Syringomyelia and Craniocervical Junction Abnormalities in Chihuahuas

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Background: Chiari-like malformation (CM) and syringomyelia (SM) are widely reported in Cavalier King Charles Spaniels and Griffon Bruxellois dogs. Increasing evidence indicates that CM and SM also occur in other small and toy breed dogs, such as Chihuahuas.

Objectives: To describe the presence of SM and craniocervical junction (CCJ) abnormalities in Chihuahuas and to evaluate the possible association of CCJ abnormalities with SM. To describe CM/SM-related clinical signs and neurologic deficits and to investigate the association of CM/SM-related clinical signs with signalment, SM, or CCJ abnormalities.

Animals: Fifty-three client-owned Chihuahuas.

Methods: Prospective study. Questionnaire analyses and physical and neurologic examinations were obtained before magnetic resonance and computed tomography imaging. Images were evaluated for the presence of SM, CM, and atlantooccipital overlapping. Additionally, medullary kinking, dorsal spinal cord compression, and their sum indices were calculated.

Results: Scratching was the most common CM/SM-related clinical sign and decreased postural reaction the most common neurologic deficit in 73 and 87% of dogs, respectively. Chiari-like malformation and SM were present in 100 and 38% of dogs, respectively. Syringomyelia was associated with the presence of CM/SM-related clinical signs ($P = 0.034$), and medullary kinking and sum indices were higher in dogs with clinical signs ($P = 0.016$ and $P = 0.007$, respectively).

Conclusions and Clinical Importance: Syringomyelia and CCJ abnormalities are prevalent in Chihuahuas. Syringomyelia was an important factor for the presence of CM/SM-related clinical signs, but many dogs suffered from similar clinical signs without being affected by SM, highlighting the clinical importance of CCJ abnormalities in Chihuahuas.

Key words: Chiari-like malformation; Magnetic resonance imaging; Neuropathic pain; Scratching.

Chiari-like malformation (CM) and syringomyelia (SM) are widely reported in Cavalier King Charles Spaniels (CKCSs) and Griffon Bruxellois dogs.[1–5] Increasing evidence indicates that CM and SM also occur in other small and toy breed dogs (e.g, Yorkshire terriers, Chihuahuas, Maltese dogs, Pugs, Miniature poodles, and Pomeranians).[6,7]

Chiari-like malformation has been defined as a multifactorial condition that includes shortening of the entire basicranium, loss of convexity of the supraoccipital bone, invagination of the cerebellum under the occipital lobes, and increased proximity of the atlas to the occiput, causing overcrowding of the caudal cranial fossa and craniocervical junction (CCJ). As a compensatory

Abbreviations:

CCJ	craniocervical junction
CKCS	Cavalier King Charles Spaniel
CM0	Chiari-like malformation grade 0
CM1	Chiari-like malformation grade 1
CM2	Chiari-like malformation grade 2
CM	Chiari-like malformation
CT	computed tomography
MRI	magnetic resonance imaging
SM0	syringomyelia grade 0
SM1	syringomyelia grade 1
SM2	syringomyelia grade 2
SM	syringomyelia

change, height of the rostral cranial cavity increases and the dorsal cranial vault lengthens.[8] Syringomyelia is characterized by fluid-filled cavities within the spinal cord.[9,10]

Morphometric studies suggest that SM-affected dogs have a smaller caudal cranial fossa and relative caudal cranial fossa overcrowding, although other studies have challenged these results.[11–17] It has further been suggested that cranial venous outflow is impaired in SM-affected dogs, which might also contribute to the pathogenesis of SM.[18,19] Furthermore, CKCSs with SM have a shortened and broader skull, and as a consequence, rostrocaudal doming of the cranium.[20] Similar findings have been described in Griffon Bruxellois dogs.[8]

Recently, in addition to CM, other CCJ abnormalities, such as dorsal spinal cord compression at the first 2 cervical vertebrae, caudal position of the obex, and atlantooccipital overlapping, have been reported to be associated with SM.[21–23]

Although not all SM-affected dogs show clinical signs, SM is an important predisposing factor for the presence of neuropathic pain in dogs.[1,2,24] In humans, type I Chiari malformation, a human counterpart of CM in dogs, also is associated with neuropathic pain, and it has been proposed that CM alone could also cause neuropathic pain in dogs.[1,2,25] Additionally, some evidence suggests that atlantooccipital overlapping, medullary elevation, and dorsal spinal cord compression are associated with clinical signs in dogs.[21–23]

The aims of our prospective study were to:

1 Describe the presence of SM and CCJ abnormalities, including CM, dorsal spinal cord compression, medullary elevation, and atlantooccipital overlapping, in Chihuahuas.
2 Evaluate the possible association of CCJ abnormalities with the presence of SM.
3 Describe the distribution of CM/SM-related clinical signs and neurologic deficits.
4 Investigate the association of CM/SM-related clinical signs with SM or CCJ abnormalities in Chihuahuas.
5 Investigate possible associations between signalment and presence of CM/SM-related clinical signs or SM.

Our hypothesis was that SM and CCJ abnormalities exist commonly in Chihuahuas and that CCJ abnormalities predispose to SM. Additionally, we hypothesized that the clinical signs and neurologic deficits are comparable to those previously described in CKCSs and Griffon Bruxellois dogs and are associated with both SM and CCJ abnormalities. Furthermore, we hypothesized that no differences in sex, breed, or weight of dogs with or without CM/SM-related clinical signs or SM will be detected. To the authors' knowledge, no previous prospective studies described CM and SM imaging findings and their associations with CM/SM-related clinical signs in Chihuahuas.

Materials and Methods

Case Selection

Client-owned Chihuahuas with or without typical clinical signs related to CM and SM[9,26] were enrolled in this prospective study, which was approved by the Finnish National Animal Experiment Board. Participation was voluntary and all owners provided written consent. Recruitment of dogs was done by selecting dogs from the case load of the Veterinary Teaching Hospital of the University of Helsinki. Additionally, a low-cost screening examination to detect CM and SM in Chihuahuas was advertised at Finnish Chihuahua breed club events and on their website from January 2012 until August 2015.

