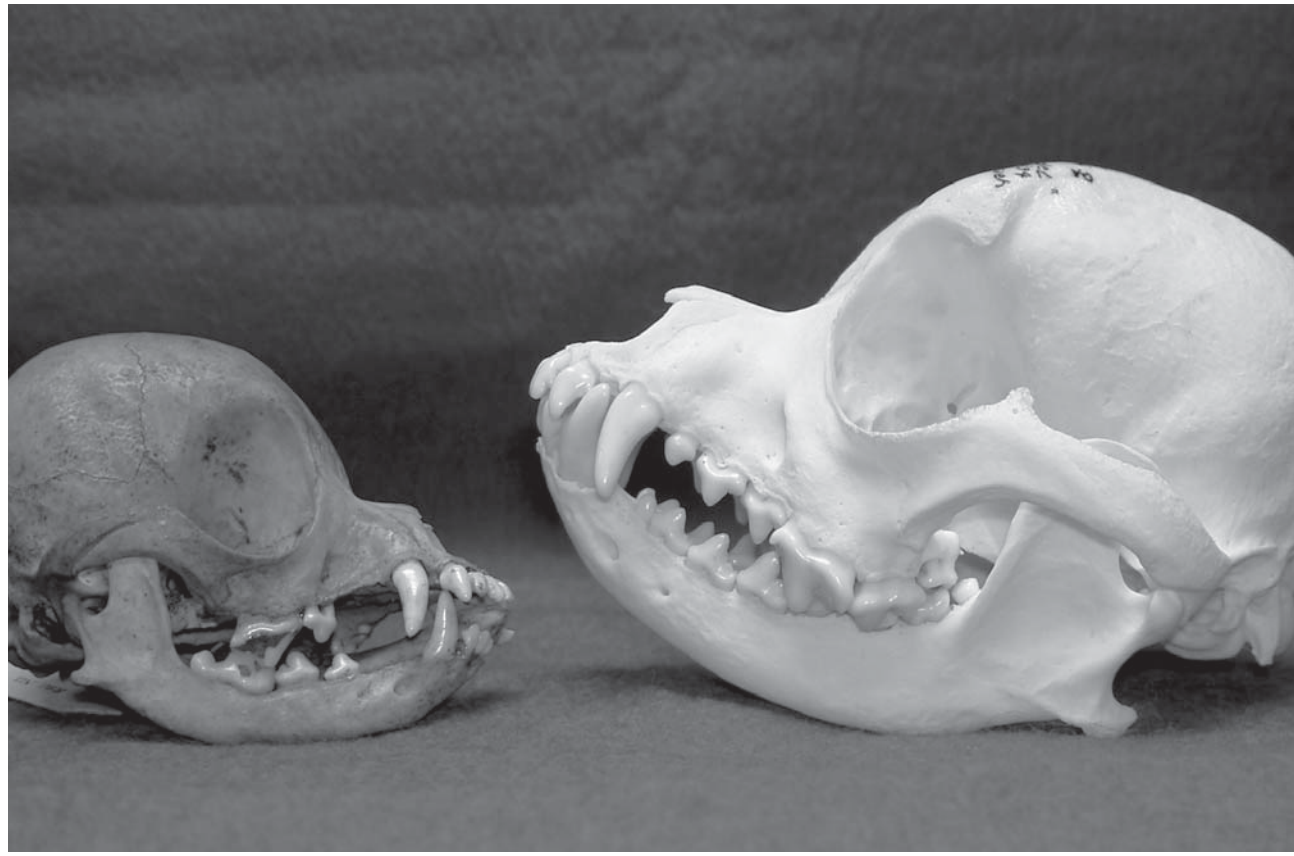

Section 4

Chiari-like malformation
in the cavalier King Charles spaniel

Chapter 4.1

Association between cervical and intracranial dimensions and syringomyelia in the cavalier King Charles spaniel

H. Carruthers [1] C. Rusbridge [1] M-P Dubé [2] M Holmes [3] N.D. Jeffrey [3]

1. Stone Lion Veterinary Centre, 41 High Street, Wimbledon Village, London, SW19 5AU, 2. Department of Medicine, Université of Montreal, and the Montreal Heart Institute, Canada, 3. Department of Veterinary Medicine, University of Cambridge, Madingley Road, Cambridge, CB3 OES

