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## Βιβλιογραφική αναφορά:

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## Chiari - like malformation and syringomyelia in a toy poodle - a potential link to central nervous system inflammation

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**ABSTRACT:** A one-year-old female Toy poodle was referred for seizures, phantom scratching behind the right ear, and inability to jump. An intracranial and cervical spinal cord disorder was suspected. The cerebrospinal fluid analysis showed pleocytosis, increased total proteins, serum amyloid A (SAA), and lactate concentration, low albumin ratio, increased lactate dehydrogenase (LDH) activity, and no active forms of matrix metalloproteinase (MMPs). Magnetic resonance imaging of the brain and cervical part of the spinal cord revealed caudal cerebellar tonsil herniation and a syrinx formation between the C2 and C7 parts of the spinal cord. Chiari-like malformation (CM) and Syringomyelia (SM) as the result of a CM was diagnosed. Histopathology verified the presence of syrinxes in the dorsal region of the spinal cord, with and without connection to the central canal. For the first time, SAA, MMPs, lactate, and LDH were measured in CSF of dogs with CMSM, suggesting a potential link to central nervous system inflammation.

**Keyword:** canine; Chiari-like malformation; syringomyelia, cerebrospinal fluid, histopathology.

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## CASE HISTORY

**C**hiari-like malformation (CM) is a complex developmental condition characterized by a disturbance of cerebrospinal fluid (CSF) flow due to the mismatch between the brain and the skull size (Hechler and Moore, 2018). Characteristics of this disease are that it does not always have a specific clinical manifestation and that some aspects do not have a clear explanation. For example, syringomyelia (SM), which may, or may not develop as part of this disease, still does not have a clearly defined pathogenesis. However, Hechler and Moore (2018) hypothesized that it occurs due to the accumulation of extracellular fluid, as a consequence of abnormal CSF flow. The Chiari-like malformation is the most common in Cavalier King Charles spaniels and their crosses, while other breeds of dogs with a high prevalence of this disease include King Charles spaniels, Griffon bruxellois, Affenpinschers, Chihuahuas, Yorkshire terriers, Maltese and Pomeranians (Rusbrige et al., 2020). Little data is available for miniature toy poodles. Previous reports about CM/SM were mainly focused on clinical signs, magnetic resonance imaging (MRI), and/or histopathology findings, whereas evaluation of CSF was frequently missing (Hu et al., 2012; Nalborczyk et al., 2017; Rusbrige et al., 2019; Rusbrige et al., 2020).

Our goal was to present biochemical changes in CSF considering serum amyloid A (SAA) and lactate concentration, matrix metalloproteinase (MMPs), and lactate dehydrogenase (LDH) activity in correlation with MRI and histopathology findings in miniature toy poodle with CM/SM.

A one-year-old female Toy Poodle weighing 2 kg was referred with a 36-hour history of cluster seizures, rolling on the left side, ataxia, and inability to jump on the bed. Between the seizures, phantom scratching appeared (under the left ear). Before referral, the dog was treated with Diazepam® (1mg/kg b.w., intravenously, BID), Prednisolone® (1mg/kg b.w., subcutaneously, SID), and Synolux® (1mg/kg b.w., subcutaneously, SID). A complete blood count (CBC) and serum biochemical profile showed no abnormalities. However, the clinical condition deteriorated.

Neurological examination revealed anxiety, cervical spinal pain, decreased proprioception on the front and back left leg, and hemiparesis on the left side ("hopping," "hemi-walking," and correction of knuckled over paw testing). Generalized seizures appeared during the examination, characterized by un-

controllable spinning on its axis (always to the left). The results of repeated CBC and biochemical analyses were within the reference interval (RI), although the erythrocyte sedimentation rate (ESR) was high (40mm/1h). Based on these results, an intracranial and cervical spinal cord disorder was suspected (CM/SM, meningoencephalomyelitis of unknown origin, suspected idiopathic epilepsy). MRI was recommended to the owner's as the additional diagnostic step, however, they preferred a less expensive diagnostic test. We suggested a CSF analysis and explained the associated risks of this procedure, including hemorrhage, infection, brain herniation, and iatrogenic trauma, particularly since we could not determine the intracranial pressure (ICP). An aggravating circumstance is that the clinical signs associated with elevated ICP are nonspecific or absent (Bittermann et al., 2014). We also noted that clinical signs such as decreased consciousness, anisocoria, abnormal pupillary light reflexes, miosis, or mydriasis, which could indicate increased ICP, were absent (Walmsley et al., 2006). The owners understood the potential risks associated with the diagnostic procedure and signed the statement of agreement for CSF sampling.

