Clinical Application of Diagnostic Imaging of Chiari-Like Malformation and Syringomyelia

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Chiari-like malformation (CM) and syringomyelia (SM) is a frequent diagnosis in predisposed brachycephalic toy breeds since increased availability of MRI. However, the relevance of that MRI diagnosis has been questioned as CM, defined as identification of a cerebellar herniation, is ubiquitous in some breeds and SM can be asymptomatic. This article reviews the current knowledge of neuroanatomical changes in symptomatic CM and SM and diagnostic imaging modalities used for the clinical diagnosis of CM-pain or myelopathy related to SM. Although often compared to Chiari type I malformation in humans, canine CM-pain and SM is more comparable to complex craniosynostosis syndromes (i.e., premature fusion of multiple skull sutures) characterized by a short skull (cranial) base, rostroventricular crowding with rostral forebrain flattening, small, and ventrally orientated olfactory bulbs, displacement of the neural tissue to give increased height of the cranium and further reduction of the functional caudalventricular space with hindbrain herniation. MRI may further reveal changes suggesting raised intracranial pressure such as loss of sulci definition in conjunction with ventriculomegaly. In addition to these brachycephalic changes, dogs with SM are more likely to have craniocervical junction abnormalities including rostral displacement of the axis and atlas with increased odontoid angulation causing craniospinal junction deformation and medulla oblongata elevation. Symptomatic SM is diagnosed on the basis of signs of myelopathy and presence of a large syrinx that is consistent with the neuro-localization. The imaging protocol should establish the longitudinal and transverse extent of the spinal cord involvement by the syrinx. Phantom scratching and cervicotoricollis are associated with large mid-cervical syringes that extend to the superficial dorsal horn. If the cause of CSF channel disruption and syringomyelia is not revealed by anatomical MRI then other imaging modalities may be appropriate with radiography or CT for any associated vertebral abnormalities.

Keywords: complex craniosynostosis syndrome, basilar invagination, COMS, Chiari type I malformation, cine MRI, balanced steady-state free precession sequence, fluid signal-void sign, MRI protocol
INTRODUCTION

Chiari-like malformation (CM) is a complex skull and cranio cervical junction disorder associated with brachycephaly with skull base shortening, low volume caudal fossa and rostro tentorial, caudotentorial and craniospinal crowding. For a detailed written and visual description of the morphogenesis see the review by Knowler et al. (1). The condition has been marred in controversy since the first description, not least by what to call it (2). The eponymic term refers to the first detailed pathological description by Hans Chiari of an analogous human condition (3). The veterinary label, chosen in a round table discussion (2, 4) was considered less restrictive than an anatomical description (for example hindbrain herniation or occipital hypoplasia), which may have proved simplistic or inaccurate in the future. This prediction was true, and over the last two decades our understanding of the complex morphology has deepened and most realize that this condition is more than a cerebellar foramen magnum herniation. As a MRI description, CM should be considered an umbrella term, as the bony and parenchymal changes between and within individuals in each breed are different but have a common tendency toward pain associated with CM and the development of syringomyelia (SM). As such, and with the common feature of being associated with brachycephaly, it was recently proposed that the disorder might be better described as a brachycephalic obstructive cerebrospinal (CSF) channel syndrome (BOCCS) with similarities to brachycephalic obstructive airway syndrome (BOAS) (1).

TABLE 1 | Pathogenesis of Chiari-like malformation and syringomyelia: summary of the existing knowledge base—skull changes.

| Anatomical feature | Study finding(s) | Possible implication |
|--------------------|------------------|----------------------|
| Brachycephaly      | Brachiocephalic breeds have early closure of the sphen-occipital synchondrosis. In CKCS closure is even earlier (49, 50) | Premature closure of the sphen-occipital synchondrosis will result in a short cranial base (basicranium). |
|                    | CKCS have shorter cranium in relation to width compared to other brachycephalic dog breeds (51) | Basiocranial shortening results in compensatory changes in the rostral cranial fossa which results in a head shape with rostrocaudal doming and is broad in relationship to the length (reduced cephalic index) |
|                    | Griffon Bruxellois with CM have shortened basicranium and supraoccipital bone, with a compensatory lengthening of the dorsal cranial vault, especially the parietal bone (52) | |
|                    | Association between increased cranial height and SM in CKCS, Griffon Bruxellois and Affenpinscher (38, 40) | May be associated with premature closure of sphen-occipital synchondrosis. This angulation occurs in rodent models where the sphen-occipital synchondrosis is damaged (1, 54) |
|                    | CKCS with broader and shorter skulls and increased rostro-cranial doming are at increased risk of developing SM (53) | CM pain is associated with increased brachycephaly |
|                    | Association between acute angulation at sphen-occipital synchondrosis (Sphenoid flexure) and SM (40) | |
|                    | Rostral forebrain flattening, short basioccipital bone associated with CM pain | There are two SM phenotypes: one typified by extreme brachycephalism and one by craniospinal junction deformation |
| Occipital Crest    | Association between reduced occipital crest and SM in CKCS, Affenpinscher and Chihuahua (40) | Suggests insufficiency of the supraocciptal bones and possibly the intraparietal bone |
| Frontal Sinus      | Association between small frontal sinuses and SM in small breed dogs (55) | Suggests that SM may be related to rostroentorial skull changes rather than being confined to a hind skull abnormality. |
| Caudal cranial fossa volume | CKCS with CM and SM have a shallower and smaller volume caudal cranial fossa compared to CKCS with CM only and other control breeds (56, 57) | Smaller caudal cranial fossa volume predisposes caudal cranial fossa overcrowding |
|                    | CKCS have a strong relationship between hindbrain volume and volume of the rostral part of the caudal cranial fossa and a weak relationship between hindbrain volume and volume of the caudal part of the caudal cranial fossa. In Labrador retrievers and other small breed dogs this relationship is reversed (56, 58) | Small breed dogs and Labrador retrievers compensate for variations in hindbrain volume by modifying growth of the occipital skull. In the CKCS, increased cerebellar size is not accommodated by increased occipital bone development and the terrotium cerebelli compensates by developing / remodeling in a rostral direction |
| Occipital bone volume | No difference in volume of the occipital bones between CKCS (with and without SM) and French Bulldogs (69) | Does not support theory of occipital bone hypoplasia |
| Jugular foramina   | CKCS with CM and SM have narrowed jugular foramina in comparison with CKCS with CM only (52, 60) | Venous narrowing at the jugular foramina associated with reduced skull base can lead to elevated venous pressure and impaired CSF absorption |
| Venous sinus volume | CKCS with CM and SM have reduced venous sinus volume in comparison with CKCS with CM only (61) | Reduced venous sinus volume could result in intracranial hypertension and impaired CSF absorption |
The analogous disease in humans was considered to be Chiari type 1 malformation, defined traditionally as a MRI finding of caudal displacement of the cerebellar tonsils inferior to the plane of the foramen magnum by at least 3 mm. However, like the canine disease, this description is problematic especially as there can be symptomatic disease and SM with smaller herniation (termed Chiari type 0). In an attempt to categorize the variations in humans there are now seven recognized types: 0, 1, 1.5, 2, 3, 3.5, and 4 (3–6). However, the distinction between types is challenging especially when the etiology is multifactorial and increasingly there is a call in human medicine that cerebellar tonsil herniation/Chiari malformation should be considered a radiographic sign and the focus of the diagnostic investigation should be to determine the cause of that herniation for example shallow posterior fossa (7), craniostenosis (8), inherited disorders of connective tissue (9), spinal cord tethering (10), intracranial hypertension (11), or intracranial hypotension (12).