Introduction

Since its first recognition in the 1990s (Rusbridge and others 2000), Chiari-like malformation (CM) of the skull, syringomyelia (SM) and their associated clinical signs have become well-known entities in the cavalier King Charles spaniel (CKCS). CM refers to the apparent mismatch in volume of the caudal brain structures to the caudal skull, which is associated with herniation of the most caudal aspects of the cerebellum through the foramen magnum (Rusbridge and others 2000). SM refers to the accumulation of fluid within the parenchyma of the spinal cord. CM is thought to cause SM through changes in the dynamics of CSF flow through the foramen magnum and in the cranial part of the cervical spinal cord (Pinna and others 2000, Iskander and others 2004, Rusbridge and others 2006) and occurrence of both disorders simultaneously is abbreviated to CM/SM in this paper.

Clinical signs typically associated with canine syringomyelia include apparent spontaneous neck or head discomfort, scoliosis and frequent scratching at the skin on the lateral aspect of the neck/ shoulder/ ear, often accompanied by signs suggesting pain, for example vocalisation (Rusbridge 1997). Comparable signs occur in affected human patients, who can report signs of headache, and neuropathic pain, such as paraesthesias and unusual sensitivity to light touch (Greenlee and others 1999, Nogajski and others 2006).

Chiari type 1 malformation in man (CMI) can remain undiscovered until adulthood although detection rates have increased with greater MRI scan availability (Masson and Colombani 2005). Whilst it appears that CM is related to underdevelopment of the posterior cranial fossa, SM is diagnosed in only 32-74% of patients with CMI, suggesting that there may be other predisposing factors in the pathogenesis (Masson and Colombani 2005). Likewise CM/SM is hypothesised to be a multifactorial disease in CKCS (Cerda-Gonzalez and others 2006) and various explanations for the occurrence of SM in the presence of skeletal abnormalities have been mooted. For example CSF flow dynamics have been studied and descriptors such as *Venturi effect* have been used to explain why a high velocity CSF jet passing through a partially obstructed foramen magnum and/or narrowed vertebral canal might cause SM (Iskander and others 2004, Rusbridge and others 2006). Whilst it is logical to conclude that skull morphology is a causal factor in development of SM in dogs, previous attempts to link specific measurements of the volume of the skull or cerebellum with the incidence of SM, or clinical signs suggestive of SM, in CKCS dogs, have met with little success (Lu and others 2003, Cerda-Gonzalez and others 2006). In this article we further describe the relationship between various anatomical measurements and the incidence of SM.

Material and methods

The population consisted of 85 CKCS that included all CKCS (25 dogs) that presented to Stone Lion Veterinary Centre (SLVC) Neurology service in a 2 year period (June 2003 to June 2005) and had a brain and/or cervical MRI scan for any reason. In addition there were also 60 breeder- owned CKCS that had a brain and cervical MRI scan either for diagnostic reasons or for screening prior to breeding. Siemens Magnetom Symphony 1.5T MRI units were used in each case. The DICOM ™ MRI images for each dog were blinded by replacing identifying information with a numerical code by a co-worker who had no role in the assessment or interpretation of the images. The anonymous images were then uploaded into a DICOM ™ viewer (Merge eFilm, Spegelt 34, 5674 CD Nuenen, Netherlands, www.merge-efilm.com). The diagnosis of SM, confirmed by detection of a fluid signal within the spinal cord parenchyma, was made independently by each of 3 of the authors from T2- weighted sagittal and transverse images of the cervical spinal cord.

Two intracranial measurements were used to represent caudal fossa area. The length of the caudal fossa was measured as the length of the basioccipital bone from its most caudal landmark to the junction between the rostral brainstem and the subarachnoid space (Figure 1; line a) as an estimate of the length

of base of the caudal fossa. In preliminary trials, this measurement was determined by the authors to be the most repeatable and consistent measurement of the floor of the caudal fossa. The height of the caudal fossa was taken as a line running perpendicular to the length of the caudal fossa, from the highest point in the caudal fossa to the skull base (Figure 1; line b). The caudal fossa area was represented by calculating the caudal fossa length multiplied by half the caudal fossa height. The product of these two measurements was termed the area of the caudal fossa triangle.

