# NEUROLOGICAL DISEASES IN THE CAVALIER KING CHARLES SPANIEL CHIARI, EPISODIC FALLING, AND MORE.

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The Cavalier King Charles Spaniel (CKCS) breed has received heightened publicity recently in relation to certain detrimental breed conformation related health issues. While it is true that over-selection for certain physical phenotypes has led to the over-expression of related, and in some cases detrimental, conformational characteristics. However the breed clubs have been proactive in improving the health of the Cavalier King Charles Spaniel and addressing these undesirable phenotypes in what is a breed with a fantastic temperament. As part of this a joint project through our clinic at the University of Glasgow and the Canine Genetics Unit of the Animal Health Trust has likely identified the mutation responsible for Episodic Falling in the breed and if this is verified eradication of the disease from the breed can begin.

**What neurological diseases are over-represented in the CKCS:**

*The Cavalier King Charles Spaniel (CKCS) breed has a number of neurological diseases that occur at an increased frequency within the breed and these include:*

- Episodic Falling in the CKCS
- Canine Chiari malformation (resulting in syringomyelia or “syrinx”).
- Cerebrovascular disease (“strokes”) – particularly within the cerebellum causing predominantly acute onset central vestibular signs.
- Neurological diseases (and other organ system diseases) associated with the brachycephalic skull phenotype: mainly related to altered brain conformation and enlarged lateral brain ventricles on MRI (although these are not necessarily pathological), obstruction of the nasolacrimal duct, brachycephalic obstructive airway syndrome (not neurological as such, but complicating anaesthesia in these dogs) and primary secretary otitis media (glue ear – most likely through occlusion of the Eustachian tube).

- Neurological diseases associated with the chondrodystrophic phenotype (mainly Hansen type-1 intervertebral disc disease).
- Middle and inner ear disease, resulting in vestibular syndrome, hearing loss and facial nerve paralysis: related to ear conformation in most cases but often idiopathic as well in the breed.

## EPISODIC FALLING IN THE CKCS

Episodic Falling is a syndrome of muscle stiffness or collapse that occurs in the Cavalier King Charles Spaniel following exercise. The amount of exercise required to induce an episode varies between cases from only mild exercise in some dogs through to prolonged running exercise in other dogs. It has been suggested that stress or excitement may exacerbate the severity or frequency of the episodes and this is certainly the finding in our clinic. The more correct medical terminology to describe the syndrome is that of 'Paroxysmal Exercise-Induced Dystonia', and forms part of a group of Movement Disorders recognised in dogs, but the terms Episodic Falling and Hypertonicity have become accepted to describe the condition.

### How do Cavalier King Charles Spaniels affected by Episodic Falling present?

Affected dogs usually start to demonstrate evidence of collapsing episodes before one year of age, with most cases having their first episode between 4 to 7-months of age, however dogs having an onset of episodes at an older age have been reported. Both male and female dogs are affected. The episodes are usually induced by exercise or excitement and as the dogs begin to demonstrate evidence of an episode the pelvic limb gait becomes more and more exaggerated and stiff, the head often is held closer and closer to the ground (the so-called 'deer-stalker gait') and in some dogs the thoracic limb are advanced higher and higher (above the level of the head in severe attacks). In the most severe cases the head may get so low that the dogs somersault over. Finally the dogs collapse but remain conscious throughout and at this stage the tone in the limbs does not appear increased. The recovery is relatively rapid and the dogs quickly return to normal, however, if they are exercised immediately after recovery then this may rapidly induce another episode.

### How is the diagnosis of Episodic Falling confirmed in suspected cases?

The main problem with the disease is confirmation of the diagnosis. Historically the diagnosis has largely been one of exclusion, combined with witnessing one of the collapse episodes in an

otherwise normal dog. The current diagnosis of episodic falling is made based on the typical appearance of the episodes, but in particular must fulfil certain criteria:

- The episodes must demonstrate the characteristic high-stepping or stiff and stilted gait.
- The episodes are usually inducible with exercise.
- There must be no evidence of heart or respiratory problems during the episodes of collapse.

Further investigation in these cases; including blood tests, spinal fluid analysis, muscle biopsies and magnetic resonance imaging (MRI) of the brain have not proved helpful in diagnosing the condition. There are two reports of muscle changes in Episodic Falling (Wright et al., 1986; Wright et al., 1987), however these changes are not specific for Episodic Falling.

Genetic testing within our clinic as part of a joint University of Glasgow and Animal Health Trust PhD project through our clinic and the Canine Genetic Unit of the Animal Health Trust has identified the probable causative mutation, but this requires further validation, but a genetic test is likely in the next few months.

**Management of cases with severe episodes:**

If the diagnosis does appear consistent with Episodic Falling then the following medications can be tried (the response is variable between dogs and in some dogs there is no effective treatment). The medication only aims to control the episodes and does not cure the dog. Many dogs will only have a few episodes, or if they are young puppies may stabilise around a year of age, and many of these cases will therefore not require treatment. We also find that the disease may appear worse when the dog is stressed or ill for a different reason, and then the disease improves again once the underlying stress has resolved.