CM is one of the most common causes of SM in the dog which is characterized by the development of cavities in the spinal cord containing a fluid similar to CSF (13, 14) however SM can develop after any obstruction to CSF channels and has been reported in a variety of disorders ranging from acquired cerebellar herniation secondary to intracranial masses (15–18) to spinal arachnoid diverticulum (19, 20) and spinal cord tethering (21). The terminology of SM is equally confused, with some veterinary papers referring to syringohydromyelia or hydrosyringomyelia. These historical terms have been mostly discarded in human medicine (4). Equally confusing is if and when the term hydromyelia is applied. The term syringomyelia was first used by Charles-Prospé d’Angers (1796–1845) deriving the term from the Greek “syringe” meaning tube or pipe, and “myelio” referring to the spinal marrow (22, 23). The term hydroamyelus was coined by Schüppel in 1865 to describe a dilatation of the central canal (24). In 1875, and after describing spinal cord cavities apparently separate from the central canal and surrounded by gliosis, Simon proposed that hydromyelia be used to describe central canal dilation and distension and that the term syringomyelia be reserved to describe cavities and cystic conditions independent of the central canal (25, 26). In 1876, Leyden concluded that hydromyelia and SM were identical conditions (26, 27) but Kahler and Pick made the observation that a hydromyelia is lined by ependyma whereas glial cells form the wall of SM cavities and recommended keeping a distinction between hydromyelia and SM (26, 28). However, it is difficult to distinguish between hydromyelia and SM, by radiological, clinical, or pathological means and consequently some used the combined terms syringohydromyelia or hydrosyringomyelia, to describe a cavity which is partially lined by ependymal but which also extends into the spinal cord substance (29). Thus, some clinicians argue that the term syringomyelia should only apply to a glia lined cavity separate from the central canal, that hydromyelia be reserved for central canal dilatation, still lined by ependyma and that the term syringohydromyelia is correct for a cavity involving a dilated central canal that is partially lined by ependyma. However, post mortem and experimental studies have suggested that the ependyma is disrupted following only minor central canal dilatation and that all syringomyelic cavities are connected to the central canal at some level of the spinal cord (4, 30–32) therefore nowadays the simpler and original term syringomyelia is used by the majority (4). In veterinary

### TABLE 2 | Pathogenesis of Chiari-like malformation and syringomyelia: summary of the existing knowledge base—craniocervical junction and cervical changes.

| Anatomical feature | Study finding(s) | Possible implication |
|--------------------|------------------|----------------------|
| Proximity of atlas to skull (atlanto-occipital overlapping) | SM risk increases with decreased distance between atlas and occipital bones (39, 62–64) | Reduced distance between the skull and the cervical vertebrae increases risk of SM |
| Odontoid peg impingement of ventral subarachnoid space/neural tissue | Commonly seen in association with CM (40, 56, 65) | Contributes to overcrowding and conformation change of craniospinal junction with loss of cisterna magna |
| Proximity of dens to atlas | Greater distance between atlas and odontoid peg is protective against SM (40) | Odontoid peg is more acutely angled, contributing to craniospinal disproportion, medullary elevation and cervical flexure (40) |
| Dorsal impingement subarachnoid space/spinal cord (atlantoaxial bands) at C1-C2 | Commonly seen in association with CM and more prominent in extended than flexed positions (56, 62, 63, 65, 66) | Significance undetermined |
| Width of spinal canal | Increased width of spinal canal at C2-C3 and C3 in CKCS with SM (67) | Questionable clinical significance |
| Atlantoaxial subluxation | Occasional comorbidity with CM (68) | No significant association with SM |
| Size of C2 spinous process | Significantly smaller in CKCSs than in non-CKCS breeds (68) | No correlation (67) |
| Angulation at C2–C3 | | |
medicine a central canal dilatation is defined as a dilatation and distension of the spinal cord with a transverse diameter <2 mm (33).

Identifying a cerebellar herniation and SM on MRI is relatively straightforward and has been defined by the British Veterinary Association and UK Kennel Club with a Health Scheme for breeding dogs based on a grading system for CM, SM, and the maximum transverse diameter of the syrinx if present (33). However, the grading for CM is simplistic and only based on the degree of cerebellar herniation. The diagnosis of symptomatic CM and SM can be challenging in some breeds such as the Cavalier King Charles spaniel (CKCS) because CM, as defined by the BVA/KC Health Scheme is ubiquitous, and SM is prevalent but may be asymptomatic (34, 35). Increasingly it has become apparent that CM alone, like the analogous human condition, can have significant impact on welfare and quality of life (36, 37). Previously we used a MRI morphometric mapping approach to define CM pain and symptomatic SM in the CKCS, Griffon Bruxellois, Chihuahua, and Affenpincher (38–40) and these traits were linked to genomic regions (41, 42). However, translating this research technique to the clinic is challenging as it involves time consuming measurements and there is no objective measure of disease presence/ risk to offspring. Consequently development of a machine learning approach and computer analysis is recommended but development of this will take considerable resources (43, 44). This article serves to review the current knowledge base and provide guidelines to the clinician for the diagnostic imaging of CM-pain and symptomatic SM.

