CHIARI-LIKE MALFORMATION

Chiari-Like Malformation and Syringomyelia in a Cavalier King Charles Spaniel

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ABSTRACT

Introduction: Bobby, a 5½-year-old neutered male Cavalier King Charles Spaniel, weighing 11.11 kg with an up-to-date vaccination and deworming status was referred and presented to the veterinary referral hospital with a chronic history of air licking, chasing shadows, auditory and neurologic deficits.

Objective: This paper aims to highlight the clinical presentation, diagnosis and management of Chiari-like syndrome and syringomyelia.

Methods: Neurological examination, revealed the presence of neck pain on full lateroflexion, vocalisation and hyperesthesia. Magnetic resonance imaging (MRI) of the brain and spinal cord, as well as cerebrospinal fluid (CSF) tap, were done. Based on the MRI images, Chiari-like malformation (CLM) and early syringomyelia at the level of C2 and C3 were diagnosed.

Findings and management: There were no evidence of lesions causing compression of the spinal cord on the sagittal images. A dry tap was obtained from cisternal CSF tap. Gabapentin and Omeprazole prescribed and significant improvements in clinical signs were observed within two weeks of treatment. Vocalisation and hindlimb ataxia were absent. While phantom scratching had reduced in frequency. Bobby is currently on a long term gabapentin and omeprazole medication and recuperating well.

Conclusion: The diagnosis of CLM is important in brachycephalic dogs that show neurologic signs as it is a progressive neurological disease especially when associated with syringomyelia. Early detection and medical management of CLM allows the slowing of progression or deterioration of syringomyelia that can lead to paralysis and eventually death.

KEY WORDS

brachycephalic, Cavalier King Charles Spaniel, Chiari-like malformation, syringomyelia

INTRODUCTION

In the 1890s, Hans Chiari, an Austrian pathologist described a condition involving deformities of the cerebellum and brainstem in children with herniation of the spinal cord which later became known as 'Arnold-Chiari malformation in 1907. It is named after Chiari and a German pathologist, Julius Arnold.

Chiari-like malformation (CLM) is a condition in dogs analogous to Chiari I malformation in humans. The suffix 'like' is added because of some features that distinguish Chiari-like malformation from 'Arnold-Chiari malformation or Chiari I malformation in humans (Cappello and Rusbridge, 2007). Dogs and cats do not have cerebellar tonsils, and the condition is not dependant on the size of cerebellar vermis herniation. CLM is a congenital condition characterised by a mismatch in the skull, and brain size (brain too big and skull too small) is the most common cause of syringomyelia in dogs (Rusbridge, 2018). It is also a condition of the craniocervical junction in which there is a mismatch of the structures of the caudal cranial fossa (CCF), often causing the cerebellum to herniate into the foramen magnum (Loughin, 2016). Syringomyelia is a disorder of cerebrospinal fluid (CSF) when there is obstruction of the flow of the fluid from the ventricles in the brain and around the spinal cord. Fluid is forced or sucked into the spinal cord resulting in dilated

fluid-filled cavities (Rusbridge, 2018).

CLM and associated syringomyelia is a breed predisposed condition for brachycephalic dogs especially Cavalier King Charles Spaniel (CKCS), Dachshund, Shih Tzu, Maltese, Staffordshire bull terrier, Pomeranian, Pug, Griffon Bruxellois and Chihuahua (Knowler et al., 2018; Limburg, 2013). The occurrence of syringomyelia has been reported to vary with age with 45% occurrence recorded for dogs one year and below, 40% in 1-4 years old dogs and 15% in dogs that are five years and above (Rusbridge, 2013). Approximately 95% of CKCS population have CLM characterised by foramen magnum cerebellar herniation (Shaw et al., 2012). Studies have revealed a 46% prevalence in asymptomatic breeder CKCS but prevalence increased with age and may be as high as 70% in dogs over six years of age (Rusbridge, 2012). In the CKCS, early closure of the spheno-occipital synchondrosis at about 8 months of age is typical, which is the earliest compared to other brachycephalic dogs that closes at 12 months and mesaticephalics (medium-sized skull) that closes at 16 months, hence supporting the theory that abnormal skull shape contributes to the CKCS predisposition to CLM (Loughin, 2016).