All drugs are given per os:

1. Diazepam:
   0.25mg/kg BID or TID for 2-weeks – if there is no favourable response after two weeks then the dose is increased to 0.5mg/kg BID or TID.
   Many dogs respond well to Diazepam but then develop tolerance after a few months.
2. Clonazepam:
   0.5mg/kg TID for 2-weeks – if there is no favourable response after two weeks then this should be stopped. .
   Most dogs respond well to Clonazepam but may develop tolerance after a few months.

3. Acetazolamide (this is usually only used as a last resort treatment in severe cases that do not respond to other treatments):

   31.5mg SID for 2-weeks (1/8 of a tablet – tablets are scored in 1/4's), then 31.5mg BID if no response to SID dosage – if there is no favourable response after two weeks then this should be stopped.

   Some dogs on treatment with acetazolamide appear unwell and in these cases the dose may need to be reduced or the treatment stopped.

## CANINE CHIARI MALFORMATION

(Also referred to as: Caudal occipital malformation syndrome)

Canine Chiari malformation occurs in the Cavalier King Charles Spaniel (and in some other small breeds) and most closely resembles the human Chiari I malformation. In affected Cavalier King Charles Spaniels there is evidence of hypoplasia of the caudal occipital bone resulting in crowding of the caudal fossa and subsequent herniation of the cerebellar vermis through the foramen magnum, dorsal to the spinal cord. The malformation is often clinically silent and is a frequent incidental finding on MRI in the Cavalier King Charles Spaniel. However, if the malformation interferes with the CSF drainage pathways, then syringohydromyelia ("syrinx") may develop with the associated clinical signs.

**Clinical Findings:**

The disease in the canine population is almost exclusively restricted to the Cavalier King Charles Spaniel breed, with affected dogs usually having a young age of onset, but varying from 6months up to 10 years of age. Canine Chiari syndrome exists in the breed at a high frequency without causing clinical signs. The clinical course of the disease varies between dogs from a few months to a matter of years. The clinical presentation is also extremely variable and in light of the frequent demonstration of canine Chiari syndrome as an incidental finding it can be a clinical challenge to decide whether the clinical signs are due to canine Chiari syndrome or an alternate cause. Affected dogs may present with a variety of clinical signs, including cervical pain, more generalised spinal pain, persistent cervical, head or flank scratching, torticollis, paresis, "bunny-hopping" pelvic limb gait, proprioceptive deficits, vestibular signs and facial nerve paralysis.

**Diagnosis:**

Diagnosis of canine Chiari syndrome depends of demonstration of the characteristic magnetic resonance imaging features of crowding of the caudal fossa due to hypoplasia of the occipital bone, with secondary syringohydromyelia of the cervical spinal cord, with variable caudal extension (in exceptional cases affecting the entire spinal cord).

**Treatment and Prognosis:**

Milder cases may be managed with moderate success with medical treatment, but in cases refractory to medical treatment (particularly those with marked spinal pain) surgical decompression of the caudal fossa and dorsal proximal cervical spinal cord may be indicated. A variety of medical managements have been proposed, with variable reported success. Of these low anti-inflammatory doses of prednisolone (0.5 mg/kg PO every other day) and analgesic therapy (in particular gabapentin, which is effective in neuropathic pain) can be tried in the first instance.

## CEREBROVASCULAR DISEASE ("STROKE")

Cerebrovascular disease is less common in dogs than in man, but does occur. Cerebrovascular disease affecting the cerebellum is over-represented in the CKCS, but is associated with a good prognosis. Affected dogs should be screened for underlying diseases, particularly cardiac, renal and hypercoagulable diseases, and in the CKCS hyperadrenocorticism.

Affected dogs with a cerebrovascular accident within the cerebellum usually present with an acute onset of central vestibular signs, but the disease is associated with a good prognosis and is non-progressive with a reasonably rapid improvement over the following days.

## HANSEN TYPE-1 INTERVERTEBRAL DISC DISEASE

Intervertebral disc disease is an important cause of canine neurological disease, accounting for over 2% of all diseases diagnosed in the dog. Affected patients typically present with clinical signs of pain or varying degrees of spinal cord dysfunction. Disc disease in the dog was first classified by Hansen as:

- Type I, where herniation of the nucleus pulposus occurs through the annular fibres of the disc into the spinal canal, and
    - Type II, where annular protrusion into the spinal canal is caused by shifting of the nucleus pulposus material. Both Hansen type I and type II disc disease are always preceded by disc degeneration.

A third type of disc extrusion may also occur:

- Traumatic disc extrusion may also occur where trauma causes rupture of a disc that demonstrated no obvious preceding degenerative changes, resulting in spinal cord injury with no or minimal residual compression.

Hansen type I intervertebral disc primarily occurs in chondrodystrophic breeds, including the CKCS. In these dogs dehydration and calcification of the nucleus pulposis occurs. Because this is a degenerative process it is very unusual to see a Hansen type I disc extrusion in a dog less than 2 years of age and virtually unheard of in dogs less than a year of age. The disc extrusions also tend to occur in specific regions: the cervical region and adjacent to the TL junction (from T10 to L3 vertebrae).