The presence or absence of CM/SM-related clinical signs was evaluated by an owner questionnaire designed for the study. The CM/SM-related clinical signs used as inclusion criteria were chosen based on previous publications.[26–28] Typical CM/SM-related clinical signs that we enquired about in the questionnaire included the presence of persistent scratching episodes (ears, shoulders, or cranial thoracic spine) with or without skin contact, facial rubbing, spinal pain, vocalization, and gait abnormalities such as incoordination or weakness. If they had at least 1 of the above-mentioned

CM/SM-related clinical signs, dogs were included in the group of dogs with CM/SM-related clinical signs.

Dogs were excluded from both groups if they had a history of another structural central nervous system disease or a severe orthopedic problem. Additionally, if during the study severe imaging artifacts or other neurologic diseases able to cause clinical signs similar to CM or SM were detected, dogs were excluded from the study. No age limits were set for dogs with CM/SM-related clinical signs, whereas dogs without CM/SM-related clinical signs needed to be at least 3 years old because of the increasing prevalence of SM until the age of 3 years in CKCSs.[4]

Assessment of Clinical Signs and Neurologic Examination and Further Case Selection

Clinical and neurologic examinations were performed on all dogs at the Veterinary Teaching Hospital, University of Helsinki, by 1 of the authors (AMK). A detailed history was obtained for each dog, confirming the information from the owner questionnaire. If the dog had dermatologic, orthopedic, or other health problems considered to affect the CM/SM-related clinical signs, such as scratching or abnormal gait, the dog was excluded from the assessment of CM/SM-related clinical signs and their association with imaging findings.

A grading system was developed for the description of the severity of CM/SM-related clinical signs assessed by the owner questionnaire. The presence and frequency of such CM/SM-related clinical signs such as:

1 persistent scratching episodes of the ears or shoulders with or without skin contact
2 persistent scratching episodes of the cranial thoracic spine with or without skin contact
3 facial rubbing
4 spinal hyperesthesia
5 vocalization
6 gait incoordination
7 weakness

were graded from 1 (occurring <2 times a week) to 5 (occurring several times a day). A percentage from the maximum points (7*5 = 35 points) was calculated for each patient.

Diagnostic Imaging Analysis

All dogs underwent magnetic resonance imaging (MRI) and computed tomography (CT) imaging of the brain and cervical spine under general anesthesia. The anesthesia protocol was planned individually for each patient by the anesthesiologist in charge.

The MRI was performed with a 0.2 Tesla MR scanner.[a] All dogs were positioned in sternal recumbency and with the base of the skull aligned perpendicular to the ventral vertebral canal at the first 2 cervical vertebrae. In dogs without CM/SM-related clinical signs, sagittal T1- and T2-weighted sequences of the brain and cervical spine, T1- and T2-weighted transverse sequences of the brain, and T1-weighted transverse sequences of the spinal cord between C1 and C4/5 were acquired. In dogs with CM/SM-related clinical signs, similar images were acquired, but additionally, the entire cervical spinal cord was imaged and T2-weighted transverse images of the cervical spine were obtained to eliminate other diseases, such as intervertebral disk disease, that could cause similar clinical signs to those of CM or SM. If considered necessary, additional sequences, such as T1-weighted dorsal, and contrast-enhanced (gadoteric acid[b] IV) transverse, and dorsal sequences of the brain and transverse sequences of the spinal cord, were obtained to eliminate other diseases such as neoplasia causing secondary SM. In

dogs with CM/SM-related clinical signs, the extent of the images occasionally was extended based on the clinical judgment of the neurologist (e.g, due to spinal pain located caudally to the cervical spine, SM extending to the caudal border of the MR images). The MRI parameters used are described in Table 1.

Computed tomographic images of the head and cranial cervical spine, including the C3 vertebra, were acquired with a helical dual slice scanner[c] with a bone algorithm. Slice thickness was 1.0 mm, feed/rotation 2 mm, and reconstruction increment 0.5 mm. The dogs were positioned so that the base of the skull was aligned perpendicular to the ventral vertebral canal in the cranial cervical spine.

The MRI images were independently evaluated by 2 board-certified neurologists (CR and TSJ) who were blinded to the signalment, CM/SM-related clinical signs, and each other's findings. The presence of CM and SM was graded according to the British Veterinary Association/Kennel Club CM and SM Health Scheme: with SM0 denoting a normal spinal cord, SM1 a central canal dilatation or a separate syrinx with <2 mm in diameter or a presyrinx alone, and SM2 a central canal dilatation or a separate syrinx with at least 2 mm in diameter (Table 2). Chiari-like malformation was assessed from the T1- and T2-weighted sagittal images, and SM from the T1-weighted transverse images. Additionally, if SM2 was present, each evaluator recorded the maximum syrinx width from the T1-weighted transverse images, and the mean width of these 2 recordings was used.

Table 1. MRI parameters used for imaging the head and cervical spine.

Sequence and plain obtained	Anatomy imaged	TR (ms)	TE (ms)
T1W sagittal	Brain and cervical spine	420–790	18
T2W sagittal	Brain and cervical spine	2,500–3,000	80
T1W transverse	Brain	600–1190	18
T2W transverse	Brain	2,500–4,870	80
T1W transverse	Cervical spinal cord	490–1110	18
T2W transverse	Spinal cord	2,500–3,770	80
T1 dorsal	Head	490–600	18

TR, time of repetition; TE, time of echo. The slice thickness was 3.5–4.5 mm and the matrix 256 × 256.

Table 2. Grading of Chiari-like malformation and syringomyelia according to the British Veterinary Association/Kennel Club Chiari-like malformation and Syringomyelia health scheme.

Chiari-like malformation	
CM0	No Chiari-like malformation
CM1	Cerebellum indented (not rounded)
CM2	Cerebellum impacted, or herniated through the foramen magnum
Syringomyelia	
SM0	Normal, no central canal dilatation, no syrinx, no presyrinx
SM1	Central canal dilatation or a separate syrinx with <2 mm diameter, or a presyrinx alone
SM2	Central canal dilatation or a separate syrinx with at least 2 mm diameter measured at maximal width in a transverse plane

CM, Chiari-like malformation; SM, syringomyelia.

To eliminate possible middle ear diseases causing scratching or facial rubbing, content in the tympanic bullae was evaluated as being present or absent in the left, right, or both ears.

To provide an objective assessment of the severity of the neural parenchymal deviation at the craniocervicomedullary junction, the dorsal spinal cord compression caused by atlantoaxial bands and medullary elevation caused by the dens were evaluated in MRI by calculating the dorsal spinal cord compression index and the medullary kinking index as previously described.[29] Each dog was measured 3 times by 1 investigator (AMK), and the mean values of the 3 measurements were used for statistical purposes. Additionally, to evaluate the effect of both dorsal and ventral compression occurring simultaneously, a sum index (dorsal spinal cord compression index + medullary kinking index) was calculated for each dog to assess the simultaneous effect of possible bidirectional deviation (Fig 1).