### CURRENT UNDERSTANDING OF THE MORPHOLOGICAL CHANGES IN CANINE CM AND SM

Many studies, mostly in the CKCS or Griffon Bruxellois, have assessed features of skull and cervical vertebral morphology in relationship to the presence or absence of SM. Not all studies had

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**TABLE 3 | Pathogenesis of Chiari-like malformation and syringomyelia: summary of the existing knowledge base—neuroparenchymal changes.**

| Anatomical feature                  | Study finding(s)                                                                 | Possible implication                      |
|-------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------|
| Parenchymal (brain) volume          | The absolute and relative volume of the CKCS skull is similar to other brachycephalic toy dog breeds but CKCS have a greater volume of parenchyma within the caudal cranial fossa (69) and CKCS with early onset SM have a larger volume of parenchyma within a smaller caudal cranial fossa compared to older CKCS with CM only (67, 61, 70) | Mismatch in skull and brain volume is associated with development of SM. |
| Cerebellar volume                   | CKCS have relatively increased cerebellar volume compared to other control breeds and this is associated with development of SM (71) | Caudal cranial fossa overcrowding is associated with development of SM. |
| Cerebellar herniation               | Typically present but size does not predict SM (62, 72, 73)                    | Obstruction of CSF channels though the foramen magnum contributes to the pathogenesis of SM but there must also be other predisposing factors. |
|                                    | Positive association with the size of foramen magnum and size of cerebellar herniation (62) | Overcrowding of the caudal cranial fossa causes supracerebral bone resorption (occipital dysplasia) and widening of the foramen magnum over time. |
| Cerebellar pulsation                | CKCS with CM and SM have significantly greater pulsation of the cerebellum compared to CKCS with CM only and other control breeds (78) | Abnormal cerebellar pulsation could lead to a mismatch in the timing of the arterial and CSF pulse waves predisposing SM (77, 78) |
| Position of cerebellum relative to occipital lobe | Rostroventral cranioencephalic disproportion results in the occipital lobes being displaced caudally so that cerebellum is invaginated under the occipital lobes (40). | Overcrowding in both cranial and caudal fossa affects position of cerebellum. |
| Medullary elevation (medullary kinking) | Higher medullary kinking index is associated with clinical signs in CKCS and Chihuahuas (47, 79) | Dogs with higher medullary elevation / kinking are more likely to have clinical signs. |
| Caudal medulla (obex) position      | Association between more caudal brainstem positions and presence of SM (79) | Caudal displacement of the obex may increase risk of SM |
| CSF flow                            | Higher peak CSF flow velocity at the foramen magnum with a lower CSF flow velocity at C2–C3 predicts SM (83) | SM is associated with alterations in the CSF velocity profile |
|                                    | Turbulence at the foramen magnum and at the C2-C3 disc significantly associated with SM (83) | Presence of CSF signal-void sign in mesencephalic aqueduct on T2W is associated with SM and increased ventricular size (81) |
| Ventricle dimensions                | In CKCS ventricle dimensions are positively correlated with syrinx width (57) | Evidence that SM is related to CSF channel obstruction |
|                                    | Are not correlated with seizures (nor is caudal cranial fossa overcrowding) (62) | Epilepsy and CM in CKCS should be considered unrelated |
good control groups, especially the earlier ones. As SM occurs secondary to CM and is more likely in older dogs (34, 35, 45, 46), it is important that the SM-clear cohort consists of dogs MRI scanned when older and typically aged 4 years or more. Equally it is important to accurately phenotype symptomatic dogs which can be challenging as the most common clinical sign is pain which is subjective and in the dog overly reliant on owner reporting (39, 47, 48).

Table 1 summarizes the existing knowledge in relationship to the skull, Table 2 the cranio cervic al junction and cervical changes, Table 3 the neuro-parenchymal changes and Table 4 the syrinx changes.

**SUMMARY OF EXISTING KNOWLEDGE OF THE MORPHOLOGICAL CHANGES IN CANINE CM AND SM**

The key feature of canine CM is craniosynostosis of particularly the sphen-occipital synchondrosis. However, premature closure of the sphen-occipital and intersphenoidal synchondrosis defines the canine brachycephalic skull (1, 49) and CM does not occur in all brachycephalic dogs. Therefore, CM is a more complex disorder and likely involves other premature suture closure (especially the lamboid) or other causes of insufficient cranium. The skull insufficiency results in rostrotentorial crowding which further reduces the functional caudotentorial space and causes hindbrain herniation. It is complicated by craniocervical junction deformation including change in angulation of the dens and increased proximity of the atlas to the skull and loss of the cisterna magna. Loss of the cisterna magna or other alteration in the CSF volume will affect the compliance of the CNS (90). In addition some predisposed breeds such as the CKCS have comparatively big brains (69, 71, 91). The pathogenesis of SM associated with CM is undetermined but is predisposed by two phenotypes (or combination); the first by extreme brachycephaly and the second by craniocervical junction deformation (39). This may be influenced by poor venous drainage, intracranial hypertension, changes in CNS compliance and conformational features of the spinal canal. Although CM is considered a naturally occurring model of adult Chiari type 1 malformation it is much closer to the hindbrain herniation seen with complex craniosynostosis such as Crouzon’s syndrome (92).