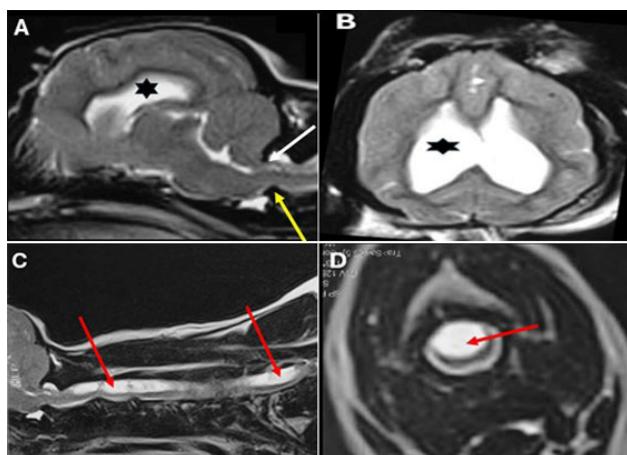
CSF was collected under general anesthesia from the cerebellomedullary cistern 24 hours after the last seizures. The sample of CSF was pale pink, cloudy, and had a total nucleated cell count (TNCC) of 360/ $\mu$ l (RI < 5/ $\mu$ l) and 50 RBCs/ $\mu$ l (determined in hemocytometer). The total protein concentration (pyrogallol red) was 11g/L (RI  $\leq$  0.30 g/L), albumin 0.4g/L (RI 0.24-0.29 g/L), lactate 3.04 mmol/L (RI 1.0-2.5 mmol/L), (Mariani et al., 2020), and total LDH activity was 50 U/L (RI 15-20 U/L), (Houle et al., 2015). The CSF to serum albumin ratio was 0.01. The CSF cytology analysis revealed a dominance of lymphocytes over neutrophils without the presence of erythrophagocytosis. The microbiological analysis did not confirm a bacterial/fungal infection. Using an ELISA kit (Tridelta®, Ireland), the concentration of SAA in the serum (434.95ng/mL) and CSF (1512.4 ng/mL) was measured. Without diluting the CSF samples, zymography in polyacrylamide gel was performed, as previously reported by Spariosu et al., (2021) for serum samples. The results showed that all gelatinolytic activity of MMPs (MMP 2, 9) in CSF originates from the inactivated form of MMP2. MMPs with an affinity for casein (MMP 3, 13) were not detected. Since the CSF findings did not help in revealing the disease's etiology, the owners accepted an MRI examination as the next diagnostic procedure.

MRI of the brain and cervical spine, T1- and T2-weighted images with 2 mm slice thickness and matrix:  $256 \times 256$ , was obtained with a 1.5 Tesla (MAGNETOM Symphony, A Tim System eco, SIEMENS) in sagittal, transverse, and dorsal planes. Midsagittal T2-weighted MRI revealed dilated lateral ventricles, and caudal cerebellar tonsillar herniation through the foramen magnum. (Figures 1A and 1B). Midsagittal and transverse T2-weighted MRI images at the level of the cervical spinal cord showed a lesion within the spinal cord consistent with a fluid-filled cavity. The CSF in the syrinx appeared hyperintense to the spinal cord parenchyma on the T2-weighted image and hypointense relative to the spinal cord itself on the T1-weighted images (Figure 1C). The diagnosis of CM/SM was concluded. According to the *British Veterinary Association/Kennel Club scheme (2019)*, CM was graded as grade 1 and SM as grade 2.

