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Behavioral and clinical signs of Chiari-like malformation-associated pain and syringomyelia in Cavalier King Charles spaniels

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Abstract

Background: Diagnosis of Chiari-like malformation-associated pain (CM-P) or clinically relevant syringomyelia (SM) is challenging. We sought to determine common signs.

Animals: One hundred thirty client-owned Cavalier King Charles spaniels with neuroaxis magnetic resonance imaging (MRI) and diagnosis of CM-P/SM. Dogs with comorbidities causing similar signs were excluded with exception of otitis media with effusion (OME).

Methods: Retrospective study of medical records relating signalment, signs, and MRI findings. Dogs were grouped by SM maximum transverse diameter (1 = no SM; 2 = 0.5-1.99 mm; 3 = 2-3.9 mm: 4 = ≥4 mm). Differences between all groups—groups 1 versus 2-4 and groups 1-3 versus 4—were investigated. Continuous variables were analyzed using 2-sample *t*-tests and analysis of variance. Associations between categorical variables were analyzed using Fisher's exact or chi-square tests.

Results: Common signs were vocalization (65.4%), spinal pain (54.6%), reduced activity (37.7%), reduced stairs/jumping ability (35.4%), touch aversion (30.0%), altered emotional state (28.5%), and sleep disturbance (22%). Head scratching/rubbing (28.5%) was inversely associated with syrinx size (P = .005), less common in group 4 (P = .003), and not associated with OME (P = .977). Phantom scratching, scoliosis, weakness, and postural deficits were only seen in group 4 (SM ≥4 mm; P = .004).

Conclusions and Clinical Importance: Signs of pain are common in CM/SM but are not SM-dependent, suggesting (not proving) CM-P causality. Wide (≥4 mm) SM is associated with signs of myelopathy and, if the dorsal horn is involved, phantom scratching (ipsilateral) and torticollis (shoulder deviated ipsilateral; head tilt contralateral).

KEYWORDS

otitis media with effusion, phantom scratching, quality of life, scoliosis, sleep disruption

Abbreviations: BOAS, brachycephalic obstructive airway syndrome; CCD, central canal dilation; CKCS, Cavalier King Charles spaniel; CM, Chiari-like malformation; CM1, Chiari type I malformation (human); CM-P, Chiari-like malformation associated pain; CNS, central nervous system; CSF, cerebrospinal fluid; IVD, intervertebral disc; MRI, magnetic resonance imaging; MVD, myxomatous mitral valve disease; OME, otitis media with effusion; PSOM, primary secretary otitis media; SM, syringomyelia; SM-S, severe SM syringomyelia with a maximum transverse diameter of 4 mm and above.

1 | INTRODUCTION

Syringomyelia (SM) is characterized by fluid filled cavities (syrinx, syringes) within the central spinal cord. The resulting damage can cause pain, phantom scratching, scoliosis, paresis, and sensory deficits.[1,2] Syringomyelia develops as a consequence of obstruction of cerebrospinal fluid (CSF) channels, and in the dog, it is most commonly associated with Chiari-like malformation (CM), a complex developmental malformation of the skull and craniocervical vertebrae characterized by a conformational change and overcrowding of the brain and cervical spinal cord, particularly at the craniospinal junction.[3]

Diagnosis of clinically relevant CM or SM can be challenging because clinical signs can be nonspecific. Chiari-like malformation alone can cause substantial morbidity and reduced quality of life[3,4]; however, an objective measure for diagnosis of CM-associated pain (CM-P) has not been translated from research studies,[3] and diagnosis is made by excluding other causes of pain together with subjective assessment of magnetic resonance imaging (MRI).[5]

Chiari-like malformation/syringomyelia is most commonly reported in the Cavalier King Charles spaniel (CKCS), and this breed is predisposed to a number of other neurological conditions[6] including fly catching,[7] idiopathic epilepsy,[8,9] idiopathic facial nerve paralysis with and without associated vestibular disease,[10] and degenerative myelopathy.[11] These unrelated conditions can be misinterpreted as a consequence of CM, SM, or both, especially as CM/SM might be the only abnormality reported on MRI investigation as CM is ubiquitous[12] and SM is also common and not always associated with clinical signs.[13] In addition, some dogs have conditions that offer an alternative explanation for the nonspecific clinical signs including intervertebral disc (IVD) disease[14] or otitis media with effusion (OME; also known as primary secretary otitis media or PSOM).[15] The presence of comorbidities increases the challenge to ascertain what clinical signs can be attributed to each condition, and, therefore, making confident diagnosis and treatment recommendations is more difficult.