**DIAGNOSTIC IMAGING OF CM AND SM**

**Radiographs**

Radiographs are not recommended for the investigation of CM and SM. However, if they have been obtained, for example by the general practitioner in the work-up for cervical pain, then there may be features that are suggestive of CM and SM such as flattened supraoccipital bone and close proximity of the atlas to the skull (Figures 1, 2). In the instance of severe SM there may be widening of the cervical spinal canal and remodeling and scalloping of the vertebrae due to increased intraspinal pressure (93) (Figure 2). Dynamic (flexion and extension) atlantoaxial radiographs may be indicted to assess stability of the atlantoaxial joint especially if a foramen magnum decompression is planned (Figure 3).

**Ultrasound**

In veterinary medicine ultrasound does not feature in management of CM and SM as it does in human medicine, where 3D ultrasound it is used intraoperatively to tailor a foramen magnum decompression and optimize re-establishment of CSF flow (94, 95). Ultrasoundography of the atlanto-occipital

| Anatomical feature | Study finding(s) | Possible implication |
|--------------------|------------------|---------------------|
| Syrinx presence    | If a syrinx is detected in an asymptomatic dog having MRI screening prior to breeding then there is a higher change that this dog may develop clinical signs of CM-SM later in life compared to a dog without a visible syrinx (83) However dogs with no clinical signs at the age of 6 are more likely to remain asymptomatic (45) | Early development of syringomyelia is more likely to be associated with clinical signs even if the dog is initially asymptomatic |
| Site of syrinx     | In CKCS, SM tends to develop first within the C2-C4, T2-T4, and T12-L2 spinal-cord segments (77, 84, 85). Axial stress increases in the cranial cervical and cervico-thoracic regions where the spinal cord has most curvature (90) In CKCS 76% of dogs with a syrinx at C1-C4 also had a syrinx in the C5-T1 and T2-L2 regions and 49% had a syrinx in the L3-L7 region (83) | SM development may be associated with subarachnoid space narrowing and/or change in the angulation of the vertebral canal Increased axial stress at the site of spinal curvature may explain the syrinx distribution in the CKCS In CKCS MRI imaging of the cranial cervical region only has high sensitivity for detection of SM however the extent of the disease may be underestimated |
| Syrinx size and symmetry | Pain is positively correlated with SM transverse width and symmetry on the vertical axis (82, 57) Phantom (fictive) scratching is associated with a mid-cervical spinal cord segment syrinx with extension to the superficial dorsal horn (88) Dogs with a wide syrinx and dorsal gray column damage are also more likely to have cervicothoracic scoliosis (57) | Dogs with a wider asymmetrical SM more likely to experience pain Phantom (fictive) scratching is associated with damage to the mid-cervical superficial dorsal horn Gray column damage can result in an imbalance of proprioceptive information and cervical dystonia (89) |

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**TABLE 4 | Pathogenesis of Chiari-like malformation and syringomyelia: summary of the existing knowledge base—syrinx features.**
junction has been described, proving it is possible to discern the cerebellar herniation (96). Hypothetically, ultrasound guidance could prove a useful aid for placement of a shunt into a syrinx or ventricle via a laminectomy or craniectomy.

**Computed Tomography (CT)**

CT should be performed if a vertebral malformation is suspected in association with SM especially if implanted surgical fixation is likely and to facilitate planning of this procedure (Figure 3). Most descriptions of CT in the investigation of CM and SM have been to answer a research hypothesis or question (51, 59, 60, 63, 97). Although CT has limited value in assessing CM and SM other than confirming a cerebellar herniation (98) and defining craniocervical junction abnormalities (63), hypothetically it could play a future role in health screening pedigree dogs assuming accurate morphometric analysis/machine learning can be translated from MRI studies and especially if risk of future disease could be predicted (99).

**Myelography**

Myelography and CT myelography can be used to investigate SM secondary to arachnoid diverticulae and webs/bands (100, 101) and CT myelography is the procedure of choice in the investigation of idiopathic SM if anatomical or cine MRI techniques are not available or have not revealed the cause of the CSF channel obstruction (102, 103). In veterinary medicine the most common application of CT myelography is when MRI is inappropriate because of metal implants and the owner wants to pursue further surgical management. An arachnoid web/band is indicated by a (often dorsal) flow block indicating CSF obstruction in combination with displacement or change in spinal cord caliber (Figure 4). An arachnoid diverticulae is a CSF containing space, lined by arachnoid mater which communicates with the subarachnoid space via a narrow “neck” enlarging via a one-way valve effect. With myelography the diverticulae will fill with contrast (101, 103, 104). Intrathecal contrast medium injections are more challenging when the spinal subarachnoid space is narrowed as a consequence of SM and should be
FIGURE 3 | Diagnostic imaging from a 5 year female CKCS presented with lethargy, ataxia, cervico-torticollis, and phantom scratching and following MRI diagnosed with symptomatic CM and SM. (A) T2-weighted mid-sagittal MRI of the brain and cranial cervical spinal cord. (B) T2-weighted mid sagittal MRI of the hindbrain and spine from C1 to T10. (C) Lateral skull and cervical spinal radiograph flexed at the atlantoaxial joint. (D) Lateral skull and cervical spinal radiograph extended at the atlantoaxial joint. (E) CT reformatted in the sagittal plane of the skull and cervical spine. MRI imaging (A,B) confirmed CM and SM with a large mid cervical SM involving the superficial dorsal horn thus explaining the cervico-torticollis and phantom scratching (insert). MRI also suggested atlantoaxial instability with spinal cord compression by the odontoid peg. Atlantoaxial instability was confirmed by a dynamic radiographic study (C,D). The CT was obtained for pre-surgical planning. The dorsal displacement of the odontoid peg (asterisk) and dorsal opening (arrow) between the atlas and axis can be appreciated (Siemens Magnetom Symphony, A Tim System, 1.5 T, Erlangen, Germany; Toshiba Aquilion Prime 160 slice, Otawara, Japan).

undertaken by an experienced operator. CT myelography is not indicated in the investigation of SM secondary to CM.

**Magnetic Resonance Imaging (MRI)**

MRI is undoubtedly the modality of choice to investigate CM and/or SM. On making a diagnosis of CM/SM there are six aims for the clinician.

