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Syringomyelia in Dogs

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Introduction

I first experienced the disease Syringomyelia twelve years ago, when our Cavalier King Charles Spaniel was diagnosed. Ruby was our much loved family pet. From her diagnosis and through her treatment I have always been very curious and intrigued as to what caused her condition and what it all meant. This all led to the decision of embarking a journey to learn and find out more about this topic.

Syringomyelia is a complex disease which can manifest itself in rather unspecific clinical signs. In this thesis work I wish to compile a clear summary but detailed explanation of the pathophysiology leading to this unusual presentation. The easily misinterpreted clinical signs are an important aspect I wish to cover as they are key to obtaining early diagnosis and to provide the dog treatment as soon as possible, which would potentially improve its quality of life.

As I experienced this disease through my dog with Syringomyelia I encountered some of the medical management options, however I am now keen to discover the reasoning for the use of each medication.

Probably one of the main aims to me, which I have developed as I have progressed towards completing my studies and soon to graduate to become a first opinion veterinarian, is on how can I improve my practise with regard of this topic and the use I will make of the information learnt in this work. I am hoping that at the end of this project I will be able to add the knowledge obtained by compiling this information into my everyday career as a general practitioner.

I will additionally discuss alternative diagnostics tools in normal practice and the role of the veterinarian to be able to educate owners and breeders to improve the quality of their pets life and also to future generations of breeds affected by this disease, to promote ways to reduce the occurrence of Syringomyelia.

Brief Background of the Disease

Syringomyelia (SM) can be translated from Latin as ‘cavity within the spinal cord’ with myelia meaning spinal cord and a syrinx being a pathological cavity. It has also previously been known as Syringo-Hydromyelia (SHM) or Hydro-syringomyelia. Hydromyelia is defined as a dilation of the central canal within the spinal cord which can lead to a cavity formation with accumulation of cerebrospinal fluid. Whereas, a syrinx is an acquired fluid filled cavity either within the spinal cord (Syringomyelia) or within the brainstem (Syringobulbia). A syrinx can either be communicating or non-communicating, depending on whether there is a connection to the cerebrospinal fluid pathways. SM was first investigated and identified by veterinary neurologists in the 1990’s, while some literature anecdotally reports the stereotypical symptoms of the disease such as the air scratching in the 1980’s. At the time it was noted of a great similarity to Arnold Chiari Type I Syndrome in humans, however with some marked differences it is not identical to it. (1)

Syringomyelia is recorded as one of the most common spinal cord disorders of the Toy Breed dogs, having being documented in the following breeds: Cavalier King Charles Spaniel, King Charles Spaniel, Griffon Bruxellois, Yorkshire Terrier, Maltese Terrier, Chihuahua, Miniature Dachshund, Miniature and Toy Poodle, Bichon Frise, Pug, Shih Tzu, Pomeranian, Staffordshire Bull Terrier, Boston Terrier, Pekingese, Miniature Pinscher and French Bulldog. There has been no measurement of the prevalence of SM in mixed breed type dogs. (2) Of this list of toy breeds that have been recorded to having cases of SM, the breeds showing exceedingly high prevalence are the Cavalier King Charles Spaniel (CKCS), with reports of up to 70% of the total population affected by the condition although many being asymptomatic. The Griffon Bruxellois with a reported 50% of its american population affected also with many asymptomatic of the disease. Maltese, Chihuahua and Pomeranians breeds also been shown to have high prevalence of the disease.

Syringomyelia is a disease that occurs in both humans and animals (cats and dogs), however the prevalence in humans is rather low in comparison to that in animals, with about one case in 10,000.(3)

SM is described as a severe progressive disease characterised by pathological fluid filled cavities called syrinx (if multiple lesions syringes) within the spinal cord. The formation of

these cavities is associated with obstruction of the cerebrospinal fluid (CSF) channels and the subarachnoid space (SAS), especially if the obstruction is located around the foramen magnum. (3) This then can lead to an explanation of why it is primarily toy breed dogs that are predisposed to this disease, as especially dogs with brachycephalic head types are shown to have particular prevalence of the Chiari-Like malformation, the most common cause of foramen magnum obstruction. Dr. Hans von Chiari was a pathologist who in 1891, classified different congenital malformations in human infants that lead to the condition now known as Syringomyelia. Sometimes it is referred to as Arnold-Chiari syndrome in humans, this originated from Dr. Arnold, who studied extensively cases of Syringomyelia. Terminology of this disease is often misused as although the Chiari malformation is the most frequently seen and famous cause of Syringomyelia, it is not exclusively the only cause of the disease so the terms should not be used interchangeably. As there is great similarity in the pathogenesis and anatomy of the malformation between humans and in veterinary patients, there are also differences so it has been questioned whether the term is appropriate to be used in veterinary fields. This led to the use of the current term of Chiari-Like malformation in animals. (4)

Figure 1: Below shows the most common breeds that Syringomyelia is found. Pomeranian (top left) Griffon Bruxellois (top right) and Cavalier King Charles Spaniel (bottom).



Theories of the Pathogenesis of Syringomyelia

Syringomyelia has been proven to be caused by a variety of primary problems. These include abnormalities of the caudal fossa (the Chiari malformation), tethered spinal cord, trauma, inflammation of the arachnoid matter or by neoplasia.

There has been multiple studies and theories proposed for the pathogenesis of Syringomyelia, I will discuss a few of the theories put forward.

Pathophysiology of Chiari-Associated Syringomyelia

As previously mentioned, Dr. Hans von Chiari was a pathologist in Prague who described four types of abnormality in the skull based on autopsy of infants with hydrocephalus. Type I malformation was detailed as “elongation of the cerebellar tonsils and the medial part of the inferior cerebellar lobes into cone-like projections, which accompany the medulla into the spinal cord.” Over years the description of the malformation was developed but still known associated with Chiari’s name, now referred to as the Chiari malformation. It is used to describe a wide range of abnormalities not all consistent with the original description of the type I malformation but all characterised by a reduced posterior fossa volume with caudal descent of the cerebellar tonsils and the brainstem. Although, the condition is very similar in the dog, characterised by decreased volume of the caudal fossa and caudal displacement of the caudal cerebella vermis into or through the foramen magnum, there has been some debate as to whether the term Chiari malformation can be used appropriately in the dog. This being because anatomically it is inconsistent with the description, with dogs not having cerebellar tonsils. It has been also explained as more correct to use an anatomical description such as occipital hypoplasia with Syringomyelia or caudal occipital malformation syndrome. (5)

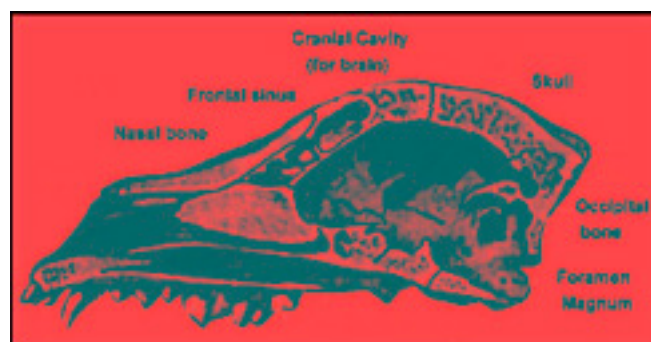


Figure 2: Lateral view of inside the skull cavity.

The cause of caudal occipital malformation syndrome is unknown, but is it most likely to be a genetically transmitted developmental disorder of the occipital bone mesoderm. In recent studies it has been proposed that the syndrome in Cavalier King Charles Spaniels is inherited as an autosomal recessive trait. The tissue i.e. cerebellum, brain stem are normal, but due to the malformation, they are crowded into an abnormally small caudal fossa. This leads to some level of cerebellar compression and also constriction of the cervicomedullary junction at the level of the foramen magnum. The bony compression and probable turbulent flow associated with pressure changes of the cerebral spinal fluid is believed to cause meningeal hypertrophy. This focal meningeal hypertrophy in turn causes the progression of the constrictive effect. Syringomyelia is a common sequela to Chiari malformation and thought to be consequence of abnormal cerebrospinal fluid dynamics. In the normal dog, cerebrospinal fluid flows caudally and rostrally between the head and vertebral column. This rapid influx and efflux results from the cardiac cycle variations of contraction and expansion of the intracranial arteries. If there is obstruction by the cerebellum at the foramen magnum in the subarachnoid space this can lead to the development of Syringomyelia. (5)