Clinical signs of CLM and associated syringomyelia include phantom scratching with or without yelping, facial rubbing, paw licking or chewing, head shaking, hyperesthesia, lip licking or air licking and vocalisation (Hechler and Moore, 2018). Other uncommon clinical signs

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Figure 1. Dorsal T2W, FLAIR, sagittal T2W images showing caudal protrusion of the cerebellum into the foramen magnum (cranial arrow) and indentation of the cerebellum with subtle focal dilation of the central canal at C2 (caudal arrow).

are seizures, unilateral facial paralysis, pelvic limb ataxia and paresis. The clinical signs shown depends on the location, size and symmetry of the syrinx in the central canal of the spinal cord (Rusbridge, 2012). A 5-year retrospective study of 37 Cavalier King Charles Spaniel (CKCS) dogs diagnosed with Chiari-like malformation and Syringomyelia revealed that all of the dogs had neuropathic pain and spontaneous vocalisation followed by scratching (81%), facial rubbing (29.7%), paw licking (10.8%) and air licking (10.8%) while fewer dogs (2.7%) had seizures and unilateral facial paralysis indicating that the latter clinical signs are uncommon (Cucos et al., 2018).

CASE DETAIL

Bobby, an 11.11 kg neutered male CKCS, was presented with a complaint of increased sensitivity to pain, intermittent hindlimb weakness or ataxia, phantom scratching, air licking, chasing shadows, and deafness which has not resolved for about a year. Further history revealed that Bobby whimpers while sleeping, struggles to rise from recumbency and is lethargic and ataxic. Medication with Carprofen (10 mg PO BID) did not resolve the clinical signs which progressed to hyperaesthesia and neuropathic pain.

On physical examination, Bobby was bright, alert and responsive upon physical examination. All his vital parameters are within the normal range with a temperature of 38.6°C (37.9-39.9°C), heart rate of 104 bpm (70-120 bpm), respiratory rate of 24 bpm (10-34 bpm) and a body condition score of 6/9 (slightly obese). Chest auscultation was clear-no heart murmurs or arrhythmias were heard. Findings from overall systemic examinations were normal except for the nervous system. Neurological examination revealed hyperaesthesia and presence of neck pain on full lateroflexion.

DIAGNOSIS

With a combination of history and physical examination findings including hyperesthesia, intermittent hindlimb weakness or ataxia, phantom scratching, air licking, chasing shadows and acute hearing loss, the differential diagnoses generated included CLM with syringomyelia, intervertebral disc disease (IVDD), granulomatous meningoencephalomyelitis, spinal tumour, and primary secretory otitis media (PSOM). The diagnostic workup revealed Chiari-like malformation and syringomyelia.

DIAGNOSTIC WORKUP

Magnetic resonance imaging (MRI) of the brain and spinal cord (Figure 1-3); and cerebrospinal fluid (CSF) tap were conducted. The dog was anaesthetised before MRI was performed using the following protocol; acepromazine (0.03 mL, IV), butorphanol (0.2 mL, IV) as premedicants. Anaesthesia was followed by the insertion of endotracheal tube and the administration of propofol (3 mL, IV) for anaesthetic induction while anaesthesia was maintained with isoflurane (2.5%) and oxygen flow. An intravenous fluid infusion was given at a slow infusion rate (5 mL/kg/hr, IV) using normal saline to maintain hydration.

Syringomyelia screening views were performed with T1 sagittal, T2 sagittal and turbo 3D T1 plain transverse views capturing the brain and

spinal cord up to C3. MRI of dorsal T2-weighted (T2W) and Fluid-attenuated inversion recovery (FLAIR), sagittal T2W images of the brain were taken while sagittal T2W, T1-weighted (T1W) and transverse T1W images of the cervical vertebrae were taken. Sagittal T1W images of the thoracolumbar vertebrae were also taken with no contrast administered. Based on the MRI images, there was the presence of Chiari-like malformation with flattening of the caudal occipital bone and protrusion of the caudal cerebellum into the foramen magnum (Figure 1). There was also mild cervical central canal dilation seen on C2 and C3 vertebrae (Figure 2) indicating early syringomyelia. However, there was no evidence of a lesion causing compression of the spinal cord on the sagittal images (Figure 3).

