VALUE OF COMBINED CEREBELLOMEDULLARY CISTERN AND LUMBAR CEREBROSPINAL FLUID ANALYSIS FOR THE DIAGNOSIS OF STEROID RESPONSIVE MENINGITIS-ARTERITIS IN DOGS

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Steroid responsive meningitis-arteritis (SRMA) is a well-defined inflammatory central nervous system disease characterised by vasculitis of the meningeal arteries and non-suppurative inflammation of the leptomeninges. Typical diagnostic features include elevated total protein (TP) and total nucleated cell count (TNCC) on cerebrospinal fluid (CSF) analysis, most commonly associated with neutrophilic pleocytosis. CSF collection is commonly performed at two different sites, the cerebellomedullary cistern (CMC) or the caudal lumbar subarachnoid space (L). Collection from both sites is considered when diffuse or multifocal pathology is suspected or when one of the samples is contaminated.

The aim of this study was to investigate whether combined CSF analysis from both CMC and L sites could be useful in the diagnosis of SRMA.

Twenty-nine dogs with clinically suspected SRMA and no previous history of corticosteroid administration were included in the study. CSF samples were collected at presentation from both the CMC and L sites in all dogs. Twenty-eight dogs presented spinal pain and 25 were pyrexic on presentation. Median duration of clinical signs was 6 days (range 1-45).

Cerebellomedullary cistern CSF analysis revealed a median TNCC of 78 cells/µl and median TP of 0.52 g/l. Lumbar CSF analysis revealed a median TNCC of 53 cells/µl and median TP of 1.7 g/l. The median percentage of polymorphonuclear cells was 62% at the CMC site and 72.5% at the L site. In two dogs, the TNCC was normal in the CMC site and in three different dogs, the TNCC was normal in the L site. In the dogs with normal CSF results at one site, 1/5 dogs did not show signs of spinal pain on clinical examination and 1/5 was not pyrexic. Median duration of clinical signs in these dogs was 14 days but there was no significant association between duration of clinical signs and a normal CSF analysis ($p=0.171$).

Based on the results of the present study, we suggest that the analysis of both CMC and L-CSF can be useful in the diagnostic investigation of dogs with suspected SRMA, as in some cases, CSF analysis may be normal at one site but not at the other.

CONVERGENCE-RETRACTION NYSTAGMUS ASSOCIATED WITH DORSAL MIDBRAIN LESIONS IN THREE DOGS.

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Convergence-retraction nystagmus is an irregular, jerky nystagmus in which both eyeballs rhythmically converge and retract into the orbit, particularly on attempting an upward gaze. It results from simultaneous contraction of all of the extraocular muscles in response to efforts to change the direction of gaze. In humans it is seen as part of Parinaud's syndrome, also known as dorsal midbrain syndrome, in which a lesion of the medial longitudinal fasciculus in the dorsal midbrain prevents upward or downward movement of the eyes.

In this retrospective case series we report three dogs that presented with acute onset convergence-retraction nystagmus. Magnetic resonance imaging (MRI) revealed focal lesions within the dorsal midbrain of all three dogs. Given the acute onset of clinical signs and the consistent imaging characteristics, the lesions were suspected to be cerebrovascular accidents. All three dogs made a prompt and complete clinical recovery.

Convergence-retraction nystagmus appears to be a highly specific neurological sign localizing to the dorsal midbrain; recognizing convergence-retraction nystagmus therefore has clear diagnostic value. To the best of our knowledge convergence retraction nystagmus has not yet been described in the dog, and should be considered one of the forms of nystagmus that may occur in this species.

SPINAL GANGLION MALFORMATION IN THE DOG – IS ITSIGNIFICANT?

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Cadaveric dissection of the lumbosacral region of a cohort of dogs was undertaken to investigate the relative anatomy of the region. The aim of this study was to identify the optimal angle to align MRI images to assess the integrity of the L7 nerve roots. During this study a gross malformation of the L7 spinal ganglion was identified. This was associated with malformation of associated structures.

Similar malformations are reported with incidence of 0.3-14% in man (Neidre 1983, Kadish 1984, Artico 2006) and at 12% in a cadaveric study on dogs (Purinton 1982). There are no reports in the veterinary clinical literature.

Given the ongoing advancement in diagnostic imaging techniques to allow better assessment of the lumbosacral spine and the development of multimodal surgical treatment strategies to address compression within the intervertebral foramina at L7-S1, accurate identification of intervertebral foraminal compression is needed. Foraminal area on diagnostic images is known to vary dependent upon body position.

It has been proposed that dorsally oriented fat suppressed images can demonstrate swelling of the L7 nerve root to help identify nerve root impingement (Godde 2012 and personal communication). Using high field MRI (1-1.5T) 2mm slices are readily available giving very detailed images of the cauda equine nerve roots, whilst on low field MRI (0.2-0.35T) Appropriately aligned 3.5mm slices can demonstrate the anatomy of the nerve roots adequate to routinely demonstrate the spinal ganglia.

Coronal STIR images of the lumbosacral region of the cadaver presented if performed *in vivo* would have been predicted to demonstrate an abnormal unilateral swelling of the L7 nerve root.

In this study we present this unusual case to provoke discussion within the community of Veterinary Neurologists who are commonly called upon to interpret MRI images of dogs with suspected lumbosacral disease. We put forward two questions for discussion:

- Why are these malformations reported only in cadaver studies and not in clinical cases?
- How should we avoid misdiagnosing these in future clinical studies?

FELINE PANLEUKOPENIA VIRUS, A POSSIBLE ANTI-GLIOMA WEAPON, THREATENS INTACT NEURONS IN CATS.

