of the brain. No primary solid mass lesion was observed. Severe hydrocephalus was observed, together with secondary lesions including syringomyelia, rupture of the septum pellucidum, and bilateral diverticula. The latter extended into the striatal body beneath the internal capsule. No lesion was present in any other organ system.

Formalin – fixed brain sections and histology through the same level as on Fig 1B with "dural tail sign" are provided on Fig. 3A, 3B and 3C). On histological examination, the leptomeninges of the brain and spinal cord were diffusely and markedly enlarged by loosely arranged sheets of monomorphous neoplastic cells. These neoplastic cells had predominantly round nuclei with a finely stippled chromatin and small nucleoli, and they had either small to moderate eosinophilic eccentric cytoplasm or perinuclear optically empty halos which were reminiscent of a honeycomb pattern. The cells were embedded in pale amphophilic to basophilic matrix compartmentalized by thin cytoplasmic processes. In some areas, the neoplastic cells had more hyperchromatic nuclei. In other areas, the cell nuclei were more irregular and arranged in different patterns such as packets, palisades and rows. Cellular atypia was moderate. Mitotic index was up to 5 mitotic figures per 10 high power fields in the denser areas of the tumor. Multifocal

areas of cystic degeneration were present. (Fig.4A). No microvascular proliferation was observed. Neoplastic cells infiltrated occasionally and superficially within the brain and spinal cord parenchyma. No primary intra-axial lesion was found upon thorough analysis.

On immunohistochemistry, neoplastic cells showed strong nuclear immunoreactivity to Olig2 (Fig. 4B), and they were negative for the following markers: vimentin, cytokeratin, GFAP, synaptophysin, PGP 9.5, Periaxin, S100, and beta-tubulin. Few intermingled cells had clear cellular processes and were GFAP positive. These cells were thus interpreted as reactive astrocytes.

Based on the pathological and immunohistochemical findings, a diagnosis of primary diffuse leptomeningeal oligodendrogliomatosis of grade II was made according to the human 2007 World Health Organization (WHO) classification of central nervous system tumors.

Discussion:

To our knowledge we describe herein for the first time the dural tail sign as a MRI characteristic of diffuse leptomeningeal oligodendrogliomatosis in a dog. Diffuse leptomeningeal oligodendrogliomatosis is a rare neoplasm characterized by widespread invasion of the CSF-containing spaces by tumor without evidence of a primary intraparenchymal focus.[1-3] In people, diffuse leptomeningeal oligodendrogliomatosis is usually the result of extension of invasion of the leptomeninges or ventricle(s) by a

primary intraparenchymal oligodendroglioma, however some cases fail to have this parenchymal involvement and are thus classified as primary diffuse leptomeningeal oligodendrogliomatosis.[4] These are rare tumors in people.[5] This tumor type was first described in two veterinary cases, with one case described as diffuse leptomeningeal oligodendrogliomatosis, with identification of the primary, parenchymal oligodendroglioma and the second case as primary diffuse leptomeningeal oligodendrogliomatosis, with no evidence of a primary parenchymal tumor.[6] This report was followed by further two cases with MRI description of diffuse leptomeningeal involvement without intraparenchymal infiltration.[2] Adding to these previous reports of brain and spinal meningeal oligodendrogliomatosis we report a fifth case and focus on the first magnetic resonance imaging findings description of this pathology.

This case of diffuse leptomeningeal oligodendrogliomatosis differs in its imaging characteristics to previously reported cases in people as well as the two previously reported canine cases. The first difference is that this case displayed the presence of a dural tail sign on post-contrast T1W images. The presence of a dural tail sign has not been reported as a characteristic sign of this neoplasm in people.[5] In this case, post-contrast images revealed thickening of the meninges adjacent to the tumor, consistent with a dural tail sign, extended laterally and caudally to the mass within the brain. The terms dural tail sign, dural thickening, flare, and meningeal sign were first used in reference to meningiomas, and were used to describe thickening of the dura adjacent to the tumor in contrast enhanced T1-MRI imaging. [6] The dural tail of the mass described herein fulfills criteria for diagnosing the dural tail sign.[7,8] When the sign was first described in humans it was thought to be pathognomonic of meningioma and not to be