1) To assess and document the anatomical changes (Figure 5, Supplementary Figure 1).
2) To determine the cause of the SM. SM is an acquired disease which occurs secondary to CSF channel disruption therefore the aim of MRI is to determine the site of that obstruction. Typically disruption at the craniocervical junction due to CM results in syrinx development in the cranial cervical region (85).
3) To determine the full extent of disease, for example the caudal extent of the syrinx in the event of holocord SM (85).
4) Eliminate other potential causes of the clinical presentation and neurological localization, for example intervertebral disc disease as an alternative explanation for spinal pain.
5) Assess whether the radiological findings are consistent with the neurological localization and severity, for example forebrain signs such as seizures or cranial nerve deficits such as facial nerve paralysis cannot be explained by SM which is a spinal cord disease.
6) To determine if other diagnostic modalities are recommended, for example CT to characterize bony abnormalities that might need surgical stabilization and therefore planning.

**MRI PROTOCOLS TO INVESTIGATE CM AND SM**

Diagnostic MRI evaluation of CM and SM should include imaging of brain and spinal cord in at least two orientations and include protocols to produce static T1-weighted and T2-weighted sequences (102). Sagittal and transverse imaging of the brain including the craniocervical junction is essential to evaluate the rostrotentorial and caudotentorial overcrowding, CSF spaces and any compromise of the craniospinal junction. Spinal MRI establishes the presence, maximum width on transverse images, dorsal horn involvement and longitudinal extent of the syrinx/presyrinx (Table 5 and Supplementary Table 1). It is recommended that at the time of scanning that the microchip or tattoo number (confirmed by the veterinary surgeon) is included on the DICOM images in addition to the Kennel Club registration number if the dog is registered. This is to permit submission to an official CMSM health scheme should the owner request it (33).

Protocols will vary between low and high field machines because of the difference in anatomical definition. T2-weighted sequences will be preferred for high field machines and T1-weighted sequences for low field machines. However, at least one region of the spinal cord, typically a sagittal sequence of
the cervical region, that includes both T1 and T2-weighting is essential to determine that the signal characteristics of the fluid filled cavity is identical to CSF and to eliminate other causes of hyperintensity on T2-weighted images for example edema associated with meningoencephalomyelitis of unknown origin. As a general rule, measurements of the width of CSF spaces are considered more accurate on T1-weighted images, however T2 weighted images are more sensitive to the presence of excessive fluid within the neural tissue and in particular presyrinx (presyringomyelia) which may eventually form a syrinx. Limited “low cost” imaging of CM or SM with a 3-sequence protocol of the hindbrain and cranial cervical spinal cord is offered by some institutions for dog breeders that wish to screen their breeding stock, however this minimal protocol does not provide information about the brain or syrinx involvement of the thoracic and lumbar regions and is not recommended for the dog presented to a veterinarian for a diagnostic work up of suspected CM or SM. Factors that influence the ability to make an accurate assessment of CM and SM are detailed in Table 6.

T2 Fluid-attenuated inversion recovery (FLAIR) imaging of the brain is a sequence which uses an inversion pulse and long echo time to suppress normal CSF signal on a heavily T2-weighted image. Pathology is suggested by high signal against background of normal signal from the brain and low or zero signal from the CSF. FLAIR sequences are also indicated if meningoencephalomyelitis is suspected. Paramagnetic contrast enhancement may be indicated especially if (i) there is evidence of a mass; (ii) if the cause of the CSF channel obstruction is not apparent; (iii) there is a presyrinx and need to eliminate other causes of spinal cord edema. Spinal intramedullary tumors may be cystic and it is important to distinguish these from SM.
FIGURE 5 | Suggested interpretation of MRI for diagnosis of CM pain and symptomatic SM—the authors’ method. With the exception of the basic scoring by the CMSM health scheme (33), there is no objective measure for the diagnosis of CM pain. The diagnosis is made by exclusion and the weight of clinical and MRI evidence. Not all dogs will have all the features. The diagnosis of symptomatic SM is more objective reflecting the size and neuro-localization. For the supporting scientific justification see Tables 1–4 however this method is also based on the authors own observations and interpretations of which the reader should take account.