A veterinary radiologist (AKL) evaluated the CT images for the presence of atlantooccipital overlapping. They were evaluated at the midsagittal plane by drawing a line extending from the caudodistal aspect of the supraoccipital bone to the caudal tip of the basioccipital bone. The CCJ was considered as overlapped when the dorsocranial border of the lamina of the atlas was at the level of the line (grade 1) or cranial to it (grade 2). The CCJ was considered normal when the dorsocranial border of the lamina of the atlas was caudal to the line (Fig 2A, B, and C).

Statistical Analysis

Statistical analysis was performed by a commercial software package.[d] Normality of the variables was evaluated by the Kolmogorov-Smirnov test, and then, the appropriate parametric or nonparametric test was used accordingly.

In all dogs eligible for the analysis of CM/SM-related clinical signs, the association between the presence of CM/SM-related clinical signs and signalment as well as imaging findings was evaluated. The pairwise associations between the presence of CM/SM-related clinical signs (yes/no) and each independent variable, including breed (shorthaired or longhaired), sex, weight, presence of SM2, atlantooccipital overlapping, and content in tympanic bullae (present/absent), CM grade (CM0, CM1, CM2), and the continuous variables of age, weight, medullary kinking index, dorsal spinal cord compression index, and sum index were studied with univariable logistic regression analysis by the method "enter" with only 1 independent variable in the model at a time. For statistical
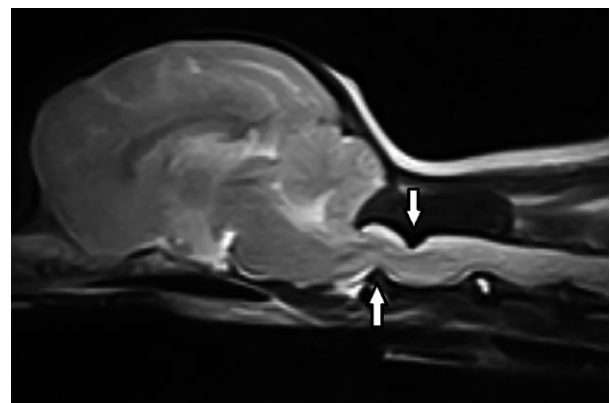

Fig 1. T2-weighted midsagittal magnetic resonance image of a Chihuahua dog with concurrent medullary elevation and dorsal spinal cord compression of the spinal cord at C1-2 cervical vertebrae. The lower arrow indicates the medullary elevation and the upper arrow the dorsal spinal cord compression.
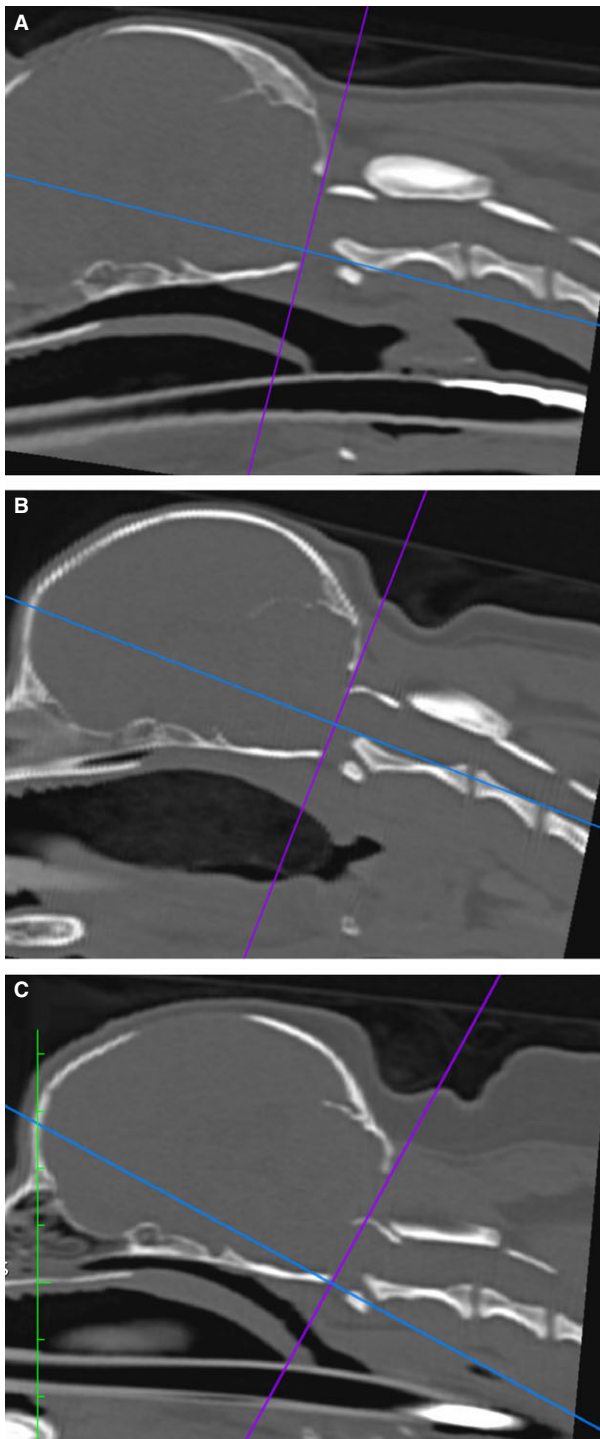
Fig 2. (A, B, and C) Classification of atlantooccipital overlapping. The craniocervical junction was considered normal when the dorsocranial border of the lamina of the atlas was caudal to the purple line **(A)**. The craniocervical junction was considered as overlapped when the dorsocranial border of the lamina of the atlas was at the level of the purple line extending from the caudodistal aspect of the supraoccipital bone to the caudal tip of the basioccipital bone (grade 1, **B**) or cranial to it (grade 2, **C**). The blue line in the images is an indicator line produced by the DICOM viewer. [Color figure can be viewed at wileyonlinelibrary.com]

purposes, dogs were considered as having content in the tympanic bullae if there was content in either or both ears. In cases with different results in estimated categorical variables, a consensus decision was reached by the evaluators. For statistical purposes, SM2 was considered to be either present or absent; hence, the dogs with SM2 were compared with both dogs with and without central canal dilatation (SM0 + SM1).