CSF tap was carried out after performing MRI. The caudal skull and cranial neck were clipped and surgically (aseptically) prepared. Then, cisternal CSF tap was performed using a 1.5-inch spinal needle, but a dry tap was obtained despite correct positioning. There was no complication during the anaesthetic recovery.

Based on the history, clinical signs and MRI findings obtained from the brain and spinal cord, Bobby was diagnosed with Chiari-like malformation and early syringomyelia.

TREATMENT AND ADVICE TO CLIENT

Since Bobby had a history of neuropathic pain and MRI finding of the presence of mild central canal dilation, Gabapentin (100 mg, orally twice daily) and Omeprazole (10 mg, orally once daily) for two weeks were prescribed to alleviate neuropathic pain and to reduce CSF production respectively.

The dog should be provided with a chest harness instead of a collar when taking the dog out for walks as wearing a collar causes rubbing of the skin at the neck area which will then irritate the superficial nerves causing hyperesthesia. The owner was advised not to breed Bobby as the conditions are hereditary.

OUTCOME AND FOLLOW-UP

After two weeks of Gabapentin and Omeprazole medication, there was an improvement in Bobby's clinical signs. There was the absence of yelping and ataxia with a drastically decreased frequency of phantom scratching. Based on the response to treatment, Bobby was placed on long-term gabapentin and omeprazole mediation to be monitored fortnightly or monthly. Clinical progress has been recorded within two months of management.

DISCUSSION

Chiari-like malformation (CLM) is a condition analogous to Chiari I malformation in humans. The suffix 'like' is added because dogs and cats do not have cerebellar tonsils and the condition is not dependant on the size of cerebellar vermis herniation compared to humans (Knowler *et al.*, 2018).

CLM and obstruction of the foramen magnum prevent transmission of the systolic cerebrospinal fluid pulse pressure wave to the distal cerebrospinal spaces. The subarachnoid space is partially occluded at the foramen magnum, partially entrapping the CSF in the spinal canal and preventing the normal rapid movement of CSF from the head to the spina. The pulse pressure is instead transmitted and reflected into the spinal cord tissues resulting in a relative increase in intrathecal pressure and a decrease in subarachnoid pressure. Also, because of the partial obstruction, the CSF displaced by each systole is forced through the narrower opening resulting in high-velocity jets of CSF ventrally within the foramen magnum. These high-velocity jets decrease the hydrostatic pressure in the subarachnoid space (Venturi effect/Bernoulli theorem). The changes in pressure have a 'suction effect' on the spinal cord. Repeated spinal cord distension results in extracellular fluid accumulation and eventually syringomyelia (Rusbridge, 2012).

Diagnosis of CLM and syringomyelia is based on history, clinical signs (neurologic signs) and diagnostic imaging. Magnetic resonance imaging (MRI) is a gold standard diagnostic tool for evaluating Chiarilike malformation and syringomyelia. Cerebellar herniation from the skull can be assessed. MRI provides greater soft tissue detail which allows for a better delineation of the cerebellum (Kromhout *et al.*, 2014).

Computed tomography (CT) scan provides lesser soft tissue detail. CT scan can be used to confirm or rule out cerebellar herniation and is used as a diagnostic tool when MRI is not available. However, CT scan

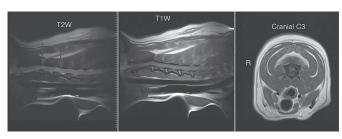


Figure 2. Sagittal T2W, T1W and transverse T1W images showing mild central canal dilation on the T2W sagittal (arrows).

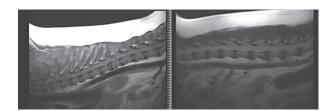


Figure 3. Sagittal T1W images are showing no evidence of T1W abnormalities of the thoracolumbar spine.

cannot replace MRI as the standard screening technique for CKCS for breeding purposes for the presence of Chiari-like malformation and syringomyelia (Kromhout *et al.*, 2014).

Ultrasonography is useful in evaluating syringomyelia and cerebellar herniation. In the sagittal view of the spine, cerebellum herniation can be seen while in the mid-dorsal portion of the cranial cervical spinal cord, a tubular anechoic fluid collection which is the syrinx can be seen (Penninck and d'Anjou, 2015).