| Anatomical Feature | Question | Rationale |
|--------------------|----------|-----------|
| **Neural tissue** | | |
| Olfactory bulbs | Size? Well-defined? Oriented rostrally? | Affected dogs are more likely to have small, ventrally oriented olfactory bulbs. |
| Restricted foramen | Rounded or flattened appearance rostrally? | Affected dogs, especially with CM pain, are more likely to have a flattened foramen at the foramen cruciatum plate and frontal sinuses. |
| Whole brain conformation | If a close fitting box was drawn around the mid-sagittal brain, would it be a rectangle or closer to a square? | CM-pains is characterized by brachycephaly with a short skull base and a compensatory increase of height in the occipital region. As a result the “box” that would approximate the brain is closer to a “square C-shaped.” |
| Cerebellar shape and position | Cerebellum rounded? | Affected dogs have a cerebellum that may be flattened/indented by the suprascalpical bone and/or occipitalfrontal lignment. Additionally alternatively it may be tilted and invaginated under the occipital lobes. |
| Cerebellar herniation | Herniation caudal to the level of the ventral edge of the suprascalpical bone? | Ubiquitous in some breeds such as the CCKS. |
| Medullary position and cranioesophageal junction conformation. | Herniation of medulla oblongata caudal to the level of the ventral edge of the suprascalpical bone? | More severe cranioesophageal conformational changes increase risk of SM. |
| **CSF spaces** | | |
| Cranial subarchnoid space | Convolutions of goi well defined by high contrast CSF on T2W images? | Narrowing of the sulci concurrently with ventriculomegaly suggests obstruction of the CSF pathways and raised intracranial pressure. |
| Lateral ventricles | Dilated? Is the corpus callosum elevated and or thinned? | Affected dogs often have dilation of the entire ventricular system and associated culmens. The corpus callosum is often thinned and elevated and the ventricles may be thinner and at an abnormal angle affected by dilation of the quadrigeminal cistern. By contrast the intraventricular adhesion appears normal. |
| Third ventricle and volum interposition | Dilated? Is intraventricular adhesion normal size? | | |
| Quadrogeminal cistern | Dilated? Is tectum position and thickness normal? | | |
| Mezzoencephalolic aqueduct | Dilated? | | |
| Fourth ventricle | Fourth ventricle a slit (normal) or triangular (distorted) in shape? | Suggests reduced outflow through the lateral apertures. |
| Cisterna magna and spinal subarchnoid space | Reduced? | Reduced cisterna magna and spinal subarchnoid space will affect the ability to buffer the systolic pulsation and the compliance of the central nervous system. |
| Fluid flow void | Fluid flow void is ventricular system? | Suggest pulsatile or turbulent flow which may be associated with progressive disease (hydrocephalus or syringomyelia). |
| **Bony tissue** | | |
| Stop and frontal sinuses | Obvious stop? Frontal sinuses evident? | Affected dogs appear to have a radience insufficiency with an absent/misshapen frontal sinus with a well-defined stop and a forehead that is a layer of skin, bone then brain. |
| Cranial base (preprosenoid, basissphenoid and basioccipital) | Short appearance? | Affected dogs have a short cranial base. |
| Suprascalpical bone | Midline portion present? Appear curved caudal to a vertical line drawn through the union of the occipital crest? | In affected dogs the suprascalpical bone may be rostral to a vertical line drawn through the union of the occipital crest. It often appears flatter. The bone is thin and the midline portion may be missing (occipital dysphasia). With extensive occipital dysphasia the cerebellum may have a more rounded shape. |
| Occipital crest | Reduced? | Affected dogs often have a reduced occipital crest. |
| Atlas | On a mid-sagittal image, when the head is in extension, what is the angulation of the dens to a basiscapital bone? | A line drawn between the union of the occipital crest and the rostral atlas should be angulated caudally. |
| Odontoid peg and axis | On a mid-sagittal image, when the head is in extension, what is the angulation of the dens to a basiscapital bone? | In the normal dog there is a slight curvature of cranioesophageal junction over the dens. In affected dogs there is increased angulation (cervical fracture). |
| **Ligament** | | |
| Occipitomastoideus ligament / membrane | On a midline sagittal image, is this ligament horizontal (normal) or it vertical and indenting the cerebellum ventrally? | This ligamentous indentation into the cerebellum is the classic feature of CM although many conflict this with the ventral suprascalpical bone because both are hypertonic. The ligament is abnormally vertical because of the close proximity of the atlas to the skull and a short suprascalpical bone. |
| Atlantoaxial bands | Dorsal impingement of the subarchnoid space at C1-C2? | Noted but significance not known. |
| **Spinal cord** | | |
| Presyn | Is there edema (pyrocytes)? | The pyrocytes is a potentially reversible myeloedema that may precede development of a syrinx. It is characterized by spinal cord oedema and amaligment with no remission. |
| Synx | Has the outline of spinal cord expanded? | An expanded syrinx suggests active filling and therefore more risk of progressive disease. By contrast a syrinx that is curvilinear on transverse images and elliptical on sagittal images with little or no change to outline of the spinal cord is more likely to be asymptomatic. |

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### TABLE 5 | Diagnostic imaging protocols for investigation of CM and SM.

| Area                              | Sequence                                                                 | Assessment of                                                                 |
|-----------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| **ESSENTIAL PROTOCOL**            |                                                                          |                                                                                |
| Brain and craniocervical junction  | - TW2 (high field) or T1W (low field) sagittal and transverse            | - Conformation brain and craniocervical junction                             |
|                                   |   - Maximum slice thickness 4 mm                                          | - CSF spaces                                                                 |
|                                   |   - Presence of SM, central canal dilation, spinal cord edema (presyrinx) | - Other differential diagnoses                                               |
| Cervical vertebral column         | - TW2 and T1W sagittal                                                   | - Measurement of maximum transverse width SM                                 |
|                                   |   - TW2 (high field) or T1W (low field) transverse with the block         | - Spinal cord dorsal horn involvement by SM                                  |
|                                   |     perpendicular to the spinal cord though the maximum width of the     | - CSF spaces including cisterna magna                                       |
|                                   |     syrinx if SM is present, or as a block centred on C3 and extending   | - Other differential diagnoses                                               |
|                                   |     from at least mid-point of the vertebral body of C2                 |                                                                                |
|                                   |   - Maximum slice thickness 4 mm                                          |                                                                                |
| Thoracic vertebral column         | - TW2 (high field) or T1W (low field) sagittal with or without transverse | - Presence of SM or central canal dilation                                   |
|                                   |     with the block perpendicular to the spinal cord though the maximum   | - Measurement of maximum transverse width SM                                 |
|                                   |     width of the syrinx if SM is present. Maximum slice thickness 4 mm    | - Spinal cord dorsal horn involvement by SM                                  |
|                                   |                                                                                | - Subarachnoid space                                                         |
|                                   |                                                                                | - Other differential diagnoses                                               |
| **ADDITIONAL OR ALTERNATIVE SEQUENCES** |                                                                          |                                                                                |
| Brain and craniocervical junction  | - Three-dimensional, T1-weighted, gradient-echo sequence (MPRAGE)       | - Used by the authors as an alternative to T1W spin echo sagittal and         |
|                                   |   - Maximum slice thickness 1mm.                                          |     transverse                                                               |
|                                   |   - Fluid-attenuated inversion recovery (FLAIR)                          | - To assess potential periventricular hyperintensive lesions for             |
|                                   |   - Maximum slice thickness 4 mm                                          |     example with acute hydrocephalus or inflammatory disease                 |
| Lumbar and lumbosacral vertebral column | - TW2 (high field) or T1W (low field) sagittal with or without transverse | - If neurolocalization suggests and/or SM extends caudally to lumbar spinal  |
|                                   |     with the block perpendicular to the spinal cord though the maximum   |     cord and to investigate spinal cord tethering by the filum terminale if  |
|                                   |     width of the syrinx if SM is present. Maximum slice thickness 4 mm    |     suspected                                                               |
| Area of suspected mass and/or     | - Paramagnetic contrast                                                   | - Cystic intramedullary tumours                                              |
| spinal cord edema of unknown       |                                                                                | - Other differential diagnoses                                               |
| anatomy                           |                                                                                |                                                                                |
| Vertebral column                   | - Half-Fourier acquisition single-shot turbo spin-echo (HASTE)            | - Used to some to make a more rapid assessment of the subarachnoid space     |
| Area of suspected arachnoid        | - Balanced steady-state free precession sequences (bSSFP)                |                                                                                |
| web/band/dilatation               | - MRI flow studies (Cine MRI)                                             | - Phase contrast cine MRI                                                   |
|                                   | - CT myelography                                                          | - Identify region of flow abnormalities/obstruction                         |
|                                   |                                                                                | - Prognostication                                                           |
|                                   |                                                                                | - Cine bSSFP                                                                |
|                                   |                                                                                | - Define the arachnoid webs or bands                                         |
|                                   |                                                                                | - If bSSFP and/or Cine MRI has not identified or not possible               |
|                                   |                                                                                |     because of metal implants and if owner/veterinarian wishes to           |
|                                   |                                                                                |     pursue possible surgical management                                       |