Additionally, a correlation between the severity of CM/SM-related clinical signs (a percentage from maximum points based on owner questionnaire) and the width of the syrinx (when SM2 was present), the medullary kinking index, and the sum index were assessed by Pearson correlation.

Before evaluating the relationship between the presence of CM/SM-related clinical signs and imaging findings with multivariable logistic regression analysis, Spearman correlation for the nonparametric variables and Pearson correlation for the parametric variables were evaluated.

A multivariable logistic regression was used to model the association of the presence of CM/SM-related clinical signs and collected signalment and imaging analysis variables by the forward likelihood ratio method. For the multivariable regression analysis, variables with Wald's $P < 0.2$ were included.

For the variables in the final model, the area under the receiver operator characteristic (ROC) curve (AUC) was calculated to estimate the optimal cut-off point to detect dogs with or without CM/SM-related clinical signs.

Similarly, associations between SM2 and signalment, presence of CM/SM-related clinical signs, neurologic deficits, and imaging findings (other than SM2) were evaluated. The pairwise associations between the presence of SM2 (yes/no) and each independent variable, including breed, sex, presence of CM/SM-related clinical signs (yes/no), postural reaction deficits (yes/no), abnormal gait (yes/no), content in tympanic bullae (yes/no), atlantooccipital overlapping (yes/no), and CM grade (CM0, CM1, CM2), and the continuous variables of age, weight, medullary kinking index, dorsal spinal cord compression index, and sum index were studied by univariable logistic regression analysis.

Finally, a multivariable logistic regression was used to model the association between SM2 and collected variables similar to that described for the presence of CM/SM-related clinical signs.

The goodness of fit of the multivariable logistic regression final models was assessed with the Omnibus test of model coefficients, Nagelkerke's R^2, and the Hosmer-Lemeshow test. The smaller the P-value in the Omnibus test, the larger the value in the Hosmer-Lemeshow test and the closer the value to 100% in Nagelkerke's R^2, the better the fit (i.e, the better the model is able to predict correctly the dogs with CM/SM-related clinical signs or the presence of SM). In all cases, significance was set at $P < 0.05$.

Results

Animals

Altogether, 65 Chihuahuas were examined, but 12 dogs were excluded for various reasons (Fig 3). The remaining 53 dogs comprised 26 (49%) longhaired and 26 (49%) smooth-haired Chihuahuas and 1 (2%) Chihuahua mix (smooth haired). Twenty-seven dogs (51%) were females, 25 dogs (47%) were males, and 1 dog (2%) was a neutered male (classified as a male in statistical analysis). The mean ± SD age of the dogs at study entry was 57 ± 27 months (range, 7–139 months), and the mean ± SD weight was 2.8 ± 0.7 kg (range, 1.4–4.3 kg).

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┌─────────────────────────────┐          ┌──────────────────────────────────────────┐
│                             │          │ 8 dogs with CM/SM-related clinical signs   │
│ Chihuahuas recruited: n= 65 │          │ excluded due to:                           │
│                             │          │                                            │
└─────────────────────────────┘          │   • microchip artifact causing undiagnostic│
              │                           │     MR images (1/8)                         │
              │                           │   • intervertebral disc disease (3/8)       │
              │                           │   • severe supracollicular fluid accumulation│
              │                           │     (2/8), additional severe hydrocephalus in│
              │                           │     one dog                                 │
              │                           │   • history of corticosteroid-responsive neck│
              │                           │     pain (1/8)                              │
              │──────────────────────────▶│   • bilateral patellar luxation (1/8)       │
              │                           │                                            │
              │                           │ 4 dogs without CM/SM-related clinical signs │
              │                           │ excluded due to:                           │
              │                           │                                            │
              │                           │   • too young (2/4)                         │
              │                           │   • acute nonambulatory paraparesis 11 days │
              │                           │     after imaging due to necropsy-confirmed │
              │                           │     granulomatous meningoencepalomyelitis   │
              │                           │     (1/4)                                   │
              │                           │   • history of corticosteroid-responsive    │
              │                           │     meningoencephalomyelitis of unknown     │
              ▼                           │     origin (1/4)                           │
┌─────────────────────────────┐          └──────────────────────────────────────────┘
│ Neurologic examination: n= 53│
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ Imaging analysis:           │
│ Magnetic resonance imaging  │          ┌──────────────────────────────────────────┐
│ (n= 53) and computed        │          │ 9 dogs excluded due to:                    │
│ tomography (n=50, three dogs │          │                                            │
│ lacking CT images)          │          │   • chronic gastrointestinal disease (4/9)  │
└─────────────────────────────┘          │   • unilateral patellar luxation (2/9)      │
              │──────────────────────────▶│   • dermatological disease (3/9), in one dog │
              │                           │     also dental disease                     │
              │                           │                                            │
              │                           │ Diseases not considered to affect the       │
              │                           │ imaging analysis or neurologic examination  │
              ▼                           └──────────────────────────────────────────┘
┌──────────────────────────────────────────┐
│ Description of CM/SM-related clinical signs │
│ and association with the imaging findings: │
│ n= 44                                      │
└──────────────────────────────────────────┘
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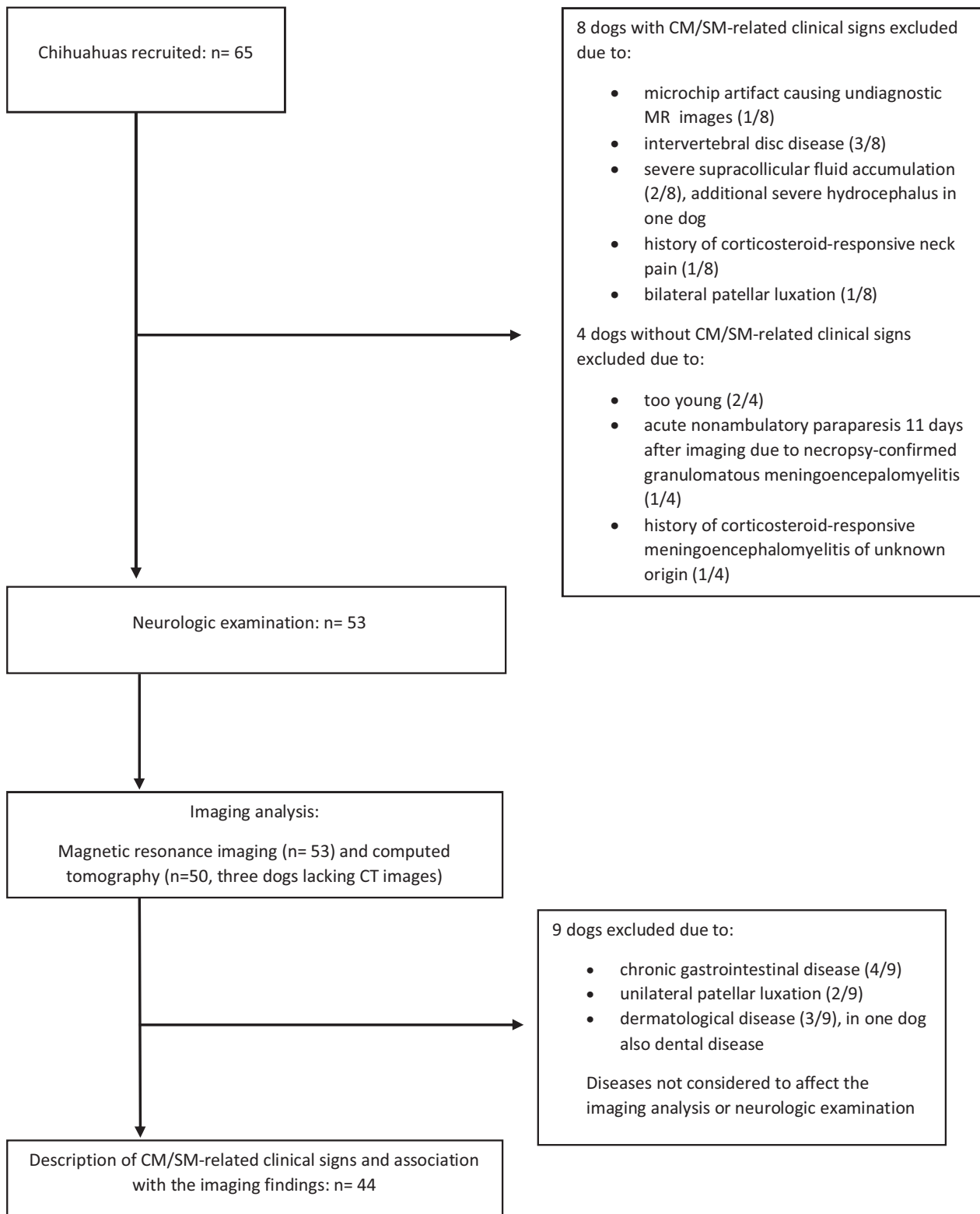
Fig 3. Flowchart describing the inclusion/exclusion of Chihuahuas in imaging analysis, description of neurological deficits, and CM/SM-related clinical signs.