Radiography has more value in predicting the breeding value of a dog than as a diagnostic test for SM by using the ratio of the height to length of the caudal skull. According to Rusbridge *et al.*, (2009), it is of value in ruling out other vertebral abnormalities such as atlantoaxial subluxation, an indication of the likelihood of intervertebral disc disease (IVDD). Myelography is also not used in the diagnosis of CLM and syringomyelia.

Chiari-like malformation and syringomyelia can be graded according to the severity of the condition based on The British Veterinary Association (BVA) and The Kennel Club (KC) scheme. As syringomyelia is a progressive neurological disease, scanning is best performed at five years of age or older, which is late for breeding. Thus, breeders are recommended to consider scanning their dogs more than once; before breeding and at five years of age or later (Freeman *et al.*, 2014).

According to the BVA and KC scheme, Chiari-like malformation is graded from Grade 0 to Grade 2. Grade 0 indicates that there is an absence of Chiari-like malformation while Grade 1 shows the cerebellum being indented (not rounded). Grade 2 indicating the cerebellum is impacted or herniated through the foramen magnum.

Syringomyelia is also graded from Grade 0 to Grade 2 based on the length of the spinal cord central canal. Grade 0 indicates that there is an absence of Syringomyelia. Grade 1 is when the central canal of the spinal cord is less than 2 mm in diameter while Grade 2 is when the central canal of the spinal cord is 2 mm or greater. The grade is qualified with a letter indicating the age group at the time of screening: a. suggests more than five years of age; b. indicates three to five years of age; and c. indicates one to three years of age (Freeman *et al.*, 2014).

The aim of these breeding guidelines provided by the BVS and KC is to remove dogs with the early onset of syringomyelia from the breeding programme (Knowler *et al.*, 2016).

TREATMENT

There are two treatment approaches for Chiari-like malformation and syringomyelia, which are medical and surgical.

Medical management

The primary goals are to alleviate neuropathic pain and also to slow

the progression of syringomyelia by decreasing CSF production. Medical management can be chosen when there is only mild pain or when there are financial constraints to allow surgical management (Rusbridge, 2014). The typical class of drugs used are antiepileptics or neuropathic pain analgesics, non-steroidal anti-inflammatory drugs (NSAID), diuretics, and corticosteroids.

Gabapentin (an antiepileptic) is currently the drug of choice for management of neuropathic pain in CLM and syringomyelia cases. Gabapentin and pregabalin (another antiepileptic drug) modulate voltage-gated calcium channels resulting in a reduction of glutamate and substance P (Rusbridge, 2006). It has been suggested that pregabalin can reduce pain as quickly as one day after it has been started in much lower doses and is quicker than gabapentin. Gabapentin, however, is more economical to use compared to pregabalin.

NSAIDs are Cyclooxygenase-1 and/ or Cyclooxygenase-2 inhibitors and suppress inflammatory pain by reducing prostaglandin E2 that contributes to the genesis of neuropathic pain (Rusbridge, 2014). NSAIDs can be useful in the management of Chiari-like malformation and syringomyelia; however, NSAID alone is unable to provide sufficient analgesia for neuropathic pain. Therefore, NSAIDs such as Carprofen (2.2 mg/kg q12h) and Meloxicam (0.1 mg/kg q24h) in combination with antiepileptics such as Gabapentin (10-30 mg/kg q8h) and Pregabalin (4 mg/kg q12h) can be used to treat neuropathic pain. Other alternative classes of drug that can be used are opioids such as methadone.

Diuretics such as furosemide can be used to reduce the production of CSF and stall the progression of syringomyelia. Recently, proton pump inhibitors such as omeprazole (Girod *et al.*, 2016) have been shown to also inhibit CSF production through mechanisms that are yet to be fully understood. Omeprazole is a specific inhibitor of H⁺-K⁺-activated ATPase in experimental models; omeprazole reduced canine CSF production by 26%. Omeprazole is unlikely to be useful long term (therapy longer than eight weeks) as it can cause stomach cancer. Cimetidine, a H₂ receptor antagonist, is proposed to also reduce CSF production by competitive H₂ receptor inhibition located in choroid plexus epithelial cell or by a direct effect on the capillaries of the choroid plexus (Girod *et al.* 2016). There is evidence that histamine may act physiologically in increasing the electrical activity of vasopressin-secretin neurons. Vasopressin reduces blood flow to the choroid plexus, thereby, reducing CSF production.