Syringomyelia-associated "phantom" scratching is considered a specific but not ubiquitous sign of SM and is associated with a large syrinx extending to the superficial dorsal horn in the C3-C6 spinal cord segments ipsilateral to the scratching limb.[16] Originally thought to represent a paraesthesia, it is more likely to be similar to fictive scratch reported in spinalized animals.[17,18] It is also recognized that dogs with CM/SM can excessively rub or scratch their heads or ears and that this is not necessarily associated with SM and is not phantom scratching.[4,19] The association of SM to scratching has led to the misconception that it causes generalized pruritus, and consequently investigation and treatment of skin disease could be missed.[20]

The aim of this study was to characterize retrospectively the clinical and behavioral signs of CM-P and SM and relate these to maximum syrinx transverse diameter. It is with a view to translating this data into a tool which can be used in prospective studies into the treatment, diagnosis, and genetics of CM/SM.

2 | MATERIALS AND METHODS

As a preparatory work for this retrospective study, the medical records of 10 CKCS that had been managed exclusively by CR for 3 years or more were examined. An inclusion criterion was regular examination (minimal of every 6 months) until the time of death. The medical notes were reviewed in detail, and all clinical signs were recorded with the aim of using these as baseline categories in the main study. These dogs were not used in the final analysis as their medical records predated the current MRI protocol.

2.1 | Animals

Medical records were searched for all CKCS examined by CR during a 5-year period (2013-2017) and that had full brain and spinal MRI. Dogs that did not have a primary diagnosis of CM-P or SM were excluded. Diagnosis of SM and CM-P was made according to previously defined criteria.[5] The date of birth, age at last MRI, sex, neuter status, and weight were recorded. The entire medical history was examined, and all clinical and behavioral signs were recorded. The assessment was made by the same clinician who had examined the dogs originally and made all the follow-up examinations. The behavioral and clinical signs were recorded under the following categories (Table 1): vocalization, spinal pain, activity, stairs/jumping, change in emotional state, sleep, other pain behaviors/signs, possibly unrelated behaviors/signs, scratching or rubbing of the head or ears, phantom scratching, neurological examination abnormalities, and comorbidities. If scratching or rubbing was noted, then the area/side to which the dog scratched/rubbed was recorded. If scoliosis was documented, then the direction of head and spine rotation was recorded.

2.2 | Image analysis

Assessment of MRI was performed separately before and after the analysis of medical records, and the results were subsequently combined. The images were not anonymized. For each dog, the MRI imaging was reviewed for adequate quality and appropriate sequences (brain and whole spine imaging in T2- and T1-weighted sagittal and T2- (high field MRI) and T1- (low field) weighted transverse images with transverse images centered on the widest point in the syringes (if present) within the cervical, thoracic, and lumbar spinal cord and also transverse imaging of any other lesion (eg, sites of IVD). Most dogs were imaged with a 1.5 Tesla unit (Symphony Maestro Class, Siemens, Enlargen, Germany); however, 23 dogs were imaged with a 0.2 Tesla MRI machine (Esaote Vet MRI, Genova, Italy). A measurement of the maximum transverse width of syrinx (if present) was made, and any spinal cord superficial dorsal horn involvement by the syrinx, including side, was noted using the methods described previously (syrinx width[17]; superficial dorsal horn involvement[16]). If both spinal cord superficial dorsal horns were involved by the syrinx, a subjective assessment of which side had more severe involvement was made. Any other MRI findings were recorded including the presence

TABLE 1 Behavioral and clinical signs of Chiari-like malformation and syringomyelia in Cavalier King Charles spaniels