If the cause of CSF channel disruption is not apparent, then balanced steady-state free precession sequences (bSSFP) such as FIESTA (Fast Imaging Employing Steady-state Acquisition) or 3D-CISS (Three-Dimensional Constructive Interference in steady state) should be employed to improve detection of arachnoid webs and diverticulae (109, 124). These are a three dimensional gradient echo sequence that produces high contrast between the CSF and structures within the subarachnoid space. They have less flow void artifact associated with turbulent CSF and allow higher detection rates of arachnoid webs and other adhesions (102, 125) (**Figure 6**) and for low field MRI where obtaining good signal-to-noise and spatial resolution is a challenge, it is recommended that a bSSFP sequence be included in any protocol that evaluates the CSF channels (or disruption of) (109). Half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequences are heavily T2W sequences that produced a myelographic effect and can be obtained in a very short time. They are also described as being useful to detect arachnoid diverticulae (126). However, the trade-off for such short imaging times is lower spatial resolution and T2 blurring artifact.

MRI flow studies are an integral part of the diagnostic work up of CM and SM in human patients (14, 102) and for review of the clinical application for SM, arachnoid webs and the subarachnoid space see Li et al. (104). Standard MRI sequences of the brain and spinal cord assume that the tissue is static with movement only occurring in blood vessels and...
Type | Example | Notes
--- | --- | ---
Protocol | Slice thickness | In the sagittal plane thinner slices (3 mm or less) are preferred to achieve 2–3 sections through the spinal canal and more chance of lesion detection. Thicker slice thickness may miss a small intramedullary lesion in an dog with a spinal cord diameter ranging between 4.1 and 10.3 mm (depending on site imaged and size of animal) [107, 108]. However, MRI machines of 1 Tesla or less cannot provide thin slices with sufficient signal-to-noise ratio. Using a balanced steady state precession sequence (bSSFP) in addition to a conventional gradient echo and spin echo sequences may help overcome this challenge [109].
Sequence | Protocols that achieve both T1W and T2W weighting are required to be confident in detecting a fluid filled cavity within the spinal cord and conformational changes with CM. Anatomical imaging of the entire brain is recommended and full extent of the syrinx should be determined. Transverse images perpendicular to the spinal cord though the syrinx are required to assess the transverse width and extent of spinal cord involvement.
Magnetic field strength | Low field vs. high field | Signal-to-noise ratio and spatial resolution is improved when imaging with higher magnetic field-strength which allows shorter imaging times for a given resolution and/or higher resolution for a given imaging time. In addition, higher signal-to-noise ratio allows better resolution with smaller voxel size and thinner slice thickness [110].
Operator factors | Inexperience/lack of training | In veterinary medicine it is possible to operate a MRI service without any Specialist qualification. By contrast an experience MRI technician has undertaken a 3–4 year radiography degree plus additional post-graduate MRI training.
Diligence | | Out with other reasons for decreasing imaging time (economic/duration of anesthesia), operator inclination is a factor for example image quality can be improved by increasing the number of averages (NEX/NSA) which will subsequently increase the acquisition time.
Interpreter factors | Inexperience/lack of training | Failure to recognize significant lesions or over-interpretation of other features for example attributing SM to epilepsy, facial nerve paralysis, fly catching and other brain disorders or interpreting a generalized pruritus as due to SM.
In humans it is reported more likely that a cervical syrinx is missed with techniques for whole spine sagittal scanning with focused lumbar spinal MRI where the physician is biased from the history for a lumbar lesion [111]. Conversely, asymtomatic localized widening of the central canal may be observed in both humans and dogs [34, 112].
Patient factors | Skull and air interface | May cause susceptibility artifacts, especially on gradient echo sequences.
Small brain and narrow spinal cord | Slice thickness should be proportional to the brain volume to achieve images with diagnostic quality i.e., animals with smaller brain volume require thinner slices. In a low field MRI this may be challenging and a bSSFP sequence is recommended.
Positioning | Assessment for CM is normally obtained with the head in extension as reproducibility is easier and anesthesia is safer as the airway may be compromised in the flexed position [33]. However, cerebellar herniation and CSF space between the cerebellum and brainstem are significantly increased in the flexed position [113].
Microchips, orthopedic implants and shrapnel | Ferromagnetic materials cause susceptibility artifacts which may compromise interpretation especially identity microchips for studies of the cervical spine. In low field MRI a T1W turbospin echo sequence is recommended [114] and for high field MRI, spin echo sequences have smaller artifacts than gradient echo sequences [115]. Titanium or oxidized zirconium implants have less susceptibly artifact than cobalt-chromium alloy implants [116].
General anesthetic | Increased time under general anesthesia may increase risk to patient and cost thus limiting length of any MRI protocol.
Motion related artifacts | Neural tissue | Standard MRI sequences are optimized for good spatial and contrast resolution, however this results in blurring of moving structures which compromises the ability to detect fine structures such as arachnoid webs and other adhesions, septations in the syrinx or appreciate dynamic compression [104]. It may also blur the edges of a syrinx cavity.
Intrasyringal fluid flow void | Pulsatile or turbulent motion of fluid within the syrinx produces low signal on T2W images because of an absence of activated protons in that region [117].
Intraventricular CSF pulsation artifact | Intraventricular hyperintensity on FLAIR imaging which result in false—negative/positive interpretations of ventricular pathology and is a particular problem for FLAIR performed on low field MRI [118]. The most common cause is pulsatile movement and un-inverted CSF flowing into the slice between the pulses [119]. It can also occur because of inadequate inversion of CSF magnetization at the edge of the transmitted coil or because of increased CSF protein or oxygen (breathing 100% oxygen) which shortens T1 [119].
CSF and the aim is to achieve higher spatial and contrast resolution typically at the expense of temporal resolution. This results in motion-related blurring of non-static structures (104). Cine MRI uses cardiac gating using electrocardiogram or pulse oximetry. Phase-contrast cine MRI (Figure 7) measures pulsatile CSF motion influenced by the cardiac cycle and can measure both CSF and syrinx fluid velocities in a defined area of interest (102, 127). By contrast cine bSSFP allows appreciation of the movement of the central nervous system and structures within the subarachnoid space. The data for a single slice is acquired multiple times over the cardiac cycle with each single image corresponding to single point in that cycle (termed a cardiac phase). All the images are then viewed sequentially as a cine loop (104). Phase contrast cine MRI is used to localize CSF channel obstruction, to demonstrate improvement (or lack thereof) post-operatively and also has a role in prognostication. Syrinx fluid movement, as detected by phase contrast cine MRI, is associated with progressive neurological signs whereas lack of syrinx fluid movement is associated with no or stable neurological signs (102, 128). However, it does not allow visualization of arachnoid membranes and so in humans, and for investigation of idiopathic SM, Phase contrast cine MRI is used to localize the area of flow abnormalities/obstruction and cine bSSFP is used to define the arachnoid webs or bands (104).