Corticosteroid such as Prednisolone is effective in reducing both pain and neurological deficits because of their ability to inhibit the production of phospholipase-A2 and it also inhibits inflammatory genes coding expression for cytokines, enzymes, receptors and adhesion molecules (Rusbridge, 2006). However, it is only used as an option if pain persists for long or where financial constraints are prohibiting the use of other drugs. It is best to avoid them as it will result in immunosuppression, weight gain, and dermatological changes.

Alternative therapy

Conditions of dogs with syringomyelia have been improved with massage and aqua therapy. Massage therapy enables improvement of muscle function and mobility (MacFarlane *et al.*, 2014). Dogs with syringomyelia have hypertonicity in their neck and shoulder muscles where their muscles hold constant tension and unable to relax. The muscles are in a steady state of spasm resulting in further irritation of the nerves. However, it is essential to have the right techniques in massaging the dog and thus require a trained therapist to be trained in 'Myofascial Release'. The massage aims to create space in the musculature and complex fascial system releasing the restrictions and improving the ability of the muscle movement. Extra pressure is placed on the cervical region via the superficial and deep fascia of the neck to help release further restriction that exacerbates the neuropathic pain.

Restoring movement in tissues by enhancing the flow of oxygen, nutrients and lymph and also to re-facilitate nerve impulses to break the pain cycle is the primary goal of canine myofascial release therapy.²¹ The therapist will look for trigger points that inhibit movement and cause nerve irritation and ischemia; and areas of reduced muscular function and myofascial pain.

Aqua therapy including pool hydrotherapy or underwater treadmill helps to strengthen the core and limb muscles as well as focusing on the dog's awareness of its hindlimbs especially those affected with Chiarilike malformation and syringomyelia having hindlimb ataxia. Hydrotherapy also helps in improving proprioception and balance problems (Kadakia *et al.*, 2008). This treatment will not help in a complete recovery but will help the dog to come to a remission resulting in slow-

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ing down the worsening of the disease.

Surgical management

Surgical management is indicated when analgesics do not relieve discomfort or when neurological deficits are present depending on its severity (Rusbrideg, 2006). The most common surgical treatment for Chiari-like malformation is foramen magnum decompression (FMD) with cranioplasty and duraplasty; and syringosubarachnoid shunt.

The principle of FMD with cranioplasty and duraplasty surgery is to allow the flow of CSF by removing the supraoccipital bone and 75% of the atlas with a high-speed drill bit and Lempert rongeurs (Schulz, 2016). This surgery successfully reduces pain and improves neurological deficits in approximately 80% of cases while 45% of cases have had two years' satisfactory quality of life postoperatively.8 Return to regular activity often takes 1-4 weeks. Omeprazole or Cimetidine and Tramadol can be prescribed to reduce CSF production and also to alleviate neuropathic pain. Exercise is limited to 5-10 minute walks 2-4 times daily over the first two weeks depending on the progress and is gradually increased over 4-8 weeks (Rusbridge, 2012).

Another surgical treatment that can be done is a syringosubarachnoid shunt. This surgery is safe and relatively effective in improving neurological signs and the quality of life of dogs affected by Chiari-like malformation and associated syringomyelia. However, there is a risk of injury causing paralysis, but commonly minor sensory disturbances are seen in shunt placement. The shunt may fail after some time due to scarring or clogged catheter resulting in the inability to diverting the fluid from the syrinx to the subarachnoid space. Generally, surgical management does not resolve syringomyelia but only helps to prevent its rapid deterioration (Sung *et al.*, 2015).

CONCLUSION

Chiari-like malformation and early syringomyelia are a relatively common hereditary condition of Cavalier King Charles Spaniels. Bobby was diagnosed based on history, neurological signs, and magnetic resonance imaging. Long-term gabapentin and omeprazole treatment was effective in improving clinical signs especially neuropathic pain, ataxia and phantom scratching. Both CLM and syringomyelia should be strongly considered by clinicians as differentials in dogs showing neurologic signs presented in this report.

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