Category	Subcategory		Notes
Vocalization	Spontaneous yelping or when changing position when recumbent		Yelping (sudden, short, high sound) described by owner as "out of now-where", spontaneous or when moved whilst lying resting or asleep
	Postural		Yelping when lifted under sternum, on rising, or both
	Defecation		Vocalization during defecation
	Scratching		vocalization during scratching
Spinal pain	Cervical		Hyperesthetic to palpation in the cervical region
	Thoracolumbar		Hyperesthetic to palpation in the T1-L4 region
	Lumbosacral		Lumbosacral or caudal lumbar (L5-L7) hyperesthesia
Activity	Reduced exercise		Described as exercise intolerant or unwilling to exercise. BOAS and heart disease ruled out as alternative causes
	Lethargy		Described as lethargy/increased sleeping
Stairs/jumping	Stairs/jumping		Described as refusing/unwilling/hesitation/ difficulty/vocalization when jumping, doing stairs, or both
Change in emotional state/behavior	Greeting		Yelping, refusal to get up and greet owner, or both
	Aggression		To other dogs/people
	Timid/anxious		Described as such by owner
	Withdrawn		Described as withdrawn/avoiding people/decreased interaction/hiding/lethargic/decreased playing
Sleep	Sleep disruption		Described as being restless in the night or having disturbed sleep
Other pain behaviors/ signs	Licking limb/paw		Without evidence of skin or joint disease
	Touch or grooming aversion	ears/head or neck 1–2 limbs or paws sternum, flank	Owner reported and specified body part and that tolerated touch, grooming elsewhere, or both
	Sleeping elevated or unusual head posture		Attempt made to rule out BOAS
	Abnormal awake head/neck posture		Head held down or reluctant to move neck
	Pain face		Described by owner that change facial expression that suggested pain
	Squinting/avoiding light		Described by owner as light avoiding/closed eyes/watery eyes/squinting Schirmer tear test performed to rule out Keratoconjunctivitis sicca
Possibly unrelated behavior	Repetitive tongue licking		Thought more likely to reflect gastroesophageal pain
	Repetitive barking		Through to reflect anxiety but not necessarily due to CM/SM
Scratching, rubbing head or ears, or both	None		Excluded cases that also had ear/skin disease (except OME)
Phantom Scratching	Phantom Scratching		Rhythmic scratching action towards, but not making contact with the skin, together with a curvature of the body and neck towards the foot. Induced by light rubbing to the neck or ear region. Side (s) recorded
Neurological abnormalities	Weakness		Anatomical location recorded
	Muscle atrophy		Anatomical location recorded
	Postural responses decreased		Anatomical location recorded
	Hypermetria		Limbs recoded. Likely only recorded if considered more than usual for the breed
	Scoliosis/cervicothoracic torticollis		Side head tilted down and shoulder pushed out recorded

(Continues)

TABLE 1 (Continued)

Category	Subcategory	Notes
Comorbidities	**Intervertebral disc disease**	Excluded if spinal pain, compression spinal cord or nerve root, or both
	Skin disease	Excluded unless separate historical diagnosis which resolved on treatment, for example, fleas
	OME/PSOMS	Left/right/bilateral recorded
	Other where CM/SM was the primary, first diagnosis, or both	Recorded not excluded unless condition a differential for one or more clinical sign
	Other primary diagnosis	Cases excluded

Bold terms indicates the exclusions and the OME category for which *p* values are given. Behavioral and clinical signs recorded from CKCS affected by CM-P and SM with explanatory notes on how these signs were identified, recorded, or both.

of OME/PSOM which was defined as the presence of uniform hyperintense material within 1 or both tympanic bullae on T2-weighted imaging with no changes suggesting infection (eg, thickening of the integument).

2.3 | Further inclusion/exclusion before analysis

All medical comorbidities were recorded. Dogs with significant IVD disease were excluded from the study. This was defined as an MRI finding of IVD herniation with impingement of the spinal cord or nerve root or IVD degeneration and any sign/history suggesting spinal pain. However, dogs with clinically insignificant IVD degeneration/minor protrusion were included in the study. This was defined as no spinal pain on neurological examination and no history of vocalization, difficulty jumping/doing stairs, lameness or exercise intolerance, and an MRI finding of 1 or more IVD with loss of signal of the nucleus pulposus on T2-weighted imaging with variable protrusion of the annulus fibrosus that might result in the displacement of the dorsal longitudinal ligament but with no spinal cord or nerve root impingement. Dogs with skin disease, ear disease, or both were excluded from the study except when the diagnosis was historical and had responded to appropriate management and only if there were no current signs of scratching, rubbing, or licking. The exception was the presence of OME/PSOM as this variable would be analyzed separately. Dogs that had other current or historical comorbidities that could be a possible alternative explanation for a 1 or more clinical or behavioral signs were excluded.

2.4 | Analysis

The dogs were grouped according to maximum transverse central canal or syrinx size as follows: group 1 with no SM or central canal dilatation (CCD); group 2 with CCD and a maximum transverse central canal of 0.50-1.99 mm; group 3 with mild SM and a maximum transverse syrinx size of 2-3.99 mm; group 4 with severe SM (SM-S) with a maximum transverse central canal or syrinx size ≥4 mm. Potential differences between the groups were analyzed in 3 ways as follows: (1) The difference among all 4 groups; (2) The difference between dogs without SM and dogs with a CCD/SM transverse diameter ≥0.5 mm, that is, groups 1 versus groups 2-4; and (3) the difference between dogs with SM-S and other dogs, that is, group 4 versus groups 1-3. Continuous variables were analyzed using 2-sample *t*-tests and analysis of variance as appropriate, and all associations between categorical variables were analyzed using either Fisher's exact or chi-square tests. A 5% level of significance was set, and all analyses were performed on IBM SPSS v24.0.