Assessment of Clinical Signs and Neurologic Deficits

Of the 53 included dogs, 9 were excluded from the assessment of clinical signs because of various health problems, but were included in the description of neurologic deficits and in imaging analyses (Fig 3). This was done because previous or concurrent non-neurologic

Table 3. (a) Association of signalment and imaging findings with CM/SM-related clinical signs (nonparametric variables), (b) the presence CM/SM-related clinical signs (parametric variables).

Variable	Number of Dogs with CM/SM-Related Clinical Signs (%)	Number of Dogs without CM/SM-Related Clinical Signs (%)	Number of Dogs/All Dogs	P
(a)				
Smooth haired	11 (25%)	9 (20%)	20/44	0.545
Longhaired	11 (25%)	13 (30%)	24/44	
Sex: M	13 (30%)	7 (16%)	20/44	**0.073**
Sex: F	9 (20%)	15 (34%)	24/44	
CM0	0 (0%)	0 (0%)	0/44	**0.111**
CM1	1 (2%)	5 (11%)	6/44	
CM2	21 (48%)	17 (39%)	38/44	
No SM2 (SM0 + SM1)	10 (23%)	17 (39%)	27/44	**0.034***
SM2	12 (27%)	5 (11%)	17/44	
No bulla tympanica content	17 (39%)	20 (45%)	37/44	0.230
Bulla tympanica content	5 (11%)	2 (5%)	7/44	
No AOO	5 (12%)	6 (14%)	11/43	0.795
AOO	16 (37%)	16 (37%)	32/43	

Variable	Dogs with CM/SM-Related Clinical Signs (mean)	SD (with CM/SM-Related Clinical Signs)	Dogs without CM/SM-Related Clinical Signs (mean)	SD (no CM/SM-Related Clinical Signs)	P
(b)					
Age (months)	53.9	35.5	63.3	17.6	0.271
Weight (kg)	2.7	0.7	2.9	0.6	**0.154**
MKI	26.9%	7.4	19.8%	8.4%	**0.016***
DSCCI	25.8%	7.1	23.8%	7.5%	0.370
SI	53.0%	8.7	44.2%	8.9	**0.007***

CM/SM, Chiari-like malformation and/or syringomyelia; M, male; F, female; CM0, no Chiari-like malformation; CM1, cerebellar indentation; CM2, cerebellar herniation or impaction into the foramen magnum; SM2, syringomyelia (syrinx width at least 2 mm in transverse plane); AOO, atlantooccipital overlapping; SD, standard deviation; MKI, Medullary kinking index; DSCCI, dorsal spinal cord compression index; SI, sum index (MKI + DSCCI). Variables with a P-value <0.2 are bolded and ones with a P-value <0.05 are indicated with an asterisk.

Table 4. Neurologic deficits detected in 31 of 53 Chihuahuas examined.

Deficit Detected	Number of Dogs	Proportion of Dogs with Neurologic Deficits (%)	Proportion of All Dogs Examined (%)
Decreased postural reactions	27	87	51
Abnormal gait (mild to moderate hypermetria in front/hindlimbs or both)	18	58	34
Decreased or absent menace (uni- or bilateral)	15	48	28
Spinal hyperesthesia	12	39	23
Abnormal posture (kyphosis, holding head down)	8	26	15

diseases might cause difficulties in interpreting the origin and severity of CM/SM-related clinical signs, but were not considered to interfere with the neurologic examination or imaging findings.

Of the remaining 44 dogs, 22 of 44 (50%) had and 22 of 44 dogs did not have CM/SM-related clinical signs. Mean age ($P = 0.271$), weight ($P = 0.154$), and sex distribution ($P = 0.073$) did not differ between the 2 groups (Table 3a and b).