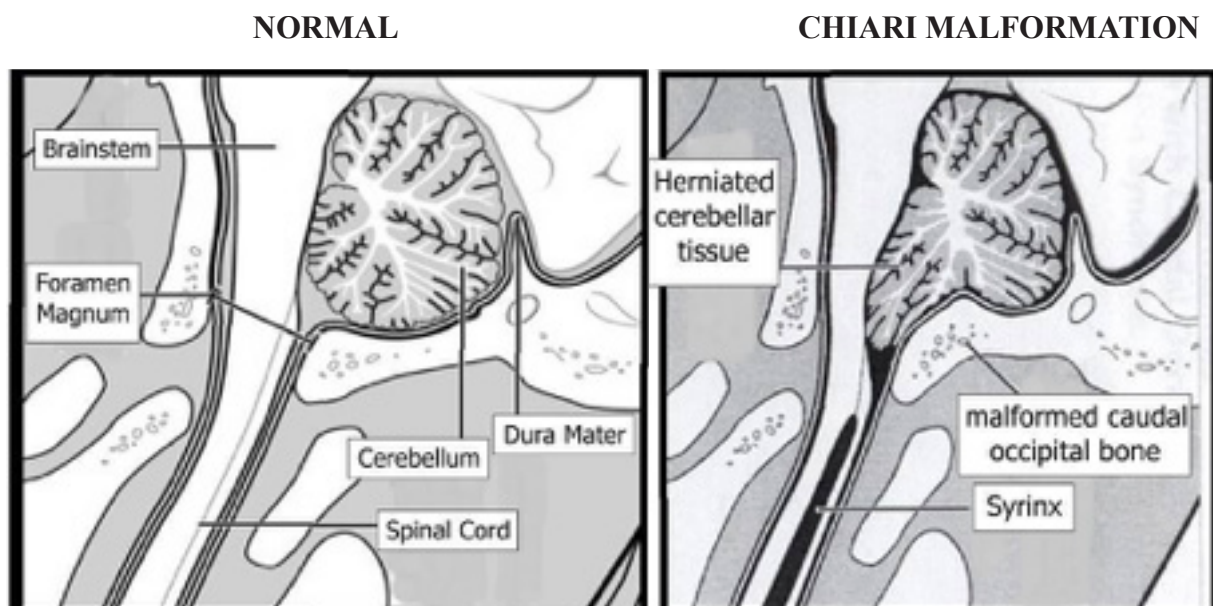


Figure 3: Diagram illustrating the Chiari malformation in the foramen magnum in comparison with the normal anatomy. The herniated cerebellar tissue is shown and also the possible location of a cervical syrinx which is the most common place for them to develop.

Theories of the involvement of cerebral spinal fluid in Syringomyelia

There are numerous theories to explain the development and progression of Syringomyelia and common to those theories is an obstruction of normal cerebrospinal fluid flow at the level of the cervicomedullary junction. The theories proposed hypothesise the pathophysiology behind the formation of a syrinx.

Cerebrospinal fluid makes up 10% of the intracranial fluid volume and is produced at a relatively constant rate, regardless of intracranial pressure, by the transport of water, potassium, chloride and bicarbonate from the choroid into the ventricles. The pathway of the cerebrospinal fluid flow starts in the lateral ventricles, courses through the inter-ventricular foramen and into the third ventricle. From there it passes through the mesencephalic aqueduct into the fourth ventricle. The majority of cerebrospinal fluid passes into the subarachnoid space through the lateral apertures adjacent to the foramen magnum, however a small fraction also passes through the central canal. Body position, physical activities, gravity, blood pressure and accelerating forces all influence the flow rate, pressure and drainage of the cerebrospinal fluid. Alterations in the cerebrospinal fluid have been implicated as a major contributing factor to the development of Syringomyelia and there are several theories as to how this may occur. (7)

In a normal dog, during systole there is pulsatile cerebrospinal fluid flow across the foramen magnum from the intracranial subarachnoid space to cervical spinal subarachnoid space and back again during diastole. If there is an obstruction, the cerebrospinal fluid does not flow well in either direction. (6) This is the first hypothesis called the ‘water-hammer theory’ suggested when systolic cerebral spinal fluid outflow from the fourth ventricle and flow through the foramen magnum were obstructed thus the cerebrospinal fluid from the ventricle was forced into the central canal with each arterial pulse causing the central canal to dilate leading to a syrinx. This theory however was flawed as it was prior to the arrival of the magnetic resonance imaging, meaning it is not supported by clinical evidence as not all patients have a patent connection between the fourth ventricle and the central canal. Although small mammals such as dogs are more likely to have a patent connection, there is a lack of evidence for this theory of a syrinx developing after the cerebrospinal fluid is forced into the central canal. (5)

Another theory that was proposed was described as the ‘suck effect theory.’: when intra-abdominal or intra-thoracic pressure is increased suddenly during manoeuvres such as coughing, sneezing, barking or exercising, a pressure difference is created between the head and the vertebral column. This change in intra-cranial and intra-spinal pressures due to epidural venous distension effectively mean that the intra-cranial pressure is higher than the cervical intra-spinal pressure, resulting in the ‘suck effect’ of the cerebrospinal fluid being drawn from the ventricles into the central canal.

However, this theory also relies on there being a connection between the fourth ventricle and central canal and implies lower pressure in a syrinx on the spinal cord whereas research has

shown that the pressure is higher in a syrinx than that outside of the spinal cord. If the syrinx pressure is higher than the cerebrospinal pressure this theory also seems implausible. (5)

Another common flaw discovered on further investigation of both these two proposed theories was the syrinx fluid was significantly lower in protein content than cerebrospinal fluid. This, along with the lack of communication between the fourth ventricle and the central canal lead to the theory of cerebrospinal fluid being forced into the spinal cord parenchyma through the perivascular spaces.(5)

The ‘slosh effect’ phenomenon caused by the combination of spinal epidural vein distension with resultant pressurisation of the subarachnoid space and obstruction to cerebrospinal fluid flow from the cervical spine to the intra-cranial compartment, may result in forcing subarachnoid cerebral spinal fluid down perivascular spaces into the spinal cord parenchyma. This leads to the cerebrospinal fluid ‘sloshing’ around, fissuring surrounding parenchyma and enlarging the fluid cavity causing the formation of a syrinx. Contradictions for this theory include two main arguments of that it relies on cerebrospinal fluid being forced into the spinal cord from the subarachnoid space and if this were true, if such a force was put on the soft spinal cord from the outside it would be more likely to be crushed than expand with a syrinx. (5)

All these previous theories of the pathophysiology are based around Chiari malformation associated Syringomyelia. Another theory proposed called the ‘intramedullary pulse pressure theory’ developed based on experimental work in laboratory rodents. This is one of the first general theories to provide an explanation of the pathophysiology regardless of aetiology. Other possible aetiologies being: post-traumatic Syringomyelia, arachnoiditis, Syringomyelia secondary to tumours in the caudal fossa or vertebral canal. This theory’s main principle suggests that Syringomyelia is secondary to repeated mechanical distension of the spinal cord and that cavitation arises from the extracellular fluid originating from the high-pressure system in the microcirculation of the spinal cord and not the cerebrospinal fluid from the low-pressure system in the arachnoid space.

The systolic cerebrospinal fluid pulse pressure, defined as the pressure waves of the cerebrospinal fluid displaced from the head during arterial pulsations, are shown to be the driving force of Syringomyelia in this theory of pathogenesis. When the subarachnoid space is obstructed, there is a significant decrease in pressure transmission to distal cerebrospinal fluid spaces. This consequently means there is increased transmission and reflection of the systolic cerebrospinal fluid pulse pressure into the spinal cord tissue in close proximity to the obstruction.

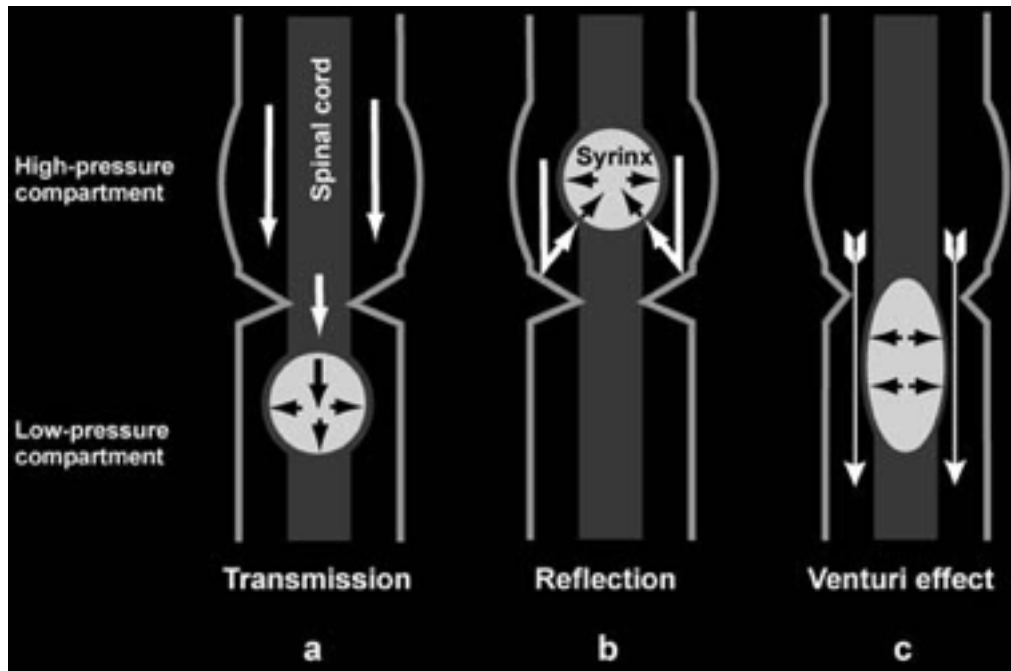


Figure 4: Diagram illustrating the possible consequences of subarachnoid adhesions (post-traumatic Syringomyelia) causing a fixed type of obstruction that decreases the transmission of systolic cerebrospinal fluid pulse pressure (the pressure wave of cerebral spinal fluid displaced during systole) distal to the obstruction.