TABLE 2 Descriptive statistics of syrinx size

Group	Number of dogs	Mean (mm)	SD (mm)	Range (mm)
1 (no SM)	11	0	0	0
2 (CCD 0.5–1.99 mm)	15	1.22	0.43	0.50-1.98
3 (SM 2.00-3.99 mm)	20	2.30	0.66	2.00-3.97
4 (SM ≥4 mm)	84	5.80	1.20	4.00-9.00
Total	130	4.34	2.34	0-9.00

Distribution of mean maximum transverse diameter of the syrinx or central canal in 130 CKCS with CM-P and SM.
Abbreviations: CCD, central canal dilatation; CKCS, Cavalier King Charles spaniel; CM-P, Chiari-like malformation associated pain; SM, syringomyelia.

3 | RESULTS

3.1 | Animals

The initial search of medical records revealed 216 CKCS with a primary diagnosis of CM-P, SM, or both, but after exclusions the final cohort was 130 CKCS (54 male, 76 female). The excluded dogs were as follows: 12 dogs with comorbidity of IVD disease; 11 dogs with comorbidity of skin disease; 30 dogs with other comorbidities which could cause exercise intolerance, pain, or both including brachycephalic obstructive airway disease (BOAS), orthopedic disease, or both; 33 dogs because of inadequate MRI study.

The mean syrinx size was 4.34 mm (SD ±2.34) distributed as detailed in Table 2 with 11 dogs in group 1, 15 dogs in group 2, 20 dogs in group 3, and 84 dogs in group 4. Table 3 and Figures 1 and 2 summarize the group statistics for age and bodyweight at MRI.

TABLE 3 Group statistics for age and weight in CKCS with and without syringomyelia

	Syrinx presence	Number of dogs	Mean	SD	SE mean
Age_MRI, y	NO	16	4.16	3.00	0.75
	YES	113	4.88	2.26	0.21
Weight, kg	NO	16	10.23	3.05	0.76
	YES	100	9.51	2.20	0.22

Group statistics for age at most recent MRI and weight in CKCS with and without SM (group 1 versus groups 2-4). From the original 130 dog cohort, the age and weight was missing from the medical records for 1 and 14 dogs, respectively.
Abbreviations: CKCS, Cavalier King Charles spaniel; MRI, magnetic resonance imaging; SM, syringomyelia.

