Chiari-Like Malformation

Elizabeth L. Hood

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Faculty Advisor: Dr. Michalea Beasley

INTRODUCTION

For many years, dog breeders have been selecting breeding stock based on the selection of physical characteristics. This process has narrowed the gene pool for many pure bred dogs leading to a variety of breed related disorders[13]. Cavalier King Charles Spaniels (CKCS) are among this group that has little genetic variation [18]. The term Chiari-like malformation (CLM) or Caudal Occipital Malformation Syndrome (COMS) is used to describe a disease process that has become prevalent in CKCS. CLM/SM was first identified in the CKCS in 1997[18]. CLM is the canine version of Chiari type 1 malformation in human medicine[7]. Syringomyelia (SM) secondary to Chiari type 1 malformation and COMS is high due to alterations in cerebrospinal fluid (CSF) hydrodynamics occurring at the level of the foramen magnum and cranial cervical spinal cord[7].

HISTORY AND PRESENTATION

In one study, the estimated prevalence of CLM in CKCS varies from 92 to 100 percent[14]. Of those 92-100% of animals, 70% developed SM[21]. Although it is overrepresented in CKCS, CLM/SM is also observed in other toy breeds including the French Bulldog, Brussels Griffon, Chihuahua, Pomeranian, Maltese terrier, Pug, and Yorkshire terrier[7]. There are a wide variety of clinical signs typically associated with CLM/SM which are caused by damage by obstruction of the flow of CSF at the foramen magnum, compression to the cerebellum and brainstem as well as damage to the cervical spinal cord for SM[18]. These include cervical scoliosis, cervical myelopathy, decreased menace with normal vision, strabismus, hearing problems, and signs that are suggestive of neuropathic pain (NeP)[10,14]. Specific characteristic behaviors have been associated with NeP including phantom scratching, unwillingness to be touched in the head or neck region, and vocalization with rubbing and circling on the floor[22.] Occasionally, dogs with

CLM and SM present with a certain type of cervical myelopathy called 'central cord syndrome'[5]. With this syndrome, the expanding syrinx causes more LMN damage to the thoracic limb muscles than white matter damage to the pelvic limbs. This results in thoracic limb paresis (typically LMN signs) that is worse than the noted pelvic limb defecits[5].Although signs of CLM are typically recognized between 6 months and 3 years of age, dogs of any age may be presented. Typically, dogs with more severe disease present earlier[18]. Maximum syrinx width, length, and asymmetry strongly predict signs of pain[21]. A puzzling feature of CLM/SM is both can, and commonly do, occur in dogs that have no apparent clinical signs[11]. Because of this factor, it can be difficult to predict which dogs will develop clinical signs following an incidental diagnosis of CLM or SM[7].

PATHOPHYSIOLOGY

In the canine patient, CLM is characterized by herniation of the cerebellum into or through the foramen magnum of the skull. In CKCS it had been noted that there is an overcrowding of the caudal cranial fossa caused by a mismatch between caudal cranial fossa volume and brain parenchyma. This leads to cerebella herniation, medullary kinking, obstruction of the dorsal craniocervical subarachnoid space, and alterations in the flow of CSF[9]. Alterations in pressure dynamics between the intracranial and spinal compartments are thought to be responsible for the clinical signs of CLM. Although this same mechanism is agreed to cause SM in CLM, the exact mechanism of this development is unknown and there are many theories proposed to explain it[5].

Morphometric studies have been used for studying anatomical abnormalities in canines with CLM. These studies look at certain anatomical features in two or three dimensions[7]. This modality has been used for studying anatomical abnormalities in canines with CLM. In CKCS,

breed selection pressure has led to popularity of brachycephaly[7]. Brachycephaly is related to paedomorphosis, meaning that it is desirable to retain a shorter skull conformation that is common to juvenile dogs. Selective breeding for this skull type has led to virtual ablation of the frontal sinuses, a large cephalic index, and subsequent effects on cerebral tissue. Given the wide brain case of CKCS, etiology of CM could be associated with a high grade of the brachycephalic phenotype[7].