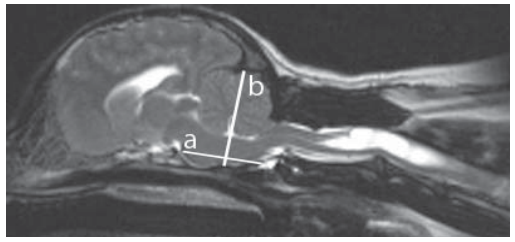

Figure 1 Midsaggittal T2 weighted MRI of the brain and upper cervical spinal cord from case 52, a 4.1 year old female neutered CKCS with syringomyelia
Line a. represents length of the caudal fossa
Line b. represents height of caudal fossa

Four measurements of the vertebral canal height were recorded (Figure 2). The greatest dorsoventral distance across the spinal canal at C1/2 (line c) C2 (line d) C2/C3 (line e) and C3 (line f.)

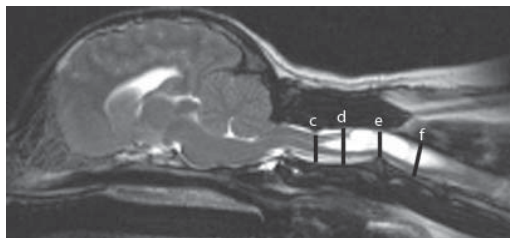

Figure 2 Midsaggittal T2 weighted MRI of the brain and upper cervical spinal cord from case 52
Line c. represents the greatest dorsoventral distance across the spinal canal at C1/C2,
Line d. the distance across C2,
Line e. the distance across C2/C3
Line f. the distance across C3

The angle across the C2/C3 junction was measured as the external angle at the intersection of lines showing the angle of the C2 and C3 vertebrae (Figure 3, line g and line h).

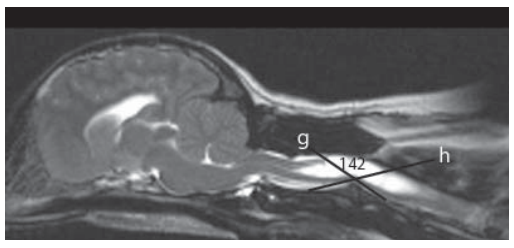

Figure3 Midsaggittal T2 weighted MRI of the brain and upper cervical spinal cord from case 52
The angle of the C2/C3 junction (in this case 142º) is indicated by external angle formed at intersection of line **g**. and line **h**.

For the study population, the mean of those measurements made by the examiners was used for further analysis. For the decision regarding appearance of syrinx (this applied only when syrinx was less or equal to 0.1mm dilatation of the central canal [3 dogs]) a consensus call was applied. Once the data analysis was complete, records were unblinded and corresponding information on age at the time of the MRI scan, gender, and clinical signs, including historical pain, could be added.

Statistical analysis was conducted using the statistical programmes SAS v9.1.3 (SAS Institute Inc., Cary, NC, USA.) and NCSS (NCSS v.2004, Hintze, J. (2001). NCSS and PASS. Number Cruncher Statistical Systems. Kaysville, Utah). Normality of variables was first evaluated and then parametric or non-parametric tests were used as appropriate, to test for differences in the two populations. Tests used were Mann-Whitney U, Chi-square, Equal-Variance T-Test and Aspin-Welch Unequal Variance Test. Significance was set to $p<0.05$.

Results

Results are shown at Table 1 (Univariate Statistics) and Table 2 (Association test results for presence of syrinx).