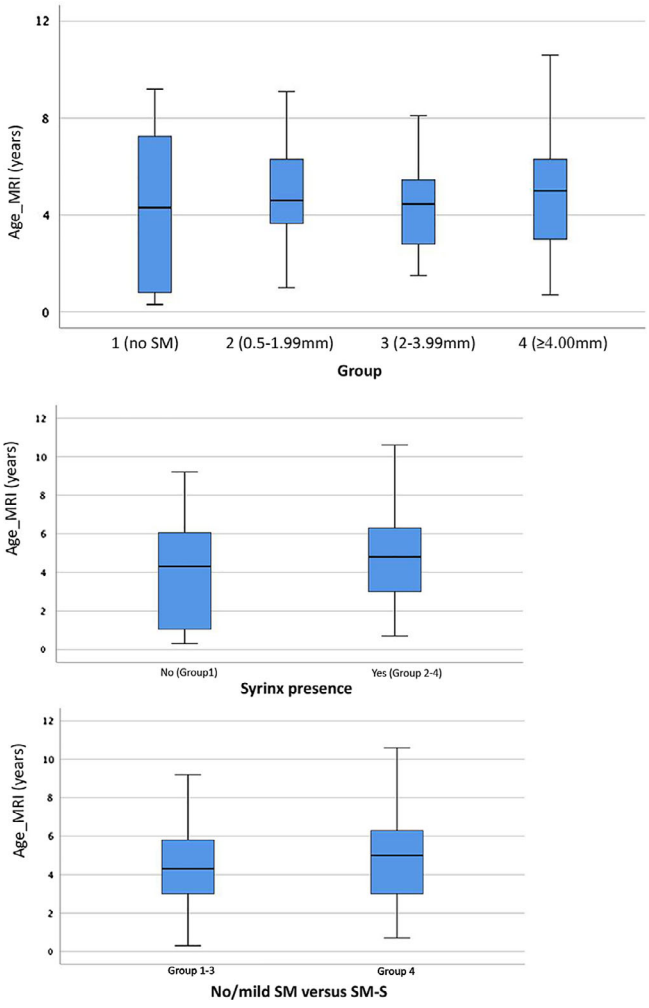

FIGURE 1 Distribution of age in CKCS with CM-P and SM Age at last MRI (years). Groups according to maximum transverse diameter of syrinx 1 = no SM; 2 = 0.5-1.99 mm; 3 = 2-3.9 mm: 4 = ≥4 mm. Top row: Comparison among all 4 groups divided according to maximum transverse diameter of the syrinx or central canal (P = .60). Middle row: Difference between dogs without SM and dogs with a CCD/SM transverse diameter ≥0.5 mm, that is, group 1 versus groups 2-3 (P = .26). Bottom row: Difference between dogs with SM-S (SM ≥4 mm) and other dogs (SM <4 mm), that is, group 4 versus groups 1-3 (P = .29). From the original 130 dog cohort, age was missing from the medical records for 1 dog: CKCS, Cavalier King Charles spaniel; CCD, central canal dilatation; SM, syringomyelia; SM-S, severe syringomyelia with a maximum transverse syrinx diameter ≥4 mm

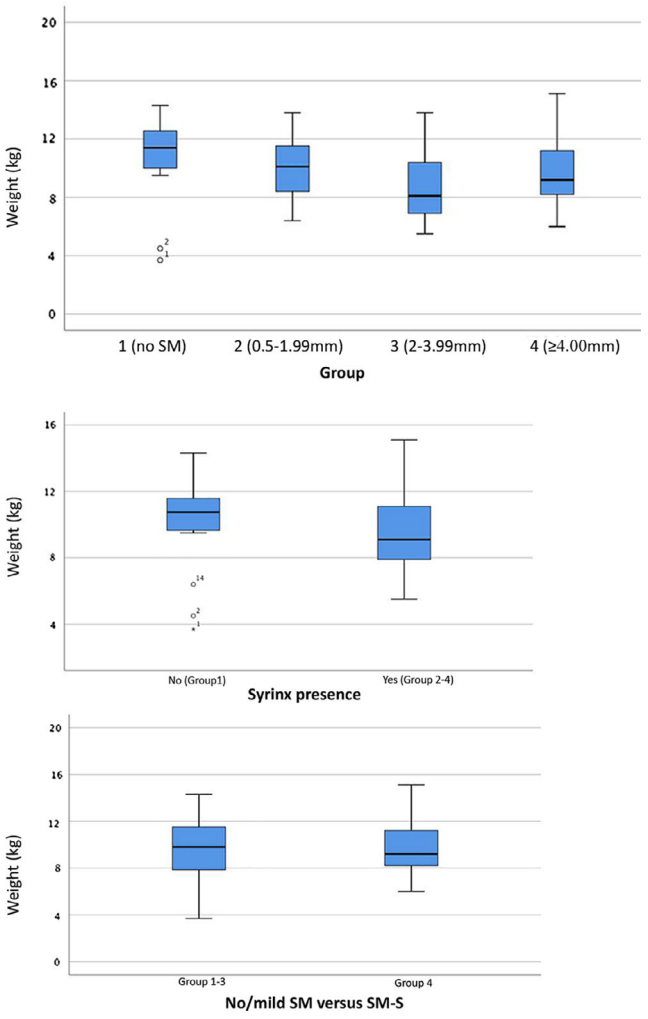

FIGURE 2 Distribution of weight in CKCS with CM-P and SM Weight (kg) at MRI. Groups according to maximum transverse diameter of syrinx 1 = no SM; 2 = 0.5-1.99 mm; 3 = 2-3.9 mm: 4 = ≥4 mm. Top row: comparison among all 4 groups divided according to maximum transverse diameter of the syrinx or central canal (P = .17). Middle row: difference between dogs without SM and dogs with a CCD/SM transverse diameter ≥0.5 mm, that is, group 1 versus groups 2-3 (P = .25). Bottom row: difference between dogs with SM-S (SM ≥4 mm) and other dogs (SM <4 mm), that is, group 4 versus groups 1-3 (P = .93). From the original 130 dog cohort, weight was missing from the medical records for 14 dogs: CKCS, Cavalier King Charles spaniel; CCD, central canal dilatation; SM, syringomyelia; SM-S, severe syringomyelia with a maximum transverse syrinx diameter ≥4 mm

The mean bodyweight was 9.61 kg (SD ±2.33 kg). The mean age at the last MRI was 4.79 years (SD ±2.36 years). The sex distribution was group 1 (3 female, 8 male); group 2 (9 female, 6 male); group 3 (14 female, 6 male); group 4 (20 female, 34 male; between all groups: $P = .14$; between dogs with and without SM (group 1 versus group 2-4): $P = .12$; between dogs with SM-S and those with mild or no SM (group 4 versus group 1-3): $P = .88$. Of the total sample, 88 dogs were neutered (55 female 33 male) and 14 dogs (3 female 11 male) were entire; neuter status was not specified in the records of 28 dogs (neuter status between groups $P = .13$).