Caudal cranial fossa (CCF) morphology has also been discussed as an etiology of CLM. The CCF is the intra-cranial compartment that contains the cerebellum, pons, and medulla oblongata[7]. Studies have been performed comparing the craniocerebral volumes of CKCS to other small breed dogs and Labrador retrievers. This study revealed that CKCS have smaller CCF than Labradors, but were found to have the same size fossa as other brachycephalic breeds. This indicates that a smaller CCF may not predispose CLM on its own[14]. However, this same study found that when compared to Labradors, CKCS had proportionately the same volume of paranchyma in their CCF. Therefore, it is this mismatch of volumes with too much parenchyma to a too small CCF that leads to overcrowding[14]. Increased parenchymal overcrowding was found to be in association with the presence and severity of SM[7].

Synringomyelia is often concurrent with developmental disorders of the craniocervical junction such as CLM. Syringomyelia is a disease in dogs characterized by fluid-cavitation of multiple spinal cord segment. The first feature of syrinx development is dilatation of the central canal, termed “hydromyelia”. At first, the cavity is lined by ependyma, but as expansion occurs, the lining is split and fluid enters into the grey matter of the spinal cord, creating a syringohydromyelia. The first fibers affected by the syrinx expansion are the fibers of the spinothalamic tracts. Damage of these fibers leads to the pain and paraesthesia associated with

the disease. As the syrinx enlarges, the ventral horn cells are damaged. Clinical signs associated with this change are muscle atrophy, weakness and decreased spinal reflexes. The syrinx may extend throughout the entire length of the spinal cord, resulting in corresponding clinical signs[15]. It is thought to be due to abnormal flow of CSF[7]. Chronic compression at the cervicomedullary junction, turbulent CSF flow, and pressure changes in this region are thought to lead to the underlying meninges becoming hypertrophied[5]. The rate of drainage of CSF is related to the venous blood pressure. CSF will only drain when CSF pressure exceeds venous pressure. Researchers have investigated reduced venous outflow as a mechanism for raised CSF pressures, especially in relation to the osseous abnormalities of CLM. Venous hypertension is thought to occur at the level of stenotic cranial foramina that causes a congestion of outflow, especially at the level of the venous sinuses. In canines, the jugular foramen is the major site of venous drainage. In a recent study, CKCS with SM had significantly narrower jugular foramina than those without SM[7].

DIFFERENTIAL DIAGNOSES

The most important differential diagnoses to consider for cervical spinal cord dysfunction include craniocervical malformations, subarachnoid diverticulae, and intervertebral disk disease (IVDD) with neoplasia less likely given the age of these patients[7]. Since scratching and ear rubbing are common clinical signs seen with CLM, otic and skin diseases need also be ruled out[19].

DIAGNOSTIC APPORACH/CONSIDERATIONS

CLM/SM can be easily confirmed through magnetic resonance imaging (MRI) or at necropsy after signalment and history have raised an index of suspicion. MRI is used to identify morphologic changes including cerebellar herniation, occipital hypoplasia, and SM[3]. However,

the correlation between morphologic changes and the presence or severity of clinical signs or SM in dogs with CLM is poor[3]. Maximum syrinx width is the strongest predictor of pain in these patients. In one study, 95% of CKCS with a maximum syrinx width of 0.64cm or more had more associated clinical signs[19]. The most helpful sequence in diagnosing CLM/SM via MRI are sagittal T2-weighted images that include the brain and the cervical spine to at least C4 as well as transverse T2-weighted images through the syrinx.

Computed tomography (CT) and MRI are both imaging modalities that are used to visualize the brain and detect a variety of intracranial lesions. Compared to MRI studies, CT imaging takes a shorter amount of time to complete, hence less anesthetic time, are less expensive, and the equipment is typically more widely available[12]. CT and radiographs have lesser value in the diagnosis of CLM compared with MRI. Certain radiographic findings that may be associated with dogs that have CLM are occipital dysplasia, widened foramen magnum, atlantoaxial subluxation, and dens abnormalities. Radiographs and CT studies are of the most value when ruling out other vertebral abnormalities such as atlantoaxial subluxation or IVDD[19].