As illustrated in the above diagram, the intra-medullary pulse pressure theory suggests during transmission the systolic cerebrospinal fluid pulse pressure (represented by the white arrows) is transmitted through the spinal cord at the obstruction. The increase of spinal cord pressure and decrease in subarachnoid pressure results in distension of the spinal cord just below the obstruction (black arrows) leading to the formation of a syrinx. Simultaneous to this transmission, is the reflection of part of the systolic cerebrospinal fluid pulse pressure, which is reflected into the spinal cord at the obstruction resulting in an increase in spinal cord pressure and consequently causing distention of the spinal cord just above the obstruction. This can also occur in partial subarachnoid obstructions, where the cerebrospinal fluid flow decreases the hydrostatic pressure in the cerebrospinal fluid (Venturi effect) which in turn distends the spinal cord. Syringomyelia develops by the collection of extra-cellular fluid in the distended spinal cord. (5)

The partial obstruction of the subarachnoid space such as the Chiari-like Malformation causes the Venturi effect (also known as the Bernoulli's theorem) which states that mechanical energy of flowing fluid remains constant. Meaning that in this case of a narrowed subarachnoid space with increased velocity there is a decrease in the hydrostatic pressure in the fluid resulting in distension of the spinal cord.

Repeated mechanical distension of the spinal cord results in dilatation of the central canal and accumulation of extracellular fluid which forms the syrinx. The Venturi effect also explains why Syringomyelia can develop at distances from the obstruction of the cerebrospinal fluid flow.

In Chiari malformations, most commonly there is formation of a syrinx in the cervical region, however, there can also be formation of syringes at any point of the spinal cord even at the medullary conus. This is due to the extended Venturi effect causing increased systolic pressure transmission to the spinal subarachnoid space meaning a shock-like pressure wave is created, which effects all parts of the vertebral canal. (7)

The latest proposed theory by Levine in 2004 is called the 'Vascular theory.' It postulates that in the event of a foramen magnum obstruction, there is a transient higher cerebrospinal fluid pressure above the obstruction than below it. This consequently leads to the dilation of blood vessels below the obstruction and collapse the ones above it, producing mechanical stress on the spinal cord especially caudal to the obstruction. The venous and capillary dilation along with the mechanical stress partially disrupts the blood-spinal cord barrier, allowing ultrafiltration of crystalloids and accumulation of a protein deprived fluid. Essentially, this theory is an expansion of the 'intramedullary pulse pressure theory', it also offers an explanation of why the syrinx pressure is higher than the cerebrospinal fluid pressure and why the composition of syrinx fluid is not identical to that of cerebrospinal fluid.

Despite substantial research focusing on the pathogenesis of Syringomyelia and multiple theories providing partial explanation, the development of further theories which cause contradictions to previous hypothesis means that it still remains unclear. The main debates amongst the studies seem to be:

- Does a syrinx form due to an increase of pressure in the subarachnoid space or because of raised pressure within the spinal cord?
- What is the source of the fluid within the syrinx - cerebrospinal fluid or extracellular fluid?

Despite extensive research on the above theories, it is still a huge topic of debate to what really explains the mechanism of syrinx formation.

Clinical signs

The most important and consistent clinical sign in Syringomyelia affected dogs is pain. Pain syndromes in dogs are challenging to identify and manage because of the subjective behaviour. Veterinarians must rely on owner observations and physical examination findings to assess the pain grade in the dog. Not only is it difficult to interpret the pain displayed in the dog, it is also challenging as there is various types of pain associated with this disease. (8)

Syringomyelia also occurs in humans, often as the result of a Chiari type I malformation similar to that seen in dogs. 50-90% of human patients report pain as a prominent feature, with around 40% reporting unpleasant burning, tingling to stretching sensations. Similarities in pathogenesis between human and animal Syringomyelia, the fact that pain is a central characteristic of the disease in humans and the nature of the behavioural clinical signs seen in dogs, strongly suggest that Syringomyelia is painful in dogs. (9)

The behaviours and clinical signs expressed by the dog can be dependent on the location of the syrinx in the spinal cord, both throughout its length and in cross sectional structure.

The figures below illustrate the normal anatomy of the spinal cord, including its pathways and relevant functions.

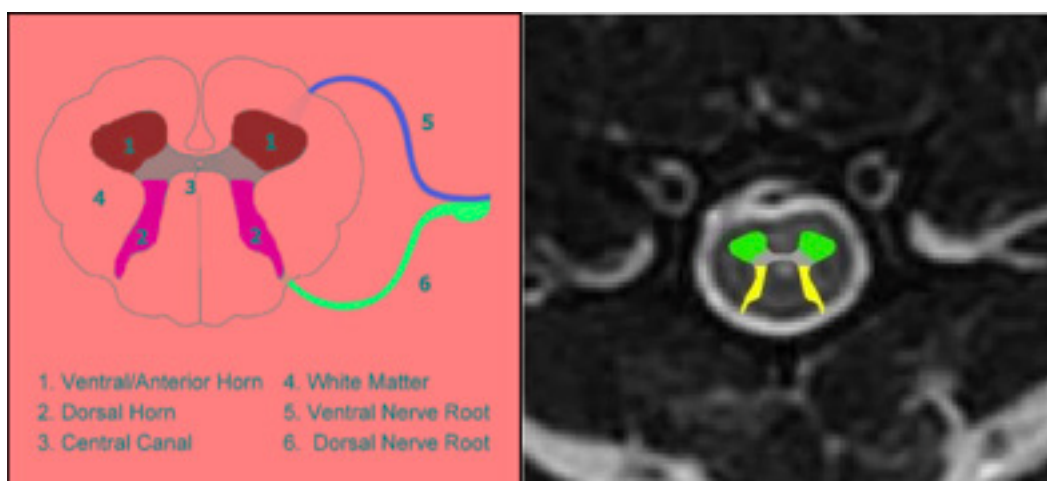


Figure 5: Transverse cross section of the spinal cord illustrating the Grey matter and White matter. The grey matter is the central ‘butterfly’ shaped area of the spinal cord containing the neurones. The White matter is the tissue through which messages pass between different areas of grey matter.

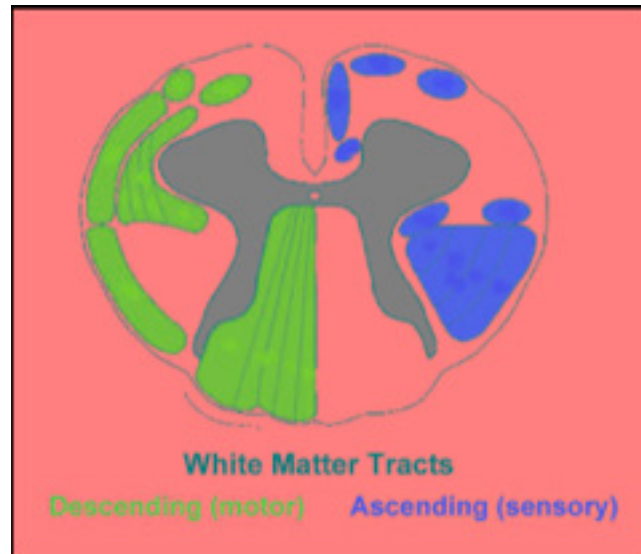


Figure 6: A simplified diagram illustrating the spinal pathways. Ascending pathways located in the dorsal horn provided sensors information such as pain, touch, temperature, vibration and proprioception. The descending pathways located in the ventral horn are for the motor function such as movement control.

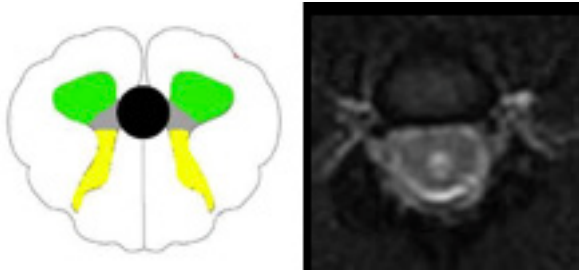
A study showed that the pain displayed in Syringomyelia was related to the syrinx location, width and symmetry. Dogs with a wider, asymmetrical syrinx are more likely to experience pain and dogs with a small, narrow syrinx may be asymptomatic.

Syrinxes that damage the ventral horn may result in neurological deficits such as decreased spinal reflexes, muscle atrophy and limb weakness. Whereas, syrinxes that invaded and damage the dorsal horn of the grey matter are most likely to cause consistent pain. It has also been found that the larger the width of the syrinx, the more likely the dog would exhibit pain and scratching. (10)

Pain can be divided into three categories: physiological, inflammatory and neuropathic. Physiological pain such as the pain in response to a needle prick serves to protect the animal from injury. Inflammatory pain is caused as a consequence to a tissue damage. Neuropathic pain is a clinical syndrome of pain due to abnormal somatosensory processing in the peripheral or central nervous system and may include spontaneous pain, paraesthesia, dyesthesia, allodynia or hyperpathia. Paraesthesia is a spontaneous or evoked abnormal sensation (not unpleasant), whereas dyesthesia is a spontaneous or evoked abnormal sensation but it described as unpleasant often as a burning sensation. Allodynia is pain from a stimulus that is not normally painful such as a light touching of a collar or harness in a particular area. Hyperpathia is the experience of increased pain than expected from stimuli which are painful. The pathophysiology of these neuropathic pains are complex and incompletely understood. (11)

Figure 7: Below is a series of simplified cross section diagrams to illustrate how the location of the syrinx, its size and symmetry effects the presentation of clinical signs of Syringomyelia.

Green: ventral horn of the grey matter. Yellow: Dorsal horn of the grey matter. Black: the syrinx.