3.2 | Clinical and behavioral signs

The frequency of the clinical signs and whether this clinical sign was related to syrinx presence or size are illustrated in Tables 4 and 5. Clinical and behavioral signs of pain were common in dogs diagnosed with CM-P and SM but were not SM dependent.

The most common historical sign was vocalization, recorded in 65.4% dogs (55.3% spontaneous or when changing position when recumbent, 29.2% postural, 2.3% during defecation). The presence of vocalization was not related to syrinx presence or size with the exception of postural vocalization (yelping when picked up under sternum), which was more common in groups 1-3, that is, dogs with no or mild SM ($P = .04$).

The next most common sign was spinal pain present in 54.6% of dogs (32.3% cervical, 36.9% thoracolumbar, 12.3% lumbosacral). Spinal pain, at any site, was not related to syrinx presence or size as defined by maximum transverse width.

A change in activity was recorded in 37.7% of dogs with 33.8% reported as having reduced exercise tolerance, 12.3% reported as lethargic, and 8.5% described as both lethargic with reduced exercise tolerance. These signs were not related to syrinx presence or size. Refusal/being unwilling/hesitating/difficulty, vocalization, or both when jumping, doing stairs, or both were also a common historical finding being reported in 35.4% of dogs and was also not related to syrinx presence or size. A change in emotional state described as becoming more timid, anxious, withdrawn, or aggressive was reported in 28.5% of dogs, and 22.3% of dogs had disrupted sleep characterized by nighttime restlessness. None of these signs was related to syrinx presence or size with the exception of withdrawn behavior, which was more common in CKCS with SM-S ($P = .03$); however, there was a low number of dogs for this variable; therefore, this finding might not be true.

Other pain behaviors, not related to syrinx presence or size, were reported in 43.1% of dogs of which the most common was aversion to touch or grooming which was present in 30.0% of dogs, with the ears, head, and neck region being the specific area in 25.4% of dogs.

The only signs that were significantly associated with syrinx presence and size were scratching (phantom and scratching or rubbing of the head or ears), scoliosis, postural deficits, and weakness. Of these phantom scratching ($P \leq .001$), scoliosis ($P \leq .001$), postural deficits ($P = .004$), and weakness ($P \leq .001$) were associated with SM-S, that is, large syringes with a maximum transverse width ≥4 mm. All affected dogs with these neurological signs were in the SM-S group 4. Phantom scratching was seen in 67% of group 4 dogs and was not seen in groups 1-3. There was a correlation with mid-cervical superficial dorsal horn involvement and the side of phantom scratching with 3 exceptions, which were dogs reported to scratch to the sternum, that is, not directed toward a side. One of these 3 dogs had a thoracic syrinx with bilateral dorsal horn involvement in the T1-T2 region with only minor cervical spinal cord involvement (CCD only); the other 2 dogs had unilateral dorsal horn involvement through the cervical and thoracic spinal cord. There were 12 dogs that phantom scratched at both sides of the neck, and for these dogs, there was bilateral superficial dorsal horn involvement in the mid-cervical region with subjectively more severe involvement of the superficial dorsal horn ipsilateral to the side most scratched. Phantom scratching was recorded in all dogs where the syrinx width was ≥6.4 mm. By contrast, scratching or rubbing of the head or ears was inversely associated to syrinx size ($P = .005$), and although present in 28% of the population, it was less common in dogs in the SM-S group 4 category ($P = .003$).

Scoliosis was found in 27% of group 4 SM-S CKCS, and this is better described as a cervicothoracic torticollis with a twisting so that the head deviated ventrally contralaterally, and the shoulder was pushed out ipsilateral to the cervical superficial dorsal horn involvement. Weakness was reported in 39% of group 4 SM-S CKCS and was most commonly reported as of 1 or both thoracic limbs; tetraparesis with the thoracic limbs more severely involved; or could also involve the core muscles with the dog presenting with lordosis. Muscle atrophy was only recorded in dogs in the SM-S category, but the frequency was low (5 dogs) and did not achieve significance.