In veterinary medicine, phase contrast cine MRI has been used to investigate CSF flow (80) and cine bSSFP used to investigate
cerebellar movement (76) (Table 3) but its application as a diagnostic tool has yet to be realized.

To make a diagnosis of symptomatic CM and or SM the diagnostic imaging should be related to the clinical history and examination findings.

**DIAGNOSIS OF CM-PAIN**

CM-pain is a difficult diagnosis because the clinical signs are non-specific and/or have alternative explanations but should be considered in a predisposed breed presenting with a signs...
suggesting pain such as; a history of vocalization described as without obvious trigger, when shifting position when recumbent and when being lifted under the sternum to a height; spinal pain; head and ear rubbing or scratching; refusal or difficulty jumping or doing stairs; exercise intolerance/reduced activity; sleep disruption; or behavioral change described as becoming more anxious, aggressive, or withdrawn (48). Morphometric studies found CM pain was associated with increasing brachycephaly with shortening of the skull base with rostroventral overcrowding resulting in rostral flattening of the forebrain, reduction and ventral displacement of the olfactory bulbs and increased height of the cranium, especially in the occipital region (39). There may be changes suggesting obstruction of CSF channels including reduction in the cranial and spinal subarachnoid space in addition to ventriculomegaly of all ventricles and cisterns except the cisterna magna which is often reduced (Figure 7). The craniocervical changes are less pronounced than in SM affected dogs and indeed this feature is hypothesized to protect this cohort from developing SM (39). Ultimately the diagnosis must be made by ruling out other causes of pain in combination with consistent clinical and MRI findings. A guide is suggested in Figures 5, 8.

**DIAGNOSIS OF SYMPTOMATIC SM**

The diagnosis of SM implies a fluid filled cavity related to disturbance of CSF flow, spinal cord tethering or intramedullary tumor; it is not an appropriate description for myelomalacia or cystic lesions (14). SM can be asymptomatic (34) and when interpreting MRI, an assessment should be made as to whether the location and severity of the syrinx would account for the signs. Signs of an “active” and filling syrinx include fluid signal-void sign within the syrinx cavity indicating pulsatile or turbulent flow (green arrow) and a pre-syrinx (edema) and central canal dilatation in the caudal thoracic spinal cord (red arrow). (C,D) The syrinx has progressed to holocord SM (red asterisk). Although conclusions cannot be drawn without pressure measurements, it is interesting that MRI signs that can suggest elevated intra-cranial pressure (129) and fluid surging and pulsation within the syrinx (117) are diminished with an appreciably greater cranial subarachnoid space indicated by high signal CSF within the sulci (blue asterisks) and less fluid signal-void sign within the syrinx (Siemens Magnetom Symphony, A Tim System, 1.5 T, Erlangen, Germany).
contralateral to the head tilt (48, 87). Phantom scratching is associated with extension to the superficial dorsal horn ipsilateral to the scratching side in the C3-C6 spinal cord segments (corresponding to C2-C5 vertebrae) (88). A guide is suggested in Figures 5, 8.

CONCLUSION

Diagnosis of CM-pain is made by appropriate clinical signs in addition to MRI brain findings of a brachycephaly with rostroventrotentorial crowding including rostral flattening, olfactory bulb reduction and rotation, increased height of the cranium with reduction of the functional caudotentorial space and hindbrain herniation. There may also be changes suggesting raised intracranial pressure such as loss of sulci definition with ventriculomegaly. The cisterna magna is reduced. In addition to these brachycephalic changes, dogs with SM are more likely to have craniovertebral junction abnormalities including rostral displacement of the axis and atlas with increased odontoid angulation causing craniospinal deformation and medullary oblongata elevation. Symptomatic SM is diagnosed on the basis of signs of myelopathy and presence of a large syrinx that is consistent with the neuro-localization. The imaging protocol should establish the longitudinal and transverse extent of the syrinx. If the cause of CSF channel disruption is not revealed by anatomical MRI then other imaging techniques such as bSSFP sequences may be appropriate.

AUTHOR CONTRIBUTIONS

CR: concept and original draft. FS: editing and reviewing draft. SK: graphics, editing, and reviewing draft.

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SUPPLEMENTARY MATERIAL

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Supplementary Table 1 | MRI parameters for a CM and SM specific protocol on a 1.5T machine.

Supplementary Figure 1 | Duplicate of Figure 5 with a higher resolution.

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