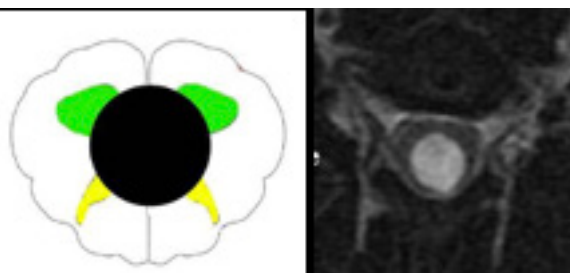
➡ Small syrinx not affecting dorsal or ventral horns likely to be asymptomatic. You can see the narrow syrinx in the MRI scan image.



➡ Syrinx affecting ventral horn meaning the motor functions will be affected.



➡ Syrinx affecting dorsal horn only meaning that pain to be the greatest symptom.



➡ The syrinx is large and spread into both the dorsal and ventral horns meaning there will be display of pain and motor function symptoms. The MRI image shows a large syrinx in the spinal cord.

Analysis of MRI scans to show the location, width and symmetry of the dog's syrinxes allow the veterinarian to estimate the clinical signs expected by the dogs behaviour. However, this is not accurate due to the variety of pain scoring and response to pain in animals. Therefore, the veterinarian is also relying on the owners reports of the animal behaviours and clinical signs to determine the grading of the disease.

The most common reported symptoms noticed by the owners of dogs diagnosed with Syringomyelia are:

- Crying out/vocalisation in pain
- Phantom scratching of the neck, flank or ear (The paw does not make contact with the skin)
- Rubbing of the face on the floor
- Sensitive to touch on one side the head, neck, shoulder or sternum
- Unable to tolerate wearing a collar on the neck
- Aversion to touch or grooming
- Reduced activity
- Reluctance to jump or climb stairs
- Weakness
- Muscle atrophy
- Ataxia/ Incoordination
- Excessive licking of paws
- Sleeping with head in raised position
- Scoliosis
- Aggression or change in behaviour towards owner or other dogs
- Becoming restless during the night/sleep disruption
- Change in facial expression demonstrating pain
- Repetitive tongue licking, repetitive barking

Owners may report that their dog's symptoms are worse at night, when first getting up, during hot or cold temperature extremes, when excited or related to posture. Due to varying demonstration of clinical signs amongst the affected dogs, the owners opinion is incredibly important in determining the pain of the animal.

A study was undertaken, in which questionnaires were filled out by dog owners to capture owner-reported clinical signs and compare them with the presence of pain on neurological examination and of Syringomyelia on magnetic resonance imaging. The questionnaire was divided into two parts: medical history and clinical signs related to Syringomyelia. The medical history portion consisted of 10 questions mostly yes/no answers. The clinical signs portion consisted of 12 questions relating to the frequency, location, lateralisation of signs, severity and types of clinical signs observed at home. Questions about frequency had the format of the following answer choices: more than twice daily, once or twice daily, once or twice a week, or not at all. For severity of discomfort associated with scratching a scale of 0-10 was used 0 being no discomfort and 10 extreme discomfort. The owners were also asked to complete diagrams outlining the areas on their pets they considered affected by pain or scratching. From this the veterinarians were able to complete their study of pain and scratch scores compared to the Syringomyelia demonstrated on the dog's MRI scan. (12)

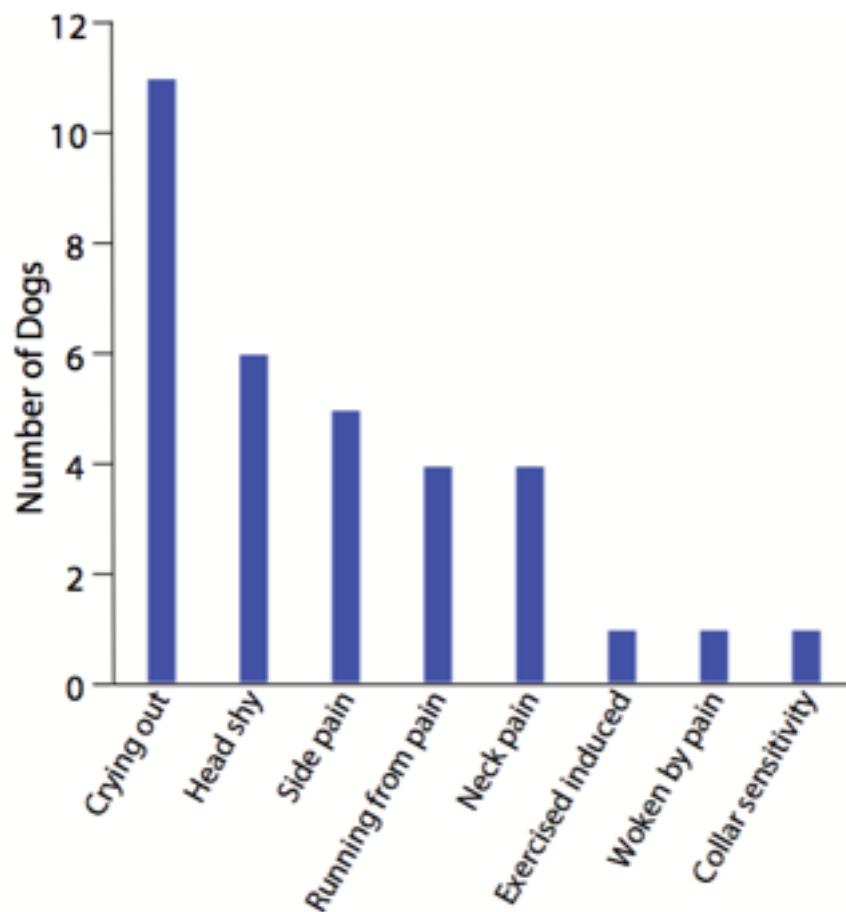


Figure 8: The range and frequency of pain signs reported by owners of dogs with Syringomyelia. Number of dogs in the study was 50.

Diagnostics

As with many diseases there are multiple diagnostic tools you can use to reach a conclusion. Each have their advantage and disadvantages. MRI scan is the 'gold standard', however this may not always be used in first opinion practice or be available to all patients so I will also explain the aspects of other forms of diagnostic tools.

Radiography

Radiographs are not indicated for the investigation of Chiari-like malformation and Syringomyelia. However, in first opinion practice it is the first line of investigation by the general practitioner in the work-up for cervical pain. There may be features noticeable that are suggestive of Chiari like malformation and Syringomyelia such as flattened supra-occipital bone and close proximity of the atlas to the skull. In case of severe Syringomyelia, there may be widening of the cervical spinal canal, remodelling and scalloping of the vertebrae due to increased intraspinal pressure. Scalloping of the vertebrae is a change in the configuration where there is an exaggeration of the normal slight concavity of the dorsal surface of the body of the vertebrae. Radiographs may be indicated to assess the atlantoaxial joint especially if surgical treatment is planned. (13)

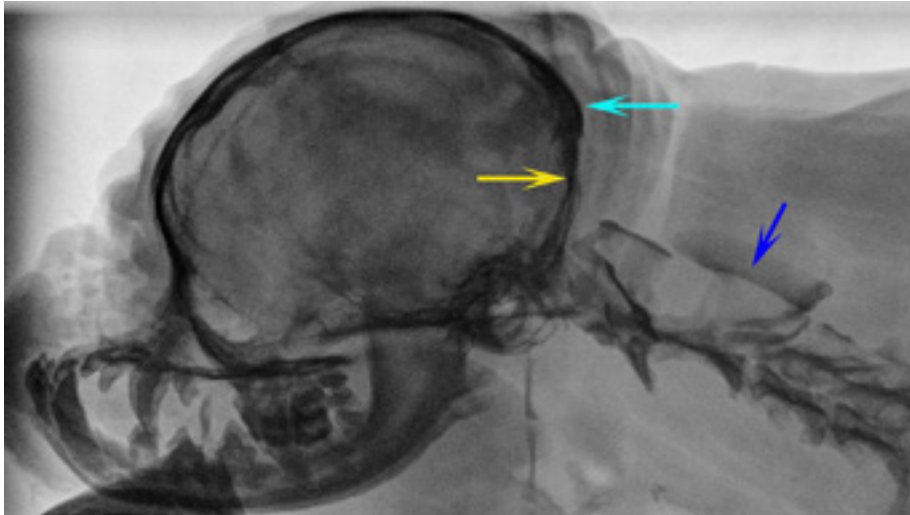


Figure 9: Lateral skull and cranial cervical spinal radiograph of a 6 year old Griffon Bruxellois. It can be observed that the skull has rostral-cranial doming and a ‘copper beaten’ appearance due to convoluted markings relating to the gyri of the brain caused by presumed raised intracranial pressure. The light blue arrow shows the small occipital crest and the supra-occipital bone is flattened shown by the yellow arrow. The dark blue arrow notes a large cervical syrinx which has resulted in widening of the cervical spinal canal with thinning and scalloping of the vertebrae.

Ultrasonography

The next diagnostic tool which is readily available in first opinion practices is ultrasound. Although it is not routinely used for examination of the spine, the atlanto-occipital junction provides a small acoustic window through which the craniocervical transition can be examined. It may be a highly skilled procedure, however sonography could be a reliable method for assessing cerebellar displacement.