seen in any other intracranial or extra-cranial tumors.[9] However, it is now reported in a growing number of human tumors, other than meningioma, as well as infectious, autoimmune and vascular diseases. Tumors that have displayed a dural tail sign in human medicine include glioblastoma, acoustic schwannoma, carcinoma, hemangiopericytoma, pituitary adenoma, other sellar tumors.[10-16] So far in veterinary medicine masses such as meningioma, pituitary macroadenoma, histiocytic sarcoma, chromophobe adenocarcinoma, lymphoma granular cell tumors and CNS blastomycosis have been reported as demonstrating a dural tail sign.[17-24] Many possible causes for the dural tail sign have been hypothesized, such as expansion of the connective tissue and hypervascularity, and different opinions exist regarding the diagnostic and prognostic value of this imaging sign. Among these causes, expansion of connective tissue secondary to tumoral invasion is important in determining the therapeutic plan, particularly for planning surgical margins and radiation therapy planning. The area of the dural tail in our case histologically was characterized by infiltration with the neoplastic cells.

Another unique imaging characteristic of this case was the degree of contrast enhancement the tumor displayed. A linear relationship has been established between the degree of contrast enhancement and volume of peritumoral edema in human gliomas.[25, 26] This does not appear to be the case in our patient. The MR images of the lesion we present here had a homogeneous appearance on all sequences with no significant perilesional edema on FLAIR sequence, yet displayed marked, homogeneous contrast enhancements on post-contrast T1W images. Histopathological examination confirmed this lack of significant peritumoral edema. Presented herein was

a mass that had imaging characteristics of a diffuse extra-axial and intradural lesion with marked, homogeneous contrast uptake. Similar MRI post contrast characteristics have been described in glioblastomas in a dog and man. [27, 28] In the current veterinary literature reported gliomas have variable contrast enhancement ranging from none to variably isointense, nonuniform or ring-like enhancement, whereas in this case the mass had marked and homogeneous contrast uptake.[25, 26] Contrast enhancement is reported to be more common in high-grade tumors (III or IV) than in low-grade tumors (II), due to microvascular proliferation. [29] No microvascular proliferation was observed in examined histopathological sections to explain this contrast uptake, and it remains to be determined whether this is a characteristic of purely leptomeningeal oligodendrogliomas. [2] However, it has been described that uptake of gadolinium by extra-axial lesions is usually seen because they lack a blood-brain barrier [30] and because of their tendency to develop congestion and interstitial edema. [31]

Due to the extensive spread of the lesion along the vertebral column in this patient surgical resection was not an option. Leptomeningeal oligodendrogliomatosis is potentially treatable with chemotherapy and radiation. [32] The suitability of radiation therapy was not explored as the owners elected euthanasia.

In conclusion, diffuse leptomeningeal oligodendrogliomatosis should be included on differential lists for dogs with an extensive, extramedullary tumor, a dural tail sign, and other MRI characteristics described in this case.

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Figure Legends:

Fig. 1 A. Sagittal T1 – weighted postgadolinium. MR images revealed presence of thickening of the adjacent meninges “dural tail” sign extending caudad (arrow) to the lesion. Dilation of the central canal consistent with syringohydromyelia is seen (white star).

Fig. 1 B. Transverse T1 - weighted postgadolinium. MR images revealed presence of thickening of the adjacent meninges “dural tail” sign extending lateral (arrow heads) to the lesion. Syrinx within the cervical spinal column also seen.

Fig. 2. Sagittal T1 – weighted postgadolinium images of the spine. MR images showed the lesion extending along the entire vertebral canal as an irregular intradural lesion ventral to the cord (arrows).

Fig. 3 A. Formalin-fixed brain section at the thalamic level showing the extra-axial mass (see arrow). Severe secondary hydrocephalus is evident.
Fig. 3 B. The area of dural tail sign (arrow heads) was histologically characterized by infiltration by the neoplastic cells. An extra-axial mass is indicated by the arrow.
Fig. 3 C. The larger magnification shows the presence of the neoplastic cells within the subarachnoid space correlating with the dural tail sign on MRI.

Fig.4. Microphophotographs through the leptomeninges of the brain, correlating with the MR images of Fig. 1A and Fig. 1B. (A) HE x20. Sheets, packets, palisades and rows of neoplastic cells are embedded in an aboundant pale eosinophilic to amphophilic matrix. (B) Oligo2 staining x 20. Neoplastic cells show strong nuclear reactivity for Oligo2.