In all, 16 of 22 dogs (73%) with CM/SM-related clinical signs had been scratching their ears, shoulders, or cranial thoracic area with or without skin contact. Facial rubbing and head or spinal hyperesthesia were both reported in 10 of 22 dogs (46%). Vocalization when scratching, excited, or moving occurred in 9/22 dogs (41%), and in 12 of 22 dogs (55%) the owners reported occasional incoordination, stumbling, or weakness in either thoracic or pelvic limbs or both.

Eighteen (82%) of the 22 dogs had multiple CM/SM-related clinical signs. Four owners (18%) of the 22 dogs reported their dogs to have only 1 CM/SM-related clinical sign, and in 3 of 4 dogs, it was scratching.

The mean ± SD onset of CM/SM-related clinical signs was 15.4 ± 19 months (range, 3–84 months), and scratching was the most common first CM/SM-related clinical sign noted in 12 of 20 dogs (60%). (Two owners did not define the onset of clinical signs.)

Neurologic deficits were detected in 31 of 53 dogs (59%). A detailed description of the deficits detected in all dogs is provided in Table 4. Neurologic deficits were observed in 21 of 22 dogs (96%) with CM/SM-related clinical signs and in 1 of 22 dogs (5%) without CM/SM-related clinical signs. The most common deficits were decreased postural reactions in 20 of 22 dogs (91%) and ataxia in 12 of 22 dogs (55%).

Diagnostic Imaging Analysis

Chiari-like malformation was observed in all 53 dogs: cerebellar indentation in 11 of 53 dogs (21%) and cerebellar herniation in 42 of 53 dogs (79%). Central canal dilatation was detected in 15 of 53 dogs (28%) and SM in 20 of 53 dogs (38%). In 18 of 53 dogs (40%), no SM or central canal dilatation was detected.

The medullary kinking index could be measured in 50 of 53 dogs, and the mean $\pm$ SD was 23.2 $\pm$ 8.5% (range, 6.1–48.0%). The dorsal spinal cord compression index was measured in all 53 dogs, and mean $\pm$ SD was 24.3 $\pm$ 7.3% (range, 8.7–37.5%). The sum index was measured in 50 of 53 dogs, and the mean $\pm$ SD was 47.8 $\pm$ 9.8% (range, 29.2–69.6%).

Content in tympanic bullae was present in 8 of 53 dogs (15%) either unilaterally (4 of 53 [7.5%] dogs) or bilaterally (4 of 53 [7.5%] dogs).

Computed tomography imaging findings were available for 50/53 dogs. In 15 of 50 dogs (30%), the atlas was positioned caudal to the foramen magnum, but in 35 of 50 dogs (70%) atlantooccipital overlapping was considered present: grade 1 in 23 of 50 dogs (46%) and grade 2 in 12 of 50 dogs (24.0%). The presence or severity of atlantooccipital overlapping was not associated with the severity of CM ($P = 0.145$).

Association between the Presence and Severity of Clinical Signs and Diagnostic Imaging Findings

The presence of SM2 was associated with the presence of CM/SM-related clinical signs ($P = 0.034$). Additionally, CM/SM-related clinical signs were more severe in SM-affected dogs than in dogs without SM2 (21.3% from maximum points in SM2-affected dogs and 9.1% in nonaffected dogs, $P = 0.041$). When SM2 was present, the mean maximum syrinx width was 3.8 mm in dogs with CM/SM-related clinical signs and 3.2 mm in dogs without CM/SM-related clinical signs, but the difference was not significant ($P = 0.490$).

Ten (45%) of the 22 dogs with CM/SM-related clinical signs did not have SM2 at the cervical spine. Six of these 10 dogs suffered from scratching (4/6 scratching their head or shoulder area), 6 of 10 dogs had facial rubbing, 4 of 10 dogs had pain on spinal palpation, 5 of 10 dogs had spontaneous vocalization, and 2 of 10 dogs had occasional incoordination, stumbling, or weakness.

The mean medullary kinking and sum indices were significantly higher ($P = 0.016$ and $P = 0.007$, respectively) in dogs with CM/SM-related clinical signs than in dogs without CM/SM-related clinical signs. Furthermore, the sum index correlated positively with the severity of CM/SM-related clinical signs ($P = 0.025$), although the medullary kinking index alone did not ($P = 0.092$). A detailed description of the variables analyzed is presented in Table 3a and b. With a cut-off value of 0.46 for the sum index, the model had a sensitivity of 0.90 and a specificity of 0.67, and the AUC was 0.76 (95% confidence interval [CI] 0.61–0.91).

Before evaluating the relationship between the presence of CM/SM-related clinical signs and imaging findings with multivariable logistic regression analysis, correlations of the selected variables (sex, CM grade, presence of SM2, weight, medullary kinking, and sum indices) were evaluated: sex and weight ($P = 0.002$) and medullary kinking and sum indices ($P = <0.001$) correlated with each other. Due to the correlation between medullary kinking and sum indices, only the sum index was selected because of its lower p-value (see Table 3b).

In the multivariable logistic regression analysis, only the sum index remained in the final model ($P = 0.007$), and it was significantly predictive for the presence of clinical signs. The goodness of fit of this final model was confirmed by an Omnibus value of 0.002 and a Hosmer-Lemeshow value of 0.079. The model could correctly predict 65.9% of the data and explain 27.4% of the variance according to the pseudo-R^2 test (Nagelkerke).

Association of Signalment, Neurologic Deficits, and Imaging Findings with the Presence of Syringomyelia

In addition to the presence of CM/SM-related clinical signs, postural reaction deficits ($P < 0.001$) were associated with the presence of SM2. A detailed description of the factors evaluated is provided in Table 5a, b, and c.

Before evaluating the relationship between the presence of SM2 and CM/SM-related clinical signs, neurologic deficits, and imaging findings with multivariable logistic regression analysis, correlations of the selected variables (presence of CM/SM-related clinical signs, presence of postural reaction deficits, presence of gait abnormalities, CM grade, and sum index) were evaluated. Multiple correlations were detected between the presence of CM/SM-related clinical signs and postural reaction deficits ($P < 0.001$), abnormal gait ($P < 0.001$), and sum index ($P = 0.003$). Additionally, the presence of postural reaction deficits and sum index was correlated ($P = 0.024$). Finally, there also was a correlation between abnormal gait and postural reaction deficits ($P = 0.005$). Because of multicollinearity, a forward stepping method was used.