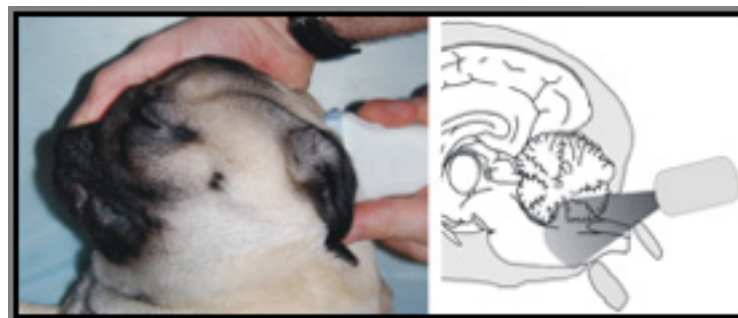


Figure 10: Schematic illustration of the transducer placement for visualising the craniocervical junction.

In a study of using ultrasound in detection of Chiari-Like malformation and Syringomyelia, twenty-five Cavalier King Charles Spaniels underwent a general anaesthetic for both magnetic resonance imaging and sonography to be able to compare the difference in grading the disease in both diagnostics. All dogs had changes consistent with caudal occipital malformation

syndrome such as cerebellar displacement into the foramen magnum, kinking of the medulla oblongata and indentation of the occipital bone. Sonographic detection of caudal cerebellar displacement was the most visible in the sagittal plane. The obex of the medulla, which represents a small medullary fold overhanging the caudal tapering end of the fourth ventricle, can be used as a leading structure for the caudal border of the hindbrain and the rostral edge of the foramen magnum. The decent of the cerebellum beyond this point into the foramen magnum could be identified by visualisation of a triangular shaped hypo-echoic structure with hypo-echoic margins dorsal to the spinal cord and ventral to the echogenic interface of the occipital bone. It was found that twenty-one of the cavaliers had mild displacement of the cerebellum which was 2mm caudal to the foramen magnum and four had marked displacement >2mm caudal to the foramen magnum. The study concluded that the grade of displacement assessed sonographically did not differ from the grade assessed in magnetic resonance imaging. (14)

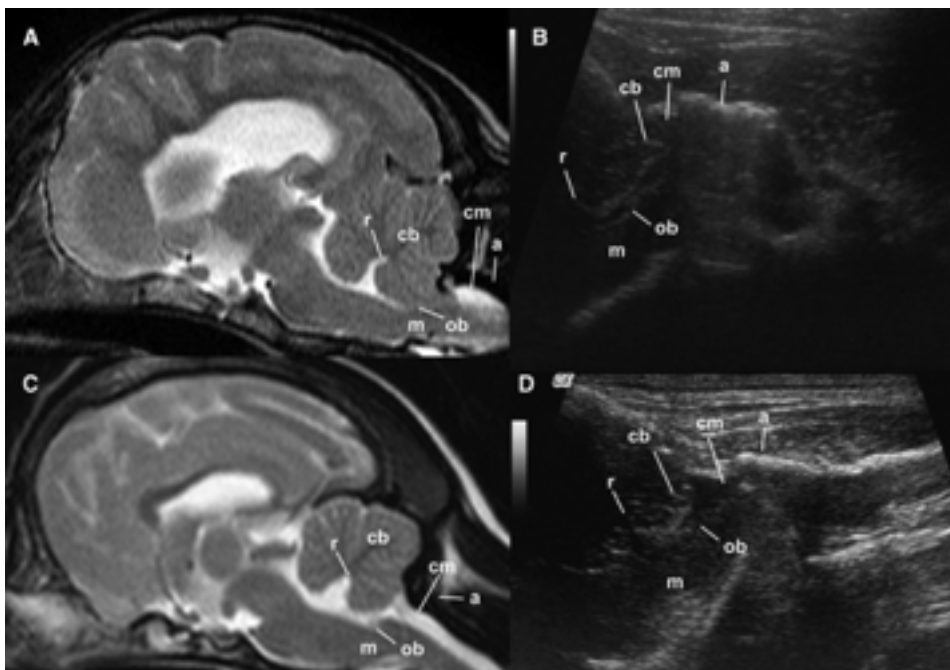


Figure 11: Mid-sagittal images of the brain. Top with cerebellar herniation and bottom without herniation. Images of MRI of each dog (A,C) matched with ultrasonographic images (B,D) centred at the caudal fossa. In figure 10B you can see a hypo-echoic structure with hyper-echoic margins triangular (label cb) in shape dorsal to the spinal cord and ventral to the occipital bone. This represents the herniated cerebellum in the foramen magnum. Labels: a-atlas, cb-cerebellum, cm-cisterna magna, m-medulla, ob-obex, r-recess of the fourth ventricle.

Computed Tomography (CT)

Most use of CT in the investigation of Chiara-Like malformation and Syringomyelia have been linked with research rather than clinical practise. It should be performed if a vertebral malformation is suspected in associated with Syringomyelia especially if implanted surgical fixation is likely to facilitate the planning of this procedure. Although, CT has limited value in assessing Chiara-Like malformation and Syringomyelia other than confirming a cerebellar herniation and defining craniocervical junction abnormalities, it could hypothetically have a role in the future in health screening pedigree dogs assuming accurate morphometric analysis can be translated from MRI studies especially if risk of future disease could be predicted. (13)

Magnetic Resonance Imaging (MRI)

As mentioned previously MRI is the gold standard choice of diagnostics and essential for the investigation of Chiara-Like malformation and Syringomyelia.

Syringomyelia diagnosis on MRI include six aims for the veterinarian:

- 1) To assess and document any anatomical changes seen.
- 2) To determine the cause of the Syringomyelia, as it is an acquired diseases which occurs secondary to disruption of cerebrospinal fluid flow, thus aim is to determine the site of that obstruction.
- 3) To assess the full extent of the disease and apply relevant grading system.
- 4) To eliminate other potential causes of the clinical signs presented or any other neurological problems such as intervertebral disc disease as an alternative explanation for spinal pain.
- 5) To asses whether the clinical presentation is consistent with the neurological localisation and severity, such as forebrain signs such as seizures or cranial nerve deficits cannot be explained by diagnosis of Syringomyelia in the spinal cord.
- 6) Finally to determine if other diagnostic modalities are recommended, such as a CT scan to characterise and assess bony abnormalities that may require surgical stabilisation. (13)

The British Veterinary Association (BVA) with the Kennel Club have developed a canine health scheme called the Chiari malformation/ Syringomyelia scheme with the aim to reduce the incidence of inherited Chiari malformation and Syringomyelia in dogs. This scheme requires magnetic resonance imaging (MRI) examination of the brain and cervical region. Although most dogs involved in the scheme will be pedigree toy breeds, the scheme is open to all dogs with relevant symptoms. The BVA and the Kennel Club aim to work along with breeders of breeds at risk of the disease to reduce to incidence. Breeders involved will be demonstrating the highest standards of testing for Chiari malformation and Syringomyelia and are doing their best to promote good health and welfare in the dogs they breed. It also allows buyers to verify that the parents of their new puppy have been MRI scanned. Potential buyers can therefore gain reassurance that they are buying from breeders who are performing all the recommended tests for this disease and are using the suggested breeding protocols. (15)

A number of veterinary centres which provide MRI services are familiar with the canine health schemes, this means they can follow the protocol recommended to ensure adequate quality of the images. Digital Imaging & Communication in Medicine (DICOM) is used for security reasons as it means it not possible to separate clients details from the images. All dogs taking part in the scheme must have permanent identification such as microchip or tattoo which must be verified as the correct details beforehand. There is a minimum age for a dog to enter the scheme, this being one calendar year but there is no upper age limit. As Syringomyelia is a progressive disease, which worsens with age, scanning is best performed at five years of age or older, however this often too late for pre-breeding screening. Therefore, it is recommended that breeders consider scanning their dogs prior to breeding regardless of the age, and possible in multiple occasions due to disease being more evident with time.

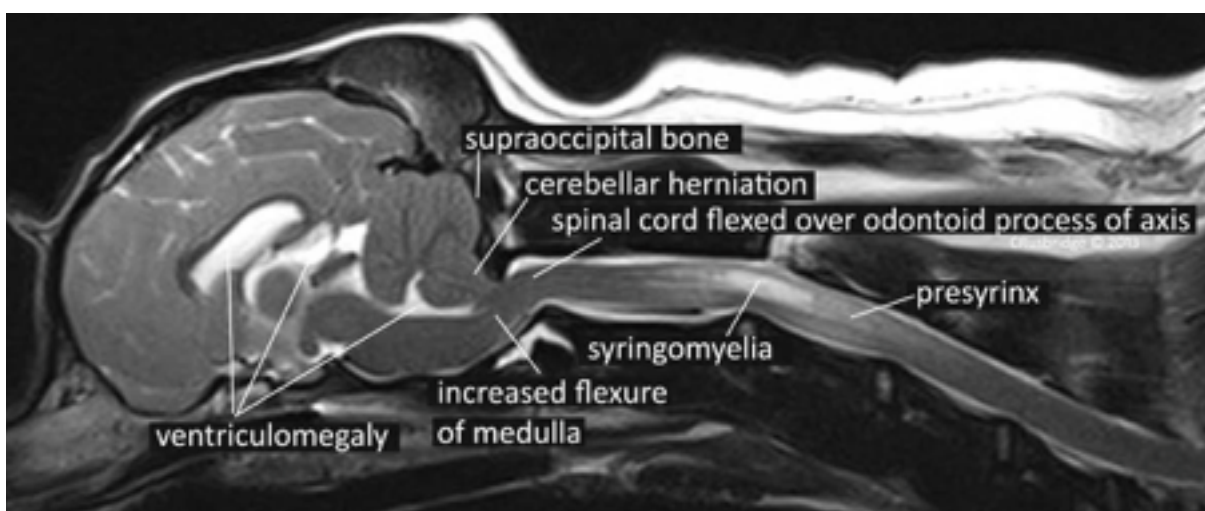


Figure 12: Midline sagittal MRI images of the brain and cervical spinal cord from a 1 year old Cavalier King Charles Spaniel with Chiari malformation and Syringomyelia which was presented with pain as the clinical sign.