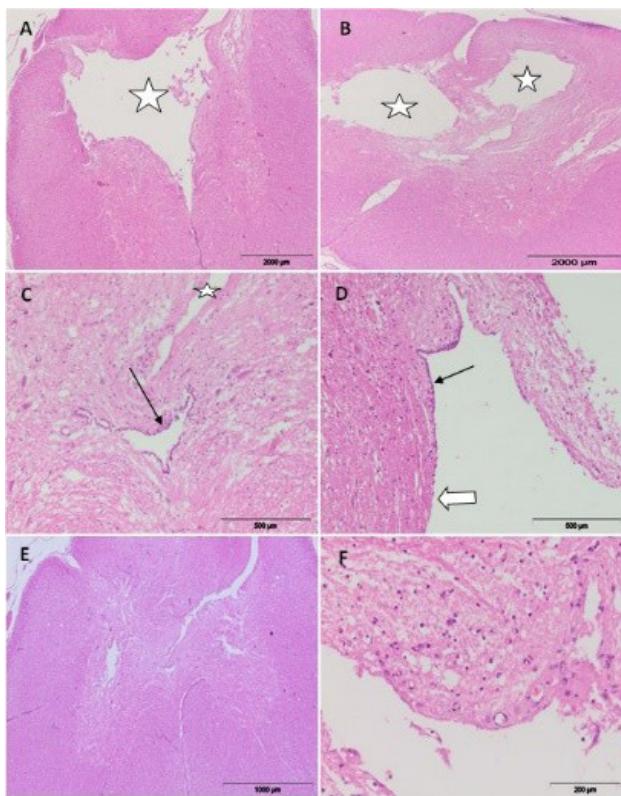
Regarding the CM/SM, we recommended that the owners consider medical treatment focused on managing neuropathic pain and phantom scratch-

ing, or a surgical approach such as cranial cervical decompression. We clarified that these proposed treatments will not cure the dog but it will maintain a good quality of life. Additionally, we suggested the beginning of the therapy for suspected idiopathic epilepsy. However, the owners did not accept any of the treatment options. At their request, the dog was euthanized, and an autopsy was performed.

The brain and spinal cord were fixed in 10% neutral formalin. The spinal cord was sliced into 12 transverse sections from C1 and one sagittal section from C1 to C8. The brain was cut in dorsal sections. The tissues were embedded in paraffin wax. The 5  $\mu\text{m}$  thick slices were stained by hematoxylin and eosin (HE) and the Masson's trichrome method. SM was discovered in the dorsal region of the spinal cord (Figure 2) and was lined by oedematous or necrotic tissue with a high concentration of astrocytes, oligodendroglia, and microglia. Cavities were seen in all cervical spinal cord tissue slices (C1-C4), with some even apparent macroscopically. The syrinx's shapes and dimensions (Figures 2A and 2B) differed depending on the segment (oval, elliptical, or irregular). In some spinal cord sections, the syrinx was connected to the central canal (Figure 2A), which was dilated (hydromielia) in some segments (Figure 2C). Also, some dorsal sections of the spinal cord exhibited two distinct chambers that were not connected to the central canal (Figures 2B and 2C). Furthermore, sections of the central canal exhibited complete ependyma, whereas others were damaged (Figure 2D). A few oval rosette-like structures (pseudorosettes) were seen at the syrinx's margin (Figures 3A and 3B). The pseudorosettes comprised ciliated or non-ciliated ependymocytes that surrounded small blood vessels. Many small blood vessels were seen in the tissue surrounding the syrinx. Substantial numbers of collagen fibers thickened the walls of some blood vessels, as evidenced by Masson's trichrome staining (Figure 3E). Masson's trichrome staining also revealed a small amount of collagen in the tissue around the syrinx (Figure 3F). In a few spinal cord slices, there was a mononuclear infiltration of macrophages and lymphocytes in the perivascular spaces and meninges only in the dorsal region (see Figures 3C and 3D). Perivascular oedema surrounding the blood vessels, located near the cavity's margin, was also seen. No pathological changes were observed in the coronary sections of the brain tissue.