In multivariable logistic regression analysis, only 1 variable remained in the final model: the presence of postural reaction deficits was significantly predictive for SM2 ($P = 0.002$). The goodness of fit of this second final model was confirmed by an Omnibus value of 0.001. The model could correctly predict 75.6% of the data and explain 33% of the variance according to the pseudo-R^2 test (Nagelkerke).

Discussion

We found that SM, CM, and several other CCJ abnormalities are commonly encountered in Chihuahuas. The CM/SM-related clinical signs in Chihuahuas are comparable with those detected in SM-affected CKCSs. Interestingly, CM/SM-related clinical signs also are commonly present in dogs without SM and may be

Table 5. (a) Association of signalment and neurologic examination findings with syringomyelia, (b) Association of imaging findings with syringomyelia, (c) Association of signalment and imaging findings with syringomyelia (parametric variables).

(a)

Variable	Dogs with SM (%)	Dogs without SM (%)	Number of Dogs/All Dogs	P
Smooth haired	12 (23%)	15 (28%)	27/53	0.307
Longhaired	8 (15%)	18 (34%)	26/53	
Sex: M	11 (21%)	15 (28%)	26/53	0.501
Sex: F	9 (17%)	18 (34%)	27/53	
CM/SM-related clinical signs	12 (27%)	10 (23%)	22/44	**0.034***
No CM/SM-related clinical signs	5 (11%)	17 (39%)	22/44	
Postural reaction deficits	16 (30%)	10 (19%)	26/53	**0.001***
No postural reaction deficits	4 (8%)	23 (43%)	27/53	
Abnormal gait	9 (17%)	8 (15%)	17/53	**0.121**
Normal gait	11 (21%)	25 (47%)	36/53	

(b)

Variable – Imaging Findings	Dogs with SM (%)	Dogs without SM (%)	Number of Dogs/All Dogs	P
CM0	0 (0%)	0 (0%)	0/53	**0.148**
CM1	2 (4%)	9 (17%)	11/53	
CM2	18 (34%)	24 (45%)	42/53	
Bulla tympanica content	4 (8%)	4 (8%)	8/53	0.441
No bulla tympanica content	16 (30%)	29 (55%)	45/53	
AOO	15 (30%)	20 (40%)	35/50	0.530
No AOO	5 (10%)	10 (20%)	15/35	

(c)

Variable – Signalment	Dogs with SM (mean)	SD (with SM)	Dogs without SM (mean)	SD (no SM)	P
Age (months)	61.8	31.6	54.1	23.7	0.319
Weight (kg)	2.7	0.7	2.8	0.6	0.418

Variable – Imaging findings	Dogs with SM (mean)	SD (with SM)	Dogs without SM (mean)	SD (no SM)	P
MKI	24.2%	7.0	22.6%	9.3	0.519
DSCCI	25.8%	7.1	23.4%	7.3	0.223
SI	50.5%	8.7	46.3%	10.1	**0.146**

M, male; F, female; CM/SM, Chiari-like malformation and/or syringomyelia; SM, syringomyelia, CM0, no Chiari-like malformation; CM1, cerebellar indentation; CM2, cerebellar herniation or impaction into the foramen magnum; AOO, atlantooccipital overlapping; SM, syringomyelia (syrinx width at least 2 mm in transverse plane); SD, standard deviation; MKI, Medullary kinking index; DSCCI, dorsal spinal cord compression index; SI, sum index. Variables with a P-value <0.2 are bolded and ones with a P-value <0.05 are indicated with an asterisk.

attributed to CCJ abnormalities. These CCJ abnormalities, including medullary elevation and dorsal spinal cord compression, especially if present concurrently and causing a bidirectional compression of the medulla or spinal cord, may play an important role in the pathogenesis of SM and neuropathic pain in Chihuahuas.

CM/SM-Related Clinical Signs and Neurologic Deficits

The most common clinical sign noted was scratching of the ears, shoulders, or cranial thoracic area with or without skin contact, seen in approximately 70% of dogs. Also, approximately half of the dogs rubbed their face, vocalized, or had spinal cord hyperesthesia indicative of neuropathic pain. In half of the dogs, the owners had noticed that their dog's gait was abnormal. Previous studies report comparable percentages of similar clinical signs in CM/SM-affected CKCSs: scratching and dysesthetic behavior, including phantom scratching or facial rubbing, was detected in 25% (3 of 12 dogs) to 100% (7 of 7 dogs) of clinically affected dogs, cervical hyperesthesia in 58–71% (5 of 7 and 7 of 12 dogs), and abnormal gait in 25–43% (3 of 7 and 3 of 12 dogs).[26,28] Unfortunately, studies describing clinical signs in detail are limited and include a low number of cases.

Occasionally, before filling out the questionnaire, owners had been unaware that repeated scratching, although present for months or years, could be a sign of disease. Commonly, the reason for veterinary consultation was some other complaint (e.g, avoidance of touch, epileptic seizures). This finding highlights the need to educate breeders and dog owners in recognizing milder signs so that neuropathic pain caused by CM or SM can be alleviated. Prospective studies with detailed questionnaires are needed to make the published research more reliable by avoiding dogs with CM/SM-related clinical signs being falsely included in the group of dogs without CM/SM-related clinical signs.

Neurologic deficits were similar to those previously described in CKCSs and Griffon Bruxellois dogs,[5,26] with the most common neurologic deficits being postural reaction deficits and ataxia in all but 1 (21/22) of the dogs with CM/SM-related clinical signs.

Diagnostic Imaging Findings and their Associations with CM/SM-Related Clinical Signs

Chiari-like Malformation and Syringomyelia

All dogs in our study had CM. This finding is similar to previous studies, with occurrence of CM in nonrandomized CKCS study populations varying between 94 and 100%, but higher than the 60.7–80% reported in Griffon Bruxellois dogs.[3,5,8,11,12,21]

Syringomyelia was detected in dogs with and without CM/SM-related clinical signs, as also reported earlier.[1] Of dogs without CM/SM-related clinical signs, 23% had SM, which is less than previously reported in CKCSs (46%) and Griffon Bruxellois dogs (46–52%).[3–5,8] However, because the prevalence of SM might increase with age and because the selection of dogs was based on voluntary participation of the owners (and hence not randomized), the prevalence of imaging findings might not reflect the true prevalence in a randomly selected population.