Grading of the disease according to MRI findings

Grading of the images is according to the severity of the Chiari malformations and the Syringomyelia changes. The grade is qualified with a letter alongside the grade indicating the age of the dog at the time of the scanning. As Syringomyelia is a progressive disease the grade is not valid without the qualifying letter. The letter indicating the age as follows:

- a = more than five years of age
- b = three to five years of age
- c = one to three years of age

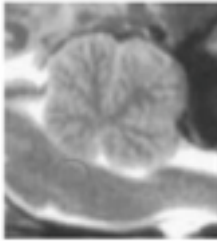
Chiari-like Malformation Grading

- Grade 0 - Normal (no central canal dilatation, no pre-syrinx, no syrinx)
- Grade 1 - Cerebellum indented (not rounded)
- Grade 2 - Cerebellum impacted into, or herniated through the opening at the foramen magnum. The size of the cerebellar herniation is not graded because there is no correlation with genetic risk of Syringomyelia yet demonstrated. Although dogs with larger cerebellar herniation may have early onset of Syringomyelia.

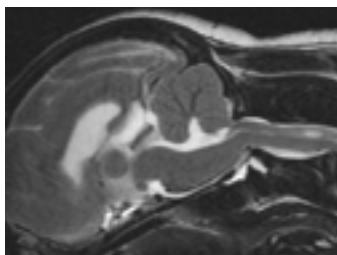
Syringomyelia Grading

- Grade 0 - Normal (no central canal dilatation, no pre-syrinx, no syrinx)
- Grade 1 - Central canal dilatation (CCD) less than 2mm in diameter
- Grade 2 - Syringomyelia - central canal has an internal diameter >2mm or greater, separate syrinx or pre-syrinx with or without central canal dilation.

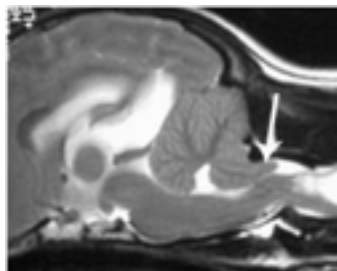
Syringomyelia is graded according to its maximum internal diameter in a transverse plane. A pre-syrinx is spinal cord oedema and maybe a transitional state prior to development of Syringomyelia, it is shown as marked increased fluid content within the spinal cord substance, not free fluid.



Grade 0 Chiari malformation ==> The cerebellum has a rounded shape with signal consistent with cerebrospinal fluid between the caudal cerebellar vermis and the foramen magnum.



Grade 1 Chiari Malformation ==> The cerebellum does not have a rounded shape, there is indentation by the supra-occipital bone but there is still a signal consistent with cerebrospinal fluid between the caudal vermis and the foramen magnum.



Grade 2 Chiari Malformation ==> The cerebellar vermis is impacted into or herniated through the foramen magnum.

Figure 13: Above MRI scans grading of Chiari malformation.

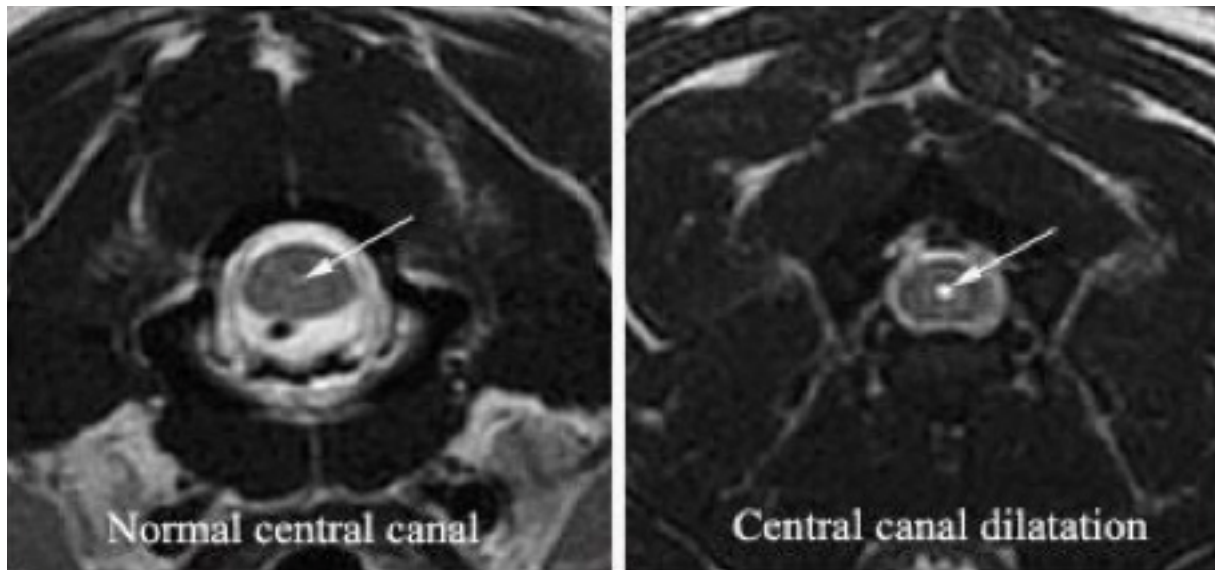


Figure 14: Above shows the comparison between the normal central canal and a central canal dilatation. Grade 1 Syringomyelia (right) with the central canal dilatation less than 2mm in transverse diameter.

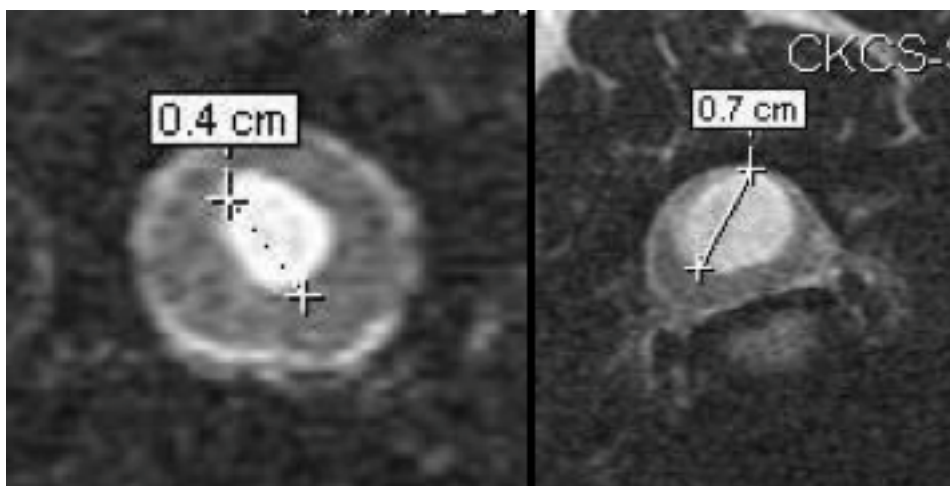


Figure 15: MRI images of examples of Grade 2 Syringomyelia where the central canal dilatation has an internal diameter of 2mm or greater.

Treatment of Syringomyelia

There are two ways of approach to treatment of Syringomyelia, either surgically or conservatively with medical management. Surgical management is indicated mostly if analgesics do not control discomfort or when neurological deficits are present. Medical management may be chosen for patients with only mild disease, when finances do not allow surgery, or when surgical management has failed to resolve the signs.(5)

Medical Management

Neuropathic pain is difficult to recognise in dogs as unlike people, they are unable to describe the discomfort and abnormal sensations. It is assumed that dogs with Syringomyelia experience neuropathic pain similar to that described by humans with the disease. From this, we assume dogs will respond to the same drugs used in humans, however many of the possible medications are not licensed for use in dogs and their adverse effects are not known. (16) The most successful approach to neuropathic pain due to the complex pathophysiology is polypharmacology, rather than addressing the entire problem with one class of medication.

The drugs used can be divided into three groups: analgesics, drugs that reduce the cerebrospinal pressure and corticosteroids.