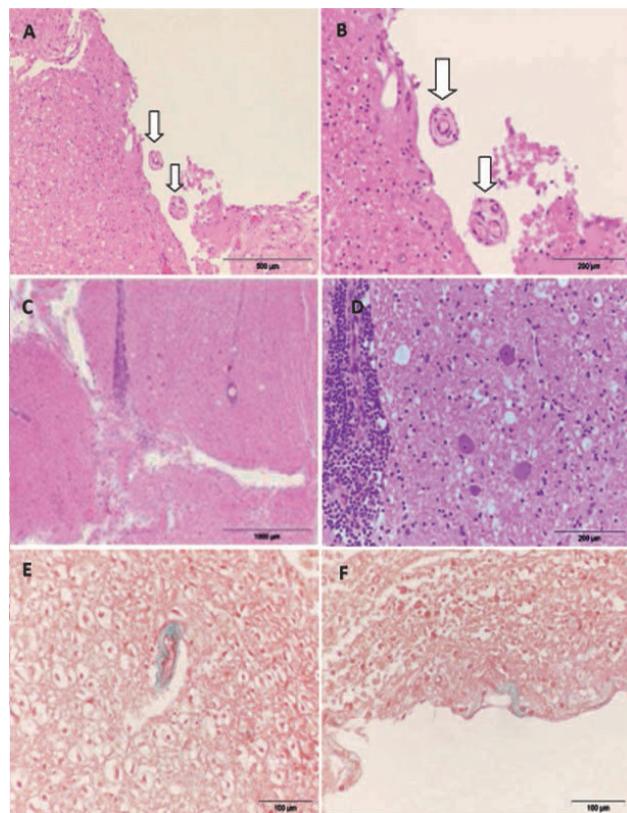
**Figure 1.** Midsagittal (A) and dorsal (B) T2-weighted MRI images of the head showing dilated lateral ventricles (asterisk), herniation of the cerebellar vermis into the foramen (white arrow) and medullary elevation, "kinked" appearance of the medulla oblongata is noticed (yellow arrow). On the midsagittal T2-weighted images of the cervical spine (C), there is syrinx formation at the level from C2 to C7 (red arrows). Transverse T2-weighted image (D) at C2-C3 revealed a syrinx centered within the dorsal half of the spinal cord (red arrow).



**Figure 2.** (A) HE, syrinx (white star) communicated with the central canal, (B) HE, two separated cavities with no connection with the central canal (white star) in the dorsal grey matter of the spinal cord, (C) HE, mild expanded central canal (black arrow) and syrinx (white star), (D) HE, black arrow indicate the region of intact ependyma, white arrow indicate a region where the integrity of the ependyma was disrupted, (E) HE, cavities in the white and gray matter of spinal cord and (F) HE, numerous blood vessels adjacent to the edge of the syrinx.

## DISCUSSION

The dog showed severe neurological signs despite being one year old and having a low-grade CM/SM. Previous observations confirmed that dogs under the age of two exhibit severe clinical signs (Rusbridge, 2020) unrelated to the size and grade of CM/SM (Harcourt-Brown *et al.*, 2015). By revealing a link between clinical signs, MRI, and histological changes, our findings supported the conclusion that large dorsolateral syringes at the C3-C6 level of the spinal cord may be associated with phantom scratching and scoliosis (Hu *et al.*, 2012; Nalborczyk *et al.*, 2017; Rusbridge *et al.*, 2019). Also, seizures are common in dogs with CM, but currently, there is insufficient data available in veterinary and human



**Figure 3.** Microscopical future of the spinal cord with syrinx: (A) HE, pseudorosette (white arrows), (B) HE, pseudorosette (white arrows) (C) HE, perivascular and meningeal mononuclear infiltrate, (D) HE, perivascular and meningeal mononuclear infiltrate and (E) Masson's trichrome staining, collagen in blood vessel wall, (F) Masson's trichrome staining, collagen in tissue adjacent to the cavity.

medicine to link CM to epilepsy. Comorbidity is still used to explain this finding (Granata and Valentini, 2011; Rusbridge 2020). Hu *et al.*, (2012) assume that blood supply is critical in developing pathogenic alterations in SM. The pseudo rosettes have a fibrovascular tissue core, and blood vessel density appears to rise approaching the central canal/syrinx. The blood arteries around the syrinx showed considerable wall thickening and perivascular edema in this case. This could be due to an auto-regulatory compensation mechanism in response to increasing pressure, as previously postulated, or inflammation.