Many members and breeders that are AKC registered have worked hard to raise awareness and funds to support clinical research into prevention of this disease[13]. The British Veterinary Association has created a canine health scheme that is aimed to reduce or eliminate the inheritance of CLM/SM in dogs. MRI images of the skull and upper neck are taken and reviewed by boarded neurologists and radiologists. The grading scale is according to the severity of CLM/SM changes seen in the images. These results are then sent to a genetics company in works toward developing estimated breeding values to reduce the prevalence of CLM/SM in future generations[2].

TREATMENT AND MANAGEMENT OPTIONS

Medical and surgical treatment options exist for dogs with CLM/SM. Since the pathophysiology of Nep is not entirely understood, the best medical treatment is through multi modal drug regimens. Medical management includes the use of drugs that reduce the CSF pulse pressure (furosemide), proton pump inhibitors (omeprazole) and carbonic anhydrase inhibitors (acetazolamide) that decrease CSF production, NSAIDs, corticosteroids, opioids, and anti-convulsant drugs that have analgesic properties (gabapentin, pregabalin)[14,17]. Even though these drugs are commonly used to relieve the symptoms of SM formation secondary to CLM, there is no scientific evidence to prove the efficacy of these drugs correcting the underlying structural abnormalities that are cause of CLM/SM. It is important to understand that although medical treatments may provide initial relief, most dogs become refractory to treatment and may require increases in dosages of medication, additional medications, or surgical intervention[20].

Surgical therapy has been recommended to improve the dog's quality of life and to slow clinical and radiographic progression of the syrinx[20]. The preferred treatment for people with symptomatic Chiari type 1 malformation is foramen magnum decompression (FMD) with duraplasty[6,24]. In canine patients, surgical procedures for treatment of CLM/SM consist of FMD with durotomy, FMD with a titanium-mesh cranioplasty and durotomy, and FMD with a durotomy and duraplasty with lyophilized swine submucosa coupled with a free adipose tissue autograft transplanted over the duroplast. These surgical techniques have been mostly successful in canine patients; however long term follow up information is being investigated[12].

OUTCOME AND PROGNOSIS

I.N. Plessas and others treated 39 dogs medically with gabapentin, pregabalin, and/or intermittent carprofen. In this study, morphometric values did not seem to play a significant role in the progression or improvement of the clinical signs. Thirty dogs showed progression of

clinical signs while nine remained static or improved with an overall survival rate of 75% at 39 months. This study shows that non-surgical management of this condition can be an acceptable option[14]. Ortinau, Vitale, Akin, Beasley, and Shores studied the long term outcome of 17 patients that underwent FMD surgery. All patients were re-evaluated 1 month after surgery, and some up to 3 years postoperatively. A questionnaire was sent out to 23 owners after a period of at least one year after surgery. 17 out of the 23 questionnaires were returned to the researchers. Out of these 17 patients, no patient required additional surgery, 94% had some improvement of quality of life after surgery, and none were judged to deteriorate to less than pre-surgical status. The researchers believe that the surgical procedure performed, combined with medical therapy, resulted in good long term outcomes[12].

CONCLUSION

CLM/SM prevalent disease in CKCS. It is a disease process that most closely resembles the human disease known as Chiari type 1 malformation. Recent advances in the study of CLM reveals that it is a naturally occurring model of Chiari type 1 malformation, and veterinarians have much to share with the human research committee[7]. CLM is a disease process that can have a wide variety of clinical signs ranging from no evidence of disease to episodes of excessive pain, making diagnosis frustrating for veterinarians. Medical and surgical treatment modalities have had good results for the treatment of CLM in dogs. CKCS breeders and the AKC are working together for funding and research on ways to reduce the prevalence of CLM/SM in future generations.

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