## PRIMARY SECRETARY OTITIS MEDIA ("GLUE EAR")

Viscous mucus accumulation within the middle ear is a common finding in the CKCS. The lesion is frequently incidental, but may be associated with pain localised to the ear or head and may result in neurological signs. The tympanic membrane is frequently normal, but in some cases may bulge outwards. Treatment in clinically affected cases is by myrinotomy with removal of the mucous material by ear flushing and following up with topical ear treatments and systemic anti-inflammatory and antibiotic therapy. Some cases may require a ventral bulla osteotomy.

## IDIOPATHIC VESTIBULAR SYNDROME AND OTITIS MEDIA / INTERNA

Vestibular disease is common in the breed, usually peripheral as a result of middle and inner ear disease or as an idiopathic syndrome.

The diagnosis of Idiopathic Vestibular syndrome is usually confirmed based on the peracute onset of clinical signs, the absence of clinical signs supportive of otitis media/interna, and negative otoscopic and radiographic (if performed) findings. While the cause is unknown in idiopathic vestibular disease, the prognosis for spontaneous remission is good. Recovery does take 2 or 3 weeks and recurrences may occur. The head tilt, return of appetite and strabismus may take the longest to return to normal.

Otitis media is another common cause of vestibular signs in the CKCS and is usually associated with extension of otitis externa into the middle and inner ears, but may arise in the absence of

external ear canal inflammation. Foreign bodies in the external ear canals, e.g. grass awns, may penetrate the tympanic membrane or cause a chronic otitis externa that results in rupture of the tympanic membrane. In the absence of otitis externa, the other two routes of infection include retrograde spread via the Eustachian tubes and haematogenous spread. The most common infectious agents are bacteria, including Staphylococcus sp., Streptococcus sp., Proteus sp., Pseudomonas sp., Enterococcus sp., and Escherichia coli. If otitis media-interna is suspected but bacterial culture results are not available then the choice of antibiotic is usually based on sensitivity to the above bacteria.

The clinical signs associated with otitis media-intena may include all the clinical signs associated with vestibular disease and may have an acute onset. The clinical signs may frequently partially improve as the animal compensates for the vestibular deficits over the next day or two. However, in contrast to idiopathic vestibular syndrome there are usually secondary clinical signs related to the ear infection. These may include:

- Discharge from the external ear canal. Head shaking, scratching or rubbing at the ears and frequent yawning.
- Abnormalities on auroscopic examination of the tympanic bulla.
- Pain on opening the mouth or palpation of the structures adjacent to the ear.
- Damage to adjacent nervous system structures, in particular the facial nerve and sympathetic supply to the head (Horner's syndrome). Facial nerve dysfunction may affect the parasympathetic lacrimal glands supply, resulting in a dry eye and nose. Facial nerve lesions occurs in about 50% of animal with otitis media-interna.
- Early irritation of the facial nerve may result in hemifacial spasm, although this is less common.

Diagnosis of otitis media-interna is based on finding of peripheral vestibular syndrome, typical clinical signs of ear disease, auroscopic examination of the tympanic membrane, radiography or advanced imaging of the ear canals and possibly surgical exploration. If there is evidence of fluid accumulation in the middle ear, on the basis of discoloration and outward bulging of the tympanic membrane then collection of a sample for culture, cytology and sensitivity should be performed via a myringotomy. The owners need to be warned that the clinical signs related to the vestibular dysfunction may temporarily deteriorate post anaesthesia.

Treatment of otitis media-interna is usually initially with appropriate antibiotics, based on bacterial culture results. Prognosis is usually good with a prolonged course of appropriate oral and topical antibiotics. Where culture and sensitivity results are not available then empirical treatment is usually attempted with an appropriate antibiotic based on the most likely bacteria. Suitable antibiotics include cephalexin (20 to 25 mg/kg PO BID); trimethoprim-sulfadiazine (15 mg/kg, PO BID) and amoxicillin-clavulanic acid (20 mg/kg BID), for 4 to 6 weeks. Where there is evidence of keratoconjunctivitis sicca then treatment with trimethoprim-sulfadiazine is avoided. If there is evidence of keratoconjunctivitis sicca then additional use of artificial tears and ocular lubricants is recommended. In advanced cases, or cases where medical treatment is not successful, surgical drainage of the middle ear via a ventral bulla osteotomy may be required.

## IDIOPATHIC FACIAL NERVE PARALYSIS

Idiopathic facial nerve paralysis: this is the most common cause of facial nerve paralysis in dogs (75% of cases in one study) and is common in the CKCS. There is an acute onset of unilateral or bilateral facial nerve paralysis with no other abnormalities evident. In some cases this may be combined with idiopathic vestibular syndrome. In some cases there will be recovery in weeks, but in the majority of cases the abnormality is permanent. The deficits are largely cosmetic, although there is an increased risk of exposure corneal ulcers in dogs with protruding eyes. In other dogs little intervention is required, besides keeping the lips clean to prevent moist dermatitis in dogs with excessive drooling and drooping lips.