Table 1 Univariate statistics for study population of 78 CKCS

Parameter	Number of Dogs	Mean	%	Standard Deviation	Standard Error	Minimum	Maximum	Range
Sex (% males)	78		39.7					
Age at time of scan (years)	78	3.0		2.05	0.23	0.6	9.3	8.7
Syrinx present	78		75.6					
Caudal fossa height (cm)	47	3.14		0.16	0.02	2.80	3.50	0.70
Caudal fossa length (cm)	47	2.54		0.14	0.02	2.27	2.80	0.53
Area caudal fossa triangle (cm^2)	47	4.00		0.33	0.05	3.36	4.73	1.36
Caudal fossa ratio	47	0.81		0.05	0.01	0.71	0.93	0.22
Widest point C2 (cm)	77	1.01		0.08	0.01	0.83	1.20	0.37
Width canal C2/C3 (cm)	77	0.73		0.06	0.01	0.60	0.87	0.27
Widest point C3 (cm)	77	0.84		0.07	0.01	0.73	1.03	0.30
C2/C3 angle (°)	77	147.11		6.15	0.70	133.67	166.33	32.67
Narrowest point C1/C2 to dens (cm)	74	0.98		0.09	0.01	0.63	1.20	0.57

Table 2 Association test results for presence of syrinx

Parameter	SM	Number of dogs	Mean	%	Standard Deviation	Standard Error	p-value	Test
Sex (% males)	N	19		36.8			0.7663	Chi-square
	Y	59		40.7				
Age at time of scan (years)	N	19	1.6		1.09	0.25	**0.0001**	Mann-Whitney U
	Y	59	3.4		2.10	0.27		
Narrowest point C1/C2 to dens (cm)	N	18	1.01		0.10	0.02	0.1299	Equal-Variance T-Test
	Y	56	0.97		0.09	0.01		
Widest point C2 (cm)	N	19	1.01		0.05	0.01	0.7693	Aspin-Welch Unequal-Variance Test
	Y	58	1.01		0.09	0.01		
Width canal C2/C3 (cm)	N	19	0.70		0.06	0.01	**0.0116**	Equal-Variance T-Test
	Y	58	0.74		0.06	0.01		
Widest point C3 (cm)	N	19	0.81		0.04	0.01	**0.0099**	Aspin-Welch Unequal-Variance Test
	Y	58	0.85		0.07	0.01		
C2/C3 angle (°)	N	19	146.16		5.89	1.35	0.4412	Equal-Variance T-Test
	Y	58	147.42		6.25	0.82		
Caudal fossa height (cm)	N	6	3.02		0.14	0.06	**0.0395**	Equal-Variance T-Test
	Y	41	3.16		0.16	0.02		
Caudal fossa length (cm)	N	6	2.53		0.12	0.05	0.8713	Equal-Variance T-Test
	Y	41	2.54		0.14	0.02		
Area caudal fossa triangle (cm^2)	N	6	3.82		0.18	0.07	0.1584	Equal-Variance T-Test
	Y	41	4.03		0.34	0.05		
Caudal fossa ratio	N	6	0.84		0.07	0.03	0.1115	Equal-Variance T-Test
	Y	41	0.81		0.05	0.01		

Significant values are in bold. Y – syringomyelia present N – syringomyelia absent

7 dogs were excluded because of missing or corrupted MRI data, which left 78 dogs for the analysis. Of those, 59 dogs had SM. This resulted in a study of 78 dogs consisting of 59 SM and 19 non-SM dogs. The average age at the time of the MRI scan was 3 ± 2.05 years (SD - standard deviation) and 40% of dogs were male. We found a significant difference in the age at the time of scan between dogs with SM versus those without (p=0.0001). Overall, older dogs were more likely to have SM. There was no difference between males and females for the presence of SM.

The area of the caudal fossa triangle had a mean of 4 ± 0.33cm^2 (SD). This parameter was not associated with presence of syrinx (p=0.158). The length of the caudal fossa was not associated with SM (p=0.8713) however the caudal fossa height was (p=0.0395). However the difference in values (0.14cm) was minimal, especially given that the smallest measurement we could appreciate was 0.1cm. Dogs with SM had a mean height of 3.16 ± 0.16cm compared to dogs without SM that had a mean of 3.02 ± 0.14cm. The narrowest point at C1/C2 had a mean of 0.98 ± 0.09cm (SD) and there was no significant association with the presence of SM, (p=0.130). The widest point at C2 had a mean of 1.01 ±0.08cm (SD) and was not associated with presence of SM (p=0.769).