The association between CM/SM and CNS inflammation was identified through CSF examination. The collected CSF sample had 50 RBCs/ $\mu$ l without erythrophagocytes on cytology smear which indicates iatrogenic contamination. Previous reports

demonstrated that iatrogenic peripheral blood contamination even when  $\geq 500$  RBC/ $\mu$ L was present poorly correlated with TNCC and protein concentration (MacNeill et al., 2018) and even when the sample contained less than 13200 RBC/ $\mu$ L (Hurt and Smith, 1997). Although the concentration of SAA in serum was high, suggesting the existence of systemic inflammation, which was supported by an elevated ESR, the concentration of SAA in CSF was higher. This result could indicate that SAA was also synthesized locally in the CNS. Furthermore, increased CSF lactate concentration and LDH activity may support the inflammation theory. In humans, CSF lactate and LDH levels are increased in inflammatory diseases, and they are especially effective in distinguishing bacterial from aseptic meningitis (Mariani et al., 2020, Houle et al., 2015). There is limited information on lactate and LDH concentration in CSF in dogs. However, it has been demonstrated that in inflammatory and neoplastic CNS diseases, lactate concentration is higher than in dogs with idiopathic or unknown epilepsy (Mariani et al., 2020). Furthermore, it was considered that seizures have little effect on lactate concentrations in CSF and that increases are more likely due to underlying illness. We assumed that an increase in lactate concentration could correspond to inflammation. In dogs diagnosed with CM and CM/SM, there is a diverse composition of CSF characterized by variations in TNCC and protein content, with more significant changes observed in cases of CM/SM. Most dogs with CM/SM exhibit alterations in both of these parameters, as noted by Whittaker et al. (2011), which is consistent with the findings in this case. To the author's knowledge, this is the first report detailing changes in acute phase proteins in both CSF and serum in dogs with CM/SM, as well as the activity of matrix metalloproteinases. In human medicine, it is widely accepted that elevated protein concentrations in CSF may be attributed to syringomyelia; however, this connection remains to be confirmed in veterinary medicine (Irani, 2009). Based on existing literature regarding CM/SM and CM, it is likely that the underlying cause of the increased protein concentration in dogs could be similar. Very high serum and CSF SAA concentrations suggest that syringomyelia may be associated with inflammation. In this case, the dog was diagnosed with CM/SM and suspected idiopathic epilepsy. The gold standard

for the diagnosis of CM/SM is magnetic resonance imaging, while the diagnosis of IE is based on the exclusion of the existence of other diseases that can result in seizures, which includes, among other things, the absence of changes on MRI and CSF examination. According to our finding, where the diagnosis of CM/SM and idiopathic epilepsy was made, the inflammatory changes registered in the CSF can only be related to the changes caused by syringomyelia. To gain a deeper understanding of the complex pathophysiological mechanisms underlying this pathology, it would be valuable to investigate whether there are histopathological changes in brain tissue that correspond to inflammatory alterations. However, a limitation of this case report is the lack of detailed descriptions of brain tissue changes.

When metalloproteinase activity was assessed, only the proenzyme form of MMP-2 was detected in the CSF, as observed in clinically healthy dogs (Bergman et al., 2002). The active forms of MMP-2 and MMP-9 are linked to ischemic and inflammatory diseases in the central nervous system. Nonetheless, the high concentration of SAA in CSF and increased enzyme activity suggest an ongoing inflammatory process. These results can be partially explained by the fact that most of the MMP-9 activity originates from neutrophil granulocytes and macrophages, rather than lymphocytes (Di Terlizzi and Platt, 2009), which constitute the dominant cell population in this case. Due to the unclear pathophysiological mechanisms and limited case studies on MMPs and acute phase proteins in CNS disorders, this finding remains partially unexplained. Nonetheless, these results are significant for future clinical discussions. Based on these findings and the low CSF/serum albumin ratio, it is most likely that the blood-brain barrier was retained and that cerebrospinal fluid results indicate a potential link between inflammation and CM/SM.

**Authors' contribution:** NA followed the clinical and neurological course of the case. IG interpreted the MRI results. SN performed an autopsy and histopathological analysis. JFA performed hematological and biochemical analyses. All authors read and approved the final article supported by the Minister of Science, Technological Development and Innovation of the Republic of Serbia (Contract number 451-03-47/2023-01/200143).

## REFERENCES

Bergman RL, Inzana KD, Inzana TJ (2002) Characterization of matrix metalloproteinase-2 and -9 in cerebrospinal fluid of clinically normal dogs. *Am J Vet Res* 10:1359-62. DOI: 10.2460/ajvr.2002.63.1359

Bittermann S, Lang J, Henke D, Howard J, Gorgas D (2014) Magnetic resonance imaging signs of presumed elevated intracranial pressure in dogs. *The Veterinary Journal* Volume 201, Issue 1, Pages 101-108. doi.org/10.1016/j.tvjl.2014.04.020.