Syringomyelia was associated with the presence of CM/SM-related clinical signs, consistent with earlier research. Previous studies also suggest an association between the presence of neuropathic pain and increased syrinx width.[1,2] In our study, the mean syrinx width was higher in dogs with CM/SM-related clinical signs, but the difference was not significant. This finding might be due to a proportionally higher number (45%) of dogs with CM/SM-related clinical signs but without SM than in a previous study (13%) of CKCSs.[2]

Dorsal Spinal cord Compression and Medullary Elevation

Dorsal spinal cord compression and medullary elevation previously have been associated with the presence of CM/SM-related clinical signs in CKCSs over 5 years of age.[21,22] In our study, the medullary kinking index was significantly higher in dogs with than without CM/SM-related clinical signs, but no statistical difference was detected in dorsal spinal cord compression index between the 2 groups. The difference between the results of these 2 studies might be due to our choice of measuring the dorsal spinal cord compression index in all dogs to avoid bias caused by initially subjectively assessing the presence of dorsal spinal cord compression, and then if compression was present, calculating the dorsal spinal cord compression index.

Despite no statistical difference in dorsal spinal cord compression index being recognized between dogs with and without CM/SM-related clinical signs, the cranial cervical spinal cord at the atlantoaxial junction commonly seemed strongly deviated and had an S-shaped appearance due to the concurrent medullary elevation and dorsal spinal cord compression (Fig 1). To study the effect of bidirectional compression deviating the spinal cord, the sum index (medullary kinking index + dorsal spinal cord compression index) was evaluated. The sum index was significantly higher in dogs with than without CM/SM-related clinical signs, and it was predictive of the presence of CM/SM-related clinical signs in multivariable logistic regression analysis. Additionally, it correlated positively with the severity of CM/SM-related clinical signs, whereas medullary kinking index or dorsal spinal cord compression index alone did not.

The CM/SM-related clinical signs, such as scratching and facial rubbing, also were detected in half of the dogs without SM at the cervical spine. In previous reports, medullary elevation was suggested to cause neuropathic pain, but the presence of multiple CCJ junction abnormalities and the high percentage of SM-affected dogs render estimation of causality problematic.[22] The high number of dogs without SM but with CM/SM-related clinical signs suggestive of neuropathic pain detected in our study supports the clinical importance of concurrent CCJ abnormalities, such as CM, medullary elevation, and dorsal spinal cord compression, in the pathogenesis of neuropathic pain, and these clinical signs are similar to those observed in dogs with only CM.[10] The exact pathomechanism and anatomical structures responsible for the clinical signs caused by these CCJ abnormalities remain to be elucidated. Compression of the spinal nucleus and tract of cranial nerve V, continuing as the substantia gelatinosa and dorsolateral fasciculus in the spinal cord and receiving sensory input related to nociception and temperature from the skin and mucous membranes of the head, might be at least partly responsible.[30]

Atlantooccipital Overlapping

Atlantooccipital overlapping was detected in 70% of dogs evaluated in our study, but it was not associated with the presence of CM/SM-related clinical signs, SM, or severity of CM. In previous studies, a subjective assessment of the presence of atlantooccipital overlapping based on 3-dimensional reconstructed CT images has been used. The studies report atlantooccipital overlapping to be present in 27.7% of small and toy breed dogs, and more specifically, in 55.2% of non-CKCS dogs.[29] Recently, a study with criteria resembling ours reported a prevalence of atlantooccipital overlapping of 80% in dogs imaged with MRI.[23] The only exception in the criteria was that in our study dogs with an atlas immediately caudal to the foramen magnum were not considered to be affected by atlantooccipital overlap. To avoid bias caused by the subjective assessment of the cranial tip of the atlas being "immediately caudal" to the foramen magnum, we considered dogs to be affected when the cranial tip of the atlas was at the caudal border of the foramen magnum (on a line drawn from dorsocaudal to ventrocaudal borders of the foramen magnum). This difference in the criteria for the presence of atlantooccipital overlapping might underestimate the number of dogs affected in our study or overestimate the number in the other study.

Previously, atlantooccipital overlapping has been reported to be associated with the presence of CM and SM, but not with the presence of CM/SM-related clinical signs.[23] The difference in the diagnostic criteria of atlantooccipital overlapping, the difference in the imaging method used, and the ubiquitous presence of CM in our study might explain why we were unable to show an association between atlantooccipital overlapping and CM or SM. Additionally, we used the British Veterinary Association/Kennel Club CM and SM Health Scheme classification for the presence of SM (Table 2). The dogs were considered to be SM-affected if the maximum width of the lesion was at least 2 mm, which differs from the criterion used in previous studies (i.e, SM present when lesion >1 mm in width).[2,21]

Limitations of the Study

Our study had some limitations. At the time of study entry, 9/22 dogs with CM/SM-related clinical signs were already medicated, which might have influenced the presence and severity of clinical signs, causing an underestimation of the severity of clinical signs. Additionally, 9/53 dogs had to be excluded from the evaluation of CM/SM-related clinical signs because of concurrent non-neurological diseases, such as dermatologic diseases, which could have affected the evaluation of clinical signs. These 9 dogs were still included in the imaging analyses. There were 8/53 dogs (15%) with either uni- or bilateral content in tympanic bullae. Despite this, they were included in the clinical analyses because the presence of content was not associated with the presence of clinical signs in statistical analysis.

All dogs in our study underwent low-field MRI. Because of the very small size of patients and the low magnetic field strength, it was occasionally difficult to differentiate a mildly dilated central canal from imaging artifacts. This might have caused underestimation of the number of dogs with central canal dilatation.

Conclusions

We have described for the first time the presence of SM, CM, and other CCJ abnormalities and their associations with clinical signs previously considered to be caused by CM or SM in Chihuahuas. The presence of CM was ubiquitous, and both SM and CCJ abnormalities occurred commonly. The clinical signs considered as CM/SM-related clinical signs in our study were similar to those reported previously in other breeds. Although SM was an important factor for the presence of these clinical signs, many dogs suffered from similar clinical signs without being affected by SM. Indices measuring medullary elevation alone or in combination with dorsal spinal cord compression were significantly higher in dogs with CM/SM-related clinical signs. These findings highlight the importance of CCJ abnormalities other than CM in the pathogenesis of neuropathic pain in Chihuahuas.

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