Non-steroidal anti-inflammatory drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs are often used in mild cases of Syringomyelia to control the pain. There is some evidence that suggests cyclooxygenase-2 enzyme (COX-2) may contribute to the development of neuropathic pain. COX inhibitors are lipophilic and achieve significant cerebrospinal fluid concentrations and may cause analgesia via a central action. Due to this commonly used, COX inhibitors such as carprofen (Rimadyl) and meloxicam (Metacam) appear to help in some dogs with Syringomyelia. Drugs that are better suited and more appropriate for the treatment of Syringomyelia are deracoxib (Deramaxx) and firocoxib (Previcox) as they are highly specific inhibitors of cyclooxygenase-2 pathway. (5)

Anti-convulsant drugs

From human use and studies it is found that anti-convulsant drugs are particularly effective for neuropathic pain such as burning and piercing sensations, having a neuro-modulatory effect on the damaged nervous system. Gabapentin (Neurontin) was originally an anti-convulsant but has been found to be successful for the treatment of neurogenic pain. Gabapentin is routinely used for dogs with Syringomyelia and reported to offer some relief. Its mechanism is thought to prevent the release of glutamate in the dorsal horn via interaction with a subunit of the voltage-gated calcium channels. (5)

Pregabalin (Lyrica) is becoming known as an effective drug for neuropathic pain in humans, however the pharmacokinetics and potential toxicity in dogs is currently unknown. There are reported side effects in people such as dizziness, drowsiness and weight gain. Its mechanism also acts by modulating the voltage-gated calcium channels resulting in reduction of glutamate release as it is a structural analogue of GABA. Individual cases have shown Pregabalin useful in treatment of pain associated with Syringomyelia but the expense of it means it is infrequently used and undesirable to owners. (5)

Opioids

Opioids are not commonly used for long term pain relief in dogs because for oral use, the effective dose can vary greatly between individuals and also is difficult to dispense being a controlled drug. In humans, neuropathic pain has been found to be only partially responsive to opioids and most people eventually become unresponsive to it due to repetitive dose escalation. Most common use of opioids in dogs in relation with Syringomyelia and Chiari malformation is in the preoperative period in the form of a Fentanyl transdermal patch. (5)

NMDA receptor antagonists

Chronic neuropathic pain such as in Syringomyelia is difficult to treat as central sensitisation has occurred. However, as this is mediated through the NMDA receptor the ideal medication would be an NMDA receptor antagonist. Ketamine is a non-competitive antagonist of NMDA receptors and blocks sodium and potassium channels in superficial dorsal horn neurones impairing the excitability. For this reason, it has benefits in the treatment of neuropathic pain but it has systemically unacceptable side effects such as neurotoxicity and behavioural disturbances. (5)

Drugs that reduce the cerebrospinal pressure

Proton pump inhibitors such as Omeprazole can theoretically inhibit cerebrospinal fluid formation and therefore useful in reduced the CSF pulse pressure which is thought to be the cause of the syrinx formation in the spinal cord. However, there is a lack of clinical data for their used effectiveness in this instance. Also, not recommended for long term use for management of Syringomyelia due to chronic gastric acid suppression results in hypergastrinaemia and some studies of increased risk of neoplasia in laboratory animals. Carbonic anhydrase inhibitors such as acetazolamide decreased the cerebrospinal fluid flow but have side effects that limit long term use. Furosemide is the most commonly used drug from this group for the treatment of Syringomyelia but does not have great effectiveness. It is said to cause decreased intracranial pressure which is desirable in the treatment of Syringomyelia but its effect is most likely to be caused by diuresis and a reduction in blood volume and no effect on cerebrospinal fluid. (5)

Corticosteroids

Corticosteroids are very effective in decreasing both pain and neurologic deficits, although the exact mechanism of action is unknown. It is believed they provide long term pain relief due to their ability to inhibit the production of phospholipase A2 and inhibit the expression of many inflammatory genes for cytokines, enzymes and adhesion molecules. As of these, corticosteroids may have a few modes of action, either by decreasing the cerebrospinal pulse pressure, reducing inflammation therefore intracranial pressure, or possibly have a direct effect on pain mediators. Oral forms such as prednisolone (Prednicare) and methylprednisolone (Medrone) have shown to provide relief in some dogs with Syringomyelia. However, an important factor to consider with corticosteroids is their side effects, which occur with long term use, some of them are immunosuppression, weight gain and dermatological changes. Also to be considered it the pharmacological interactions of concurrent medical treatments. Corticosteroids can be used with Gabapentin but not with non-steroidal anti-inflammatories. (4)

Surgical Management

The origin of Syringomyelia is an obstruction that causes the change in cerebrospinal fluid pressure so its most direct treatment would be to correct the underlying anatomical or functional abnormality. Surgical management is indicated for dogs with refractory pain or worsening neurological signs which cannot be controlled with medication. The aim of the surgery is to restore the cerebrospinal fluid dynamics, if this can be achieved then the syrinx can resolve. The most common procedure is sub-occipital decompression for caudal fossa overcrowding. Most of the supra-occipital bone and the cranial dorsal laminae of the atlas are removed to decompress the foramen magnum.



Figure 16: Diagram shows the extent of the bone removal (dotted line) from the supra-occipital bone and dorsal laminae of the atlas.

1 - supra-occipital bone 2 - wing of atlas.

The success reported postoperatively in studies vary from no improvement at all to resolution of clinical signs. Although, many reported improvement or complete resolution of clinical signs after surgery, there is a very high incidence of reoccurrence of the clinical signs. In identical procedures carried on in humans with progressive Syringomyelia, even though the surgery resulted in collapse of the syrinx, patients still experienced significant pain, especially if the dorsal horn of the spinal cord was affected by the disease. It appears that surgery in dogs is less successful than in humans, as despite there may be clinical improvement, there is high reoccurrence, meaning Syringomyelia is persistent. (11) It has also been reported that a successful postoperative outcome is more likely if surgery was performed early in the course of the disease. Unfortunately for surgery to be indicated early diagnosis is key but for this at a young age, the disease must be very severe. Sub-occipital decompression is the first procedure of choice for surgical management. If this results in recurrence or failure draining of the syrinx by the insertions of a shunt or stent, diverting to the subarachnoid space or to the pleural cavity is indicated. Unfortunately, it is not associated with good long term outcomes because the stents and shunts often become obstructed and can result in tethering. (5)

Due to low success rate and long term prognosis after the surgery, medical management of the clinical signs is the main choice of treatment for Syringomyelia.

Summarised clinical approach to treatment



Figure 17: A flow diagram illustrating the possible treatment approaches following diagnosis of Syringomyelia or Chiari-Like Malformation.

After presentation of clinical signs of Chiari-like malformation and Syringomyelia, the first diagnostic for the veterinarian to use is an MRI scan. Most importantly to investigate any evidence of dorsal horn damage of the spinal cord as this will alter the following treatment. If there is evidence of dorsal horn damage and clinical signs of neuropathic pain such as phantom scratching, first line medical management is the use of Gabapentin. However if there are no signs of dorsal horn damage and/or clinical signs of pain such as yelping on changing of posture, the first line of medical management unless contraindicated by other co-morbidities, is to commence non-steroidal anti-inflammatories such as Carprofen or Meloxicam. Following the start of both first line medical managements, if there is insufficient improvement in the patients symptoms, the veterinarian is to consider polypharmacy, adding an additional agent. This can be by changing the anti-convulsant drug to Pregabalin or adding a drug to reduce cerebrospinal fluid pressure such as Omeprazole or Cimetidine. If gait abnormalities were to develop such as ataxia, weakness or proprioceptive deficits, the addition of corticosteroids would be best after discontinuation of the NSAIDs. Another approach of medical management is the restricted use opiates, which can be used sporadically under the owners discretion of 'bad days'.

The Breeding of Syringomyelia

Studies into the inheritance of Syringomyelia and Chiari-like malformation have shown it to be a complex trait with a moderately high heritability. (18)

The dogs most commonly affected by Chiari-like malformation and Syringomyelia such as Cavalier King Charles Spaniel or the Griffon Bruxellois, all derive from a small number of individuals, meaning there is very little genetic variation. The problem is compounded by the repeated use of particular stud dogs. It is not unusual for a popular stud dog to produce over fifty separate litters and hundreds of progeny. This reduced variation breeding practice encourages the emergence of recessive genetic diseases. A common feature for these breeds, which has increased incidence of the disease is that often, they are bred to produce certain traits, an example of this is the selection of coat colours in the Cavalier King Charles Spaniel. Phenotypically, four colour variations are recognised: on one hand its ruby and black&tan, which are whole colours, where white colour is undesirable, and on the other hand, blenheim and tricolours, which are parti-colours consisting of two or more colours. Parti-colours and red colours are recessive traits meaning if they are desired in the offspring, breeders will only use particular lines, this in turn leads to the production of other recessive traits such as Syringomyelia and Chiari-like Malformation. (17)

Along with Syringomyelia and Chiari-like malformation, other recognised diseases with hereditary influence are to be avoided via selective breeding. Common amongst toy breeds, is mitral valve disease, breeders are advised to follow a suggested programme to reduce the occurrence of the disease. They are warned to select to breed from systolic murmur free dogs over the age of two and a half years old that have systolic murmur free parents over 5 years old.

The Kennel Club Assured Breeders Scheme members are responsible to get their breeding dogs tested and record the results with the association. A list is then compiled of all the registered 'clear' breeding dogs. Access to this online pedigree database allows the breeders to select for health and longevity of their dogs. Although, this practice is working positively to reduce inherited diseases in pedigree dogs it further narrows the gene pool with dogs with mitral valve disease are removed from the gene pool. (17)

The main problem with selective breeding to reduce the incidence of Syringomyelia and Chiari-like malformation is the varying onset of the disease. Severely affected dogs may be symptomatic and diagnosed as early as less than two years of age, however, the majority of affected dogs will progress over time and will only exhibit symptoms over the age of five years old. This in turn means that MRI screening before breeding is not reliable as the dog may still develop the disease in the future. (18) As of this problem, age is taken into consideration when grading the MRI scans.

The Chiari-like malformation and Syringomyelia scheme created by the British Veterinary Association with support of the Kennel club encourages breeders and owners to breed responsibly and participate in the screening process. The resulting MRI images will be graded according to the severity of the Chiari-like malformation and Syringomyelia. Alongside the grading of the severity, the age of the dog is taken into account and given a letter corresponding to this. From the final grading of the dog a breeding guideline is created for suggested mate selection. The aim of these breeding guidelines is to remove dogs with early onset Syringomyelia from the breeding programme. Nonetheless, it is known that affected offspring may arise from parents without Syringomyelia or only mildly affected.