The height of the cervical canal at the C2/C3 junction had a mean of 0.73 ± 0.06cm (SD). Dogs with SM had a mean width of 0.74 ±0.06cm (SD) versus 0.70 ± 0.06cm (SD) for dogs without SM. Although this difference was statistically significant (p=0.012) the actual value (0.04cm) is not measurable within a clinical setting. Likewise there was a significant association between the height at C3 and the presence of SM (p=0.010). Dogs with SM had a mean height of cervical canal of 0.85 ±0.07cm (SD) versus 0.81(±0.04) cm in dogs without SM. The association remained significant after adjustment for age (p=0.015) however again the difference (0.04cm) was not measurable within a clinical setting. The angle at C2/C3 did not show a significant correlation to the appearance of syrinx (p=0.4412).

Discussion

This study found that the caudal fossa height and the height of the vertebral canal at C2/C3 and C3 were significantly larger in dogs with SM. However for all of these parameters the mean difference between the two groups was so small that they are not or only barely measurable with standard techniques and it is debatable whether they could be truly associated with SM. Further study is needed before drawing any conclusions. This is especially true for the measurements of vertebral canal height at C2/C3 and C3 as a chronic expanding syrinx may cause vertebral canal widening by bone resorption and therefore the apparent difference could be a consequence rather than a cause of SM.

The area of the caudal fossa triangle was not correlated to SM. This may be either because there is no relationship between overcrowding of the caudal skull and SM, or that the dimensions measured in this study did not accurately represent caudal fossa volume. Although conclusions cannot be drawn because of these limitations, this study does support the general view that the pathogenesis of SM involves more than foramen magnum overcrowding. Cerda-Gonzalez and others (2006) also found no difference in caudal fossa volume in CKCS with and without SM. This finding also has implications for MRI screening of potential breeding stock. Most importantly it is not possible to predict whether or not a young dog with CM is at risk of developing SM.

The *intramedullary pulse pressure theory* (Rusbridge and others 2006) suggests SM occurs because of

repeated mechanical distension of the spinal cord due to abnormal pressure differences between the spinal cord and the subarachnoid space. It was hypothesised that an important contribution were the changes in CSF flow and/or turbulence that occur as the vertebral canal narrows particularly in the C1 to C3 area (*Venturi effect*). However this study found no association between vertebral canal narrowing and development of SM. There was also no association between the angulation at C2/C3 and development of SM. The older dogs in the study had a greater incidence of SM than the younger ones. The reason for this association is not clear. It is likely that SM develops with time and/or that clinical signs in presence of SM take longer to appear in some dogs than in others. A similar situation occurs in CMI in humans where symptoms of SM often take time to develop (Masson and Colombani 2005). An alternate argument is that the apparent relationship of SM and age is skewed by sampling techniques; for example it is not known whether those dogs that presented for MRI as part of a diagnostic work-up were more likely to represent the population's older cohort. Correspondingly, animals undergoing MRI, but as part of a screening programme, may represent the younger cohort, which may have tended to be asymptomatic. It is not obvious therefore whether anatomical parameters should have been adjusted for age prior to assessing the significance of their association with SM. Nor is it clear whether allowance should have been made in this study for parameters such as the size, or weight of individuals, which may have helped to amplify the differences between the SM and non-SM groups. Further studies are required to analyse matched groups of CKCS at various ages to determine the effects of age and body size on occurrence of SM.

Conclusion

This study did not find a significant correlation between a small caudal fossa and development of SM. There was also no correlation between narrowing of the cranial cervical canal and development of SM. The study did find a significant association with widening of the vertebral canal at C2/C3 and C3 however we recommend caution in drawing a conclusion from these results because the actual difference was smaller than our ability to measure using standard techniques. Considerable further reasearch into this disorder is required for example a study in age and weight matched young CKCS with and without SM is planned. Finally, in order to establish if reduced caudal fossa area is a widespread problem within the CKCS breed, comparative studies of caudal fossa size between various breeds are required.

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