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Despite improvements in surgical methods, advances in chemotherapy and radiotherapy, brain gliomas still carry a grim prognosis, and other treatment options are explored. Among which, oncolytic viruses use is promising. Parvoviruses intrinsically need the cell division machinery to complete their cycle and their major non-structural protein NS1 is cytotoxic. The rat parvovirus H-1 displays oncontropic and oncolytic properties on cultured human glioma cells and grafted glioma in rats, and is currently in phase I/IIa study for treatment of human patients with glioblastoma. Safety studies did not disclose adverse effect.

The closely related Feline Panleukopenia virus (FPV) is also able to infect and destroy subsets of rapidly dividing cells. Should the virus infect feline foetuses or newborns, the dividing neuroblasts of the cerebellar external granular layer would be destroyed leading to the “feline cerebellar hypoplasia”. However, in 1971, Sciza et al. also evidenced FPV proteins in some post mitotic, non-dividing Purkinje cells, and the loss of Purkinje cells can be dramatic. Recently, FPV proteins were found in the brain of cats affected by FPV-associated enteritis (Marigliani et al., 2016). Viral proteins were also present in neuronal cytoplasm raising the hope to catch the course of the process.

We retrospectively looked for FPV protein expression by immunohistochemistry in the brain of 11 kittens with FPV-associated cerebellar hypoplasia. In 4/11 kittens, FPV VP1/2 capsid proteins were expressed in cells, notably neurons and their cytoplasm, of the brain stem, thalamus, hippocampus and/ or cortex. Using double immunostainings, cyclin A, cdk2 (its associated cyclin-dependent kinase), and proliferating nuclear antigen could be evidenced in the nuclei of thalamic neurons, while cyclin D, a marker of the G1 cell cycle phase, and cdk4 (its associated cyclin dependent kinase) were consistently absent. Consequently, some post mitotic neurons not only allow translation of FPV proteins but also display three proteins characteristic of the S phase of the cell cycle, which are mandatory for the first step of the parvoviral cycle: the conversion of its single stranded DNA into a duplex form.

The adenovirus E1A$_{12S}$ protein is able to drive the host cell cycle directly into the S phase, skyping the G phase, a situation that might be similar to that observed in this study. Co-infection of those kittens by an adenovirus was looked for by PCR, using pan-adeno primers (300 bases product). No evidence of co-infection with an adenovirus could be evidenced by this method.

FPV protein production in post mitotic neurons is a paradox that remains unexplained since nearly a half century. This study broadens the description of the process, but also should be a warning about the possible use of this parvovirus as an anti-glioma weapon in cats.

VERTEBRAL VENOUS SYSTEM ABNORMALITIES OF SIGHTHOUNDS IDENTIFIED ON MAGNETIC RESONANCE IMAGES.

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The vertebral venous system (VVS) is composed of the internal vertebral venous plexus (IVVP), external vertebral venous plexus (EVVP) and basivertebral veins (BVV). Anatomical variations or pathological changes causing enlargement of this venous network are infrequently described in both human and veterinary medicine and may be associated with clinical signs. In the authors' experience VVS abnormalities are more common in sighthound dog breeds. The aim of this retrospective study is to describe such abnormalities, as identified on magnetic resonance imaging (MRI), in a population of sighthounds.

The MRI database of the University of Glasgow Small Animal Hospital was retrospectively searched for vertebral column studies of breeds classified as sighthounds. One hundred MRI studies fitted these criteria and were reviewed by a single observer. Cases that had abnormal enlargement of VVS components were then confirmed by a second observer. The vertebral level, side and the anatomical location (IVVP, intervertebral vein (IVV), EVVP, BVV) were noted for each abnormality. Finally, the signalment, clinical signs, neurological examination findings and final diagnosis for each case were recorded.

Eleven cases with abnormal enlargement of the VVS were identified. They included 5 Greyhounds, 4 Deerhounds, 1 Irish Wolfhound, and 1 Lurcher. 7/11 cases were females and the mean age was 6 years 3 months (range: 1.5-10.5 years). The most common clinical signs exhibited were pain (neck 6/11 and lumbar 2/11), ataxia (4/11), paresis (3/11) and lameness (3/11). The abnormalities found included enlargement of the IVVP unilaterally (10/11) and bilaterally (1/11) at one or more locations; enlargement of the IVVs unilaterally (8/11), bilaterally (2/11) or a combination of the two (1/11) at one or more locations; and enlargement of the EVVP in 7/11 cases. No abnormalities of the basivertebral veins were found, possibly due to the difficulty in identifying these vessels on imaging. Abnormalities were most common in the C4-T1 region (9/11), especially at the level of C6/7. Additionally, most abnormalities were unilateral with the right side more commonly affected. All eleven cases had more than one abnormality and 4/11 cases had abnormalities in nonadjacent anatomical locations. Interestingly one Greyhound had bilateral enlargement of the IVVP causing significant spinal cord compression. In only 2/11 cases was a definitive diagnosis achieved. Of the remaining nine cases, seven had VVS abnormalities in a neuroanatomical location that could possibly explain, either wholly or in part, the clinical signs exhibited by these patients.

The results of this study suggest that abnormalities of the VVS in sighthounds are not uncommon findings (11%) and can be incidental, as evidenced by their presence in two cases with an unrelated definitive diagnosis. However, it is possible some of them may be clinically relevant as indicated by the number of cases where a diagnosis was not achieved, coupled with the correlation of the neuroanatomical location of the abnormalities and the clinical signs display. Further prospective study would be indicated to fully elucidate the clinical significance of these abnormalities.