BVA - British Veterinary Association, Chiari Malformation / Syringomyelia Scheme, (2019), <https://www.bva.co.uk/media/2800/20190710-chs-cmsm-leaflet-0719-v1-web.pdf>

Di Terlizzi R, Platt SR (2009) The function, composition and analysis of cerebrospinal fluid in companion animals: part II - analysis. *Vet J* Apr;180(1):15-32. doi: 10.1016/j.tvjl.2007.11.024.

Granata T, Valentini LG (2011) Epilepsy in type 1 Chiari malformation. *Neurol Sci* 32:303-306. DOI: 10.1007/s10072-011-0697-y

Harcourt-Brown TR, Campbell J, Warren-Smith C, Jeffery ND, Granger NP (2015). Prevalence of Chiari-like malformations in clinically unaffected dogs. *J Vet Intern Med* 29:231-237. DOI: 10.1111/jvim.12477

Hechler AC, Moore SA (2018) Understanding and treating Chiari-like malformation and syringomyelia in dogs. *Top Companion Anim Med* 2018;(33):1-11. DOI: 10.1053/j.tcam.2018.03.002.

Houle JC, Chen AV, Brenna AC, Mealey KL, Kiszonas AM (2015) Determination of optimal storage temperature and duration for analysis of total and isoenzyme lactate dehydrogenase activities in canine serum and cerebrospinal fluid. *Vet Clin Pathol* 2:253-261. DOI: 10.1111/vcp.12263

Hu HZ, Rusbridge C, Constantino-Casas F, Jeffery N (2012) Histopathological Investigation of Syringomyelia in the Cavalier King Charles Spaniel. *J Comp Path* 146:192-201. DOI: 10.1016/j.jcpa.2011.07.002

Hurtt, AE. and Smith, M (1997) Effects of iatrogenic blood contamination on results of cerebrospinal fluid analysis in clinically normal dogs and dogs with neurologic disease 866-867. <https://pubmed.ncbi.nlm.nih.gov/9333087/>.

MacNeill AL, Andre BG, Zingale Y, Packer RA, McGrath (2018) The effects of iatrogenic blood contamination on total nucleated cell counts and protein concentrations in canine cerebrospinal fluid. *Veterinary clinical pathology* Sep;47(3):464-70 DOI: 10.1111/vcp.12639

Mariani CL, Nye CJ, Ruterbories L, Tokarz DA, Green L, Lau J, Zidan N, Early PJ, Muñana, KR, Olby NJ, Lee CS, Guevar J (2020) Cerebrospinal fluid lactate concentrations in dogs with seizure disorders. *J Vet Intern Med* 34:2562-2570. DOI: 10.1111/jvim.15953

Nalborczyk ZR, McFadyen AK, Jovanovik J, Tauro A, Driver CJ, Fitzpatrick N, Susan PK, Rusbridge C (2017) MRI characteristics for Phantom scratching in canine syringomyelia. *BMC Vet Res* 13:340. DOI: 10.1186/s12917-017-1258-2

Rusbridge C (2020) New considerations about Chiari-like malformation, syringomyelia, and their management. In *Practice* 42(5):252-267. DOI: 10.1136/inp.m1869

Rusbridge C, McFadyen AK, Knower SP (2019) Behavioral and clinical signs of Chiari-like malformation-associated pain and syringomyelia in Cavalier King Charles spaniels. *Journal of Veterinary Internal Medicine* 33(5): 2138-2150. DOI: 10.1111/jvim.15552

Spariosu K, Janjic F, Radakovic M, Francuski Andric J, Baletic A, Kovacevic Filipovic M (2021) Low serum levels of promatrix metalloproteinase-2 and -9 occur during acute *Babesia canis* infection in dogs. *Veterinary Parasitology* 300 109612.

Walmsley GL, Hertrage ME, Dennis R, Platt SR, Jeffery ND (2006) The relationship between clinical signs and brain herniation associated with rostroventorial mass lesions in the dog. *The Veterinary Journal* 172, 258-264. doi:10.1016/j.tvjl.2005.05.012.