3.3 | Comorbidities

The study cohort had following comorbidities: BOAS (10.0% of population); chronic or historical pancreatitis (6.2%); inflammatory bowel disease, chronic diarrhea, or both (6.9%); keratoconjunctivitis sicca (6.9%); myxomatous mitral valve disease (MVD) (18.5%); oral eosinophilic granuloma (0.8%); previously excised type 1 dermoid sinus (0.8%); minor orthopedic disease, for example, grade I patellar luxation (12.3%); epilepsy (3.8%); fly catching (0.8%); episodic falling (1.5%); and historical skin disease (3.1%). Cases where these comorbidities could be a possible explanation for the clinical signs, for example, scratching with a comorbidity of skin disease, had already been excluded from the study population. Some CKCS developed new (presumed) unrelated neurological conditions during the study period as follows: head and neck myoclonus[21] (13.1%), cognitive function deficit (0.8%), orthostatic pelvic limb tremor (3.8%), uncategorized paroxysmal events (1.5%), facial nerve paralysis (3.8%), vestibular disease (3.8%), and deafness (0.8%). None of the comorbidities was significantly associated to any of the 4 groups with the exception of myoclonus in which 12 of 17 cases were in group 4 ($P < .001$). Otitis media with effusion (PSOM) was present in 44.6% of the dogs with the SM-S (SM ≥4 mm) group having 48% of the cohort with 1 or both ears affected ($P = .27$) and 30% having bilateral OME ($P = .14$). Otitis media with effusion (PSOM) was analyzed separately for an association to clinical signs of scratching or head rubbing ($P = .98$).

TABLE 4 Distribution of behavioral and clinical signs according to group

Category	Subcategory		Number of dogs and percentage of that group (parenthesis)				
			Total 130 dogs	Group 1: 11 dogs No SM	Group 2: 15 dogs CCD	Group 3: 20 dogs Mild SM	Group 4: 84 dogs SM-S
Vocalization	Spontaneous/changing position when recumbent		72 (55.3)	6 (55)	11 (73)	12 (60)	43 (51)
	Postural		38 (29.2)	5 (45)	5 (33)	9 (45)	19 (23)
	Defecation		3 (2.3)	0	1 (7)	0	2 (2)
	Scratching		7 (5.4)	0	1 (7)	0	6 (7)
	Either/both spontaneous or postural		**85 (65.4)**	**7 (64)**	**13 (87)**	**14 (70)**	**51 (61)**
Spinal pain	Cervical		42 (32.3)	6 (55)	8 (53)	5 (25)	23 (27)
	Thoracolumbar		48 (36.9)	3 (27)	7 (47)	7 (35)	31 (37)
	Lumbosacral		16 (12.3)	2 (18)	1 (7)	1 (5)	12 (14)
	Any spinal pain		**71 (54.6)**	**7 (64)**	**10 (67)**	**11 (55)**	**43 (51)**
Activity	Reduced exercise		44 (33.8)	2 (18)	3 (20)	7 (35)	32 (38)
	Lethargy		16 (12.3)	3 (27)	2 (13)	2 (10)	9 (11)
	Both (lethargic and reduced exercise)		11 (8.5)	1 (9)	2 (13)	1 (5)	7 (8)
	Any activity change		**49 (37.7)**	**4 (36)**	**3 (20)**	**8 (40)**	**34 (40)**
Stairs/jumping	Refusal/ hesitation/difficulty		46 (35.4)	3 (27)	9 (60)	8 (40)	26 (31)
Change in emotional state/behavior	Greeting		6 (4.6)	1 (9)	0	2 (10)	3 (4)
	Aggression		10 (7.7)	1 (9)	2 (13)	3 (15)	4 (5)
	Timid/anxious		18 (13.8)	0	1 (7)	2 (10)	15 (18)
	Withdrawn		17 (13.1)	0	0	2 (10)	15 (18)
	Any behavior change		**37 (28.5)**	**2 (18)**	**2 (13)**	**6 (30)**	**27 (32)**
Sleep	Sleep disruption		29 (22.3)	1 (9)	2 (13)	3 (15)	23 (27)
Other pain behaviors	Touch/grooming aversion	Ears/head and/or neck	33 (25.4)	3 (27)	3 (20)	6 (30)	21 (25) `
		1–2 limb/paw	4 (3.1)	0	0	0	4(5)
		sternum/flank	7 (5.3)	0	1 (7)	2 (10)	4 (5)
		Any touch aversion	**39 (30.0)**	**3 (27)**	**3 (20)**	**7 (35)**	**26 (31)**
	Abnormal awake head/neck posture		11 (8.5)	0	0	1 (5)	10 (12)
	Sleeping elevated or unusual head posture		7 (5.4)	0	1 (7)	1 (5)	5 (6)
	Squinting/avoiding light		6 (4.6)	0	0	1 (5)	5 (6)
	Licking limb/paw		5 (3.8)	0	0	0	5 (6)
	Pain face		4 (3.1)	0	0	0	4 (5)
	1 or more pain behaviors/signs		**56 (43.1)**	**3 (27)**	**3 (20)**	**8 (40)**	**42 (50)**

(Continues)

TABLE 4 (Continued)