SM grade	Age (years)	Breed to
0a (normal)	Over 5	Any
0b (normal)	3 - 5	SM grade 0a, 0b, 0c, 1a
0c (normal)	1 - 3	SM grade 0a, 0b, 1a
1a (CCD)	Over 5	Any
1b (CCD)	3 - 5	SM grade 0a, 1a
1c (CCD)	1 - 3	SM grade 0a, 1a
2a (SM)	Over 5	SM grade 0a, 1a
2b (SM)	3 - 5	SM grade 0a, 1a
2c (SM)	1- 3	Do not breed
Any dog with clinical signs of CM7/SM	Any	Do not breed

Figure 18: Table of breeding guidelines suggested to breeders for selection of choosing breeding partners for their dogs. CCD - central canal dilatation. SM - Syringomyelia.

In addition to obtaining safer breeding lines by recognising the potential of Chiari-like malformation and Syringomyelia, the programme is able to generate Estimated Breeding Values (EBV) from the overall results. The Kennel Club encourages breeders to use their Mate Select programme, which is a free online resource. It cannot recommend possible breeding dogs, but provide health related information about individual dogs under consideration.

Estimated breeding values are a statistical estimate of the genetic risk for a given disease of individual dogs and a measure of the likelihood of transmitting the disease to their offspring. For complex traits such as Syringomyelia, estimated breeding values are the best method of genetic evaluation and can even be calculated for most dogs even before undergoing an MRI scan by simply using the grading from MRI scans of dogs they are related to. Knowing the estimated breeding values, breeders and owners will be able to make more informed choices and safer breeding combinations. To ensure the validity of the estimated breeding values it is essential to have an accurate population-wide data. To achieve this and for the scheme to be successful, every MRI form scanned dogs must be submitted for assessment, regardless of whether the animals is required for breeding or not. It is also incredibly advantageous to ascertain the Syringomyelia status of dogs especially breeding dogs above the age of five years old, even if they are no longer being used for breeding. This information will be of value to accurately determine estimated breeding values for descendants of the dog and for future breeding decisions.

A highly controversial part of the breeding recommendations shown in the above table is that older clinically asymptomatic Syringomyelia affected dog can be bred. This is due to the lack of current Syringomyelia free breeding individuals. It was thought that overuse of these low number of individuals would in turn limit genetic diversity and cause further genetic problems and even though these low grade affected dogs can produce Syringomyelia free dogs, it was later found that the number of affected dogs bred was much greater. The controversy this caused brings to the question to whether is it ethical to breed a dog knowing it has an inheritable disease, especially when the majority of the offspring may be defined for the pet-owning public. In this case it is arguable that Syringomyelia affected dogs should not be used for breeding at all. However, with the prevalence of Syringomyelia in these breeds as high as 70% this will have dire consequences for the population size of the breed. Currently, it is hoped with the ongoing use of the Kennel Club's scheme and the estimated breeding value Mate Select Programme that safer parental crosses will be chosen, allowing for the maintenance of genetic diversity while decreasing the number of syringomyelia affected offspring. (18)

Discussion

From my literature review of Syringomyelia in dogs, I have explored in depth some of the contrasting theories and opinions with regard to its pathogenesis, clinical presentation, diagnostic tools and the future of the disease.

I have acquired a better understanding of the pathogenesis of the disease even though it is still of debate. The latest theories: 'Vascular theory' and the "Intramedullary pulse pressure theory' both account for the discrepancy in the origin of the fluid in the syrinx and also about difference of pressure between the syrinx and the spinal cord. Unfortunately, the true underlying mechanism behind the formation of the syrinx remains undecided amongst researchers.

The clinical presentation of Syringomyelia remains a challenge to first opinion veterinarians. Although it is a disease with high occurrence in many toy breeds, its clinical presentation can be initially confused with more common ailments. This is to some extent due to low awareness of the disease amongst veterinary professions in general practice along with the very subjective nature of its clinical signs. The interpretation of the clinical symptoms, first by the owner and then the veterinarian can be very subjective. Not only this, but each dog will have its own response to neuropathic pain thus the clinical signs can be broad and unspecific. Equally individual dogs have different tolerance to pain, in some a mild case of Syringomyelia may be easily recognised whereas a very severe case may go unnoticed if the dog is particularly resilient in its display of pain and stress.

Another problem regarding the diagnosis of Syringomyelia in first opinion practice is that a referral is needed for an MRI scan. Most owners will see this as a great cost and may be reluctant unless the dog is insured. From having explored the other diagnostic possibilities, using the tools available in a first opinion practice it is possible to identify the Chiari-like malformation and Syringomyelia by other means, however for a definitive diagnosis an MRI scan is required, especially to characterise the grade of the disease. In this way, the Kennel Club and the British Veterinary Association are encouraging owners and breeders to take part in their canine health scheme by promoting subsidised MRI scan fees as well as 'mini' MRI scans which only image the cervical region of the dog therefore reducing cost.

All of these has helped me realise that the key towards greatly improving the future of Syringomyelia, in terms of first opinion practice, is to increase the education of owners, breeders

and the veterinarians. Better education on the display of the clinical signs and recognition of pain in the dogs, meaning the owners and breeders will bring them sooner to the veterinarian. The veterinarian should be better educated in what is available for them to differentiate from other suspected ailments.

An example of this is the use of ultrasound as a diagnostic tool. This being greatly under used, however studies have proven it to be an excellent tool, which is readily available in most clinics, but there is a void in expertise and training to exploit it.

With this greater education for all, there would be earlier recognition and diagnosis of the disease which can greatly effect the dogs quality of life and prognosis and can significantly reduce costs of treatment.

Upon reaching a diagnosis of Syringomyelia, the assessment of the dogs condition and grading of the disease leads to the choice of treatment. Surgical management is less attractive at this stage as it often is not successful and even if it results in a successful outcome of reduction of clinical signs, there still is high rate of later progression and reoccurrence. Therefore, medical management is most commonly used, even though this is not curative and is merely a trial and error of symptomatic treatment. Medical treatment can also be seen as palliative care of dogs with Syringomyelia as unfortunately, without the exact understanding of the pathogenesis, there can be no correction of the cause and medication is only used to manage pain aiming for comfort.

From this thesis work, the take away points that I will remember as a practicing veterinarian in first opinion, include the importance of educating owners about the breeds with high risk of Syringomyelia and on how to spot its clinical signs, even if very subtle and may be misunderstood as something else. Moreover, I will try to encourage my colleagues to have a good understanding of the disease so they are able to educate owners and breeders.

With greater recognition of the disease and enhanced knowledge for breeders on what resources are available to them to make well informed mating choices, I hope it this will impact the future of the disease, aiming to greatly reducing the incidence of Syringomyelia.

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Figure Bibliography

Figure 1 top left:

[https://en.wikipedia.org/wiki/Pomeranian_\(dog\)#/media/File:Pomeranian.JPG](https://en.wikipedia.org/wiki/Pomeranian_(dog)#/media/File:Pomeranian.JPG)

Figure 1 top right:

<https://www.pets4homes.co.uk/dog-breeds/griffon-bruxellois/>

Figure 1 bottom - own picture.

Figure 2, 3, 5, 6 and 7:

Karen Kennedy. *Understanding Canine Chiari Malformation and Syringomyelia*. Health Committee of the Cavalier King Charles Spaniel Club of Canada.

Figure 4:

C Rusbridge, D Greitz, B.J. Iskandar. Syringomyelia: *Current concepts in pathogenesis, diagnosis and treatment*. Journal of Veterinary Internal Medicine 2006.

Figure 8:

Lynda Rutherford, Annette Wessmann, Clare Rusbridge, Imelda M. McGonnell, Siobhan Abeyesinghe, Charlotte Burn, Holger A. Volk. *Questionnaire-based behaviour analysis of Cavalier King Charles spaniels with neuropathic pain due to Chiari-like malformation and syringomyelia*. The Veterinary Journal 194 (2012).

Figure 9:

Clare Rusbridge, Felicity Stringer, Susan P. Knowler. *Clinical Application of Diagnostic Imaging of Chiari-Like Malformation and Syringomyelia*. Veterinary Neurology and Neurosurgery, Journal Frontiers in Veterinary Science.

Figure 10 and 11:

Martin J. Schmidt, Antje Wigger, Sebastian Jawinski, Tanja Golla, Martin Kramer. *Ultrasonographic appearance of the craniocervical junction in normal brachycephalic dogs and dogs with caudal occipital (Chiari-like) malformation*. Veterinary Radiology & Ultrasound, Vol. 49, No. 5, 2008.

Figure 12:

Clare Rusbridge. *Chiari-like malformation and syringomyelia*. FECAVA for the Special issue of EJCAP, Genetic/Hereditary Disease and Breeding.

Figure 13,14 and 15:

Guide to the British Veterinary Association / Kennel Club Chiari malformation / Syringomyelia (CM/SM) Scheme

Figure 16:

C. Rusbridge. *Chiari-like malformation with syringomyelia in the cavalier King Charles spaniel; long term follow up after surgical management*

Figure 17:

http://www.veterinary-neurologist.co.uk/resources/treatment_-_algorithim_-_2013-1.jpg

Figure 18:

British Veterinary Association, The Kennel Club. *Canine Health Scheme, Chiari Malformation/ Syringomyelia Scheme (Information Leaflet)*. Adapted from: Report from the Chiari-Like Malformation and Syringomyelia Working Group round table. Cappello R, Rusbridge C; Chiari-Like Malformation and Syringomyelia Working Group. *Veterinary Surgery* (2007) 36 509-12.

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