Category	Subcategory	Number of dogs and percentage of that group (parenthesis)				
		Total 130 dogs	Group 1: 11 dogs No SM	Group 2: 15 dogs CCD	Group 3: 20 dogs Mild SM	Group 4: 84 dogs SM-S
Possibly unrelated behavior	Repetitive tongue licking	8 (6.2)	1 (9)	1 (7)	1 (5)	5 (6)
	Repetitive barking	2 (1.5)	0	0	0	2 (2)
Scratching and/or rubbing head or ears		37 (28.5)	3 (27)	7 (47)	11 (55)	16 (19)
Phantom Scratching	Phantom scratching	56 (43.1)	0	0	0	56 (67)
Neurological abnormalities	Weakness	33 (25.4)	0	0	0	33 (39)
	Muscle atrophy	5 (3.8)	0	0	0	5 (6)
	Postural responses decreased	13 (10.0)	0	0	0	13 (15)
	Hypermetria	13 (10.0)	0	2 (13)	2 (10)	9 (11)
	Scoliosis/cervicothoracic torticollis	23 (17.7)	0	0	0	23 (27)
	Any neurological abnormality	**46 (35.4)**	**0**	**2 (13)**	**2 (10)**	**42 (50)**
OME/PSOM	Total affected by PSOM	58 (44.6)	4 (26)	5 (33)	9 (45)	40 (48)
	Left (unilateral/ bilateral)	43 (33.1)	2 (18)	3 (20)	6 (30)	32 (38)
	Right (unilateral/ bilateral)	46 (35.4)	4 (36)	4 (27)	7 (35)	31 (37)
	Bilateral	33 (25.4)	2 (18)	2 (13)	4 (20)	25 (30)

Number of CKCS and percentage of that group with a certain historical or clinical signs. A total of 130 CKCS were grouped according to the maximum transverse central canal or syrinx size as group 1 with no SM or CCD; group 2 with CCD and a maximum transverse central canal size of 0.50-1.99 mm; group 3 with mild SM and a maximum transverse syrinx size of 2-3.99 mm; group 4 with SM-S and with a maximum syrinx size ≥4 mm.

Abbreviations: CKCS, Cavalier King Charles spaniel; CCD, central canal dilatation; OME, otitis media with effusion; PSOM, primary secretory otitis media; SM, syringomyelia; SM-S, severe syringomyelia.

TABLE 5 Distribution of behavioral and clinical signs in CKCS with clinically relevant CM or SM

Category	Sub category		Dogs (%)	Presence and size of SM (p value)		
				Size	Presence <0.5 mm/ ≥0.5 mm	SM-S < 4 mm/ ≥4 mm
Vocalization	Spontaneous yelping or when changing position when recumbent		55	.44	.29	.26
	Postural		29	.13	.56	**.04**
	Defecation		2	.57*	.33	.99*
	scratching		5	.51	.60	.42
	Either/both spontaneous or postural		**65**	.26	.58	.19
Spinal pain	Cervical		32	.07	.15	.15
	Thoracolumbar		37	.78	.59	.99
	Lumbosacral		12	.55*	.42	.42
	Any spinal pain		**55**	.65	.29	.38
Activity	Reduced Exercise		34	.36	.26	.23
	Lethargy		12	.46*	.11	.64
	Both (lethargic and reduced exercise)		8	.86*	.62	.99
	Any activity change		**38**	.51	.78	.49
Stairs/jumping	Refusal/ hesitation/difficulty		35	.16	.99	.22
Change in emotional state/behavior	Greeting		5	.43*	.55	.67*
	Aggression		8	.36*	.36	.16
	Timid/Anxious		14	.28*	.70	.11
	Withdrawn		13	.12*	.13	**.03**
	Any behavior change		**28**	.42	.56	.29
Sleep	Sleep disruption		22	.30*	.12	.078
Other pain behaviors	Touch/grooming aversion	ears/head and/or neck	25	.92	.99	.99
		1–2 limb/paw	3	.52*	.99	.30
		sternum or flank	5	.65*	.60	.70
	Abnormal awake Head/neck posture		8	.26*	.36	.10
	Sleeping elevated or unusual head posture		5	.86*	.60	.99
	Squinting/Avoiding light		5	.66*	.99	.42
	Licking limb/paw		4	.42*	.99	.16
	Pain face		3	.52*	.99	.30
	1 or more pain behaviors/signs		43	.37*	.30*	.12*
Possibly unrelated behavior	Repetitive tongue licking		6	.97*	.99	.99
	Repetitive barking		2	.77*	.99	.54
Scratching and/or rubbing head or ears			28	**.005**	.77	**.003**
Phantom Scratching	Phantom Scratching		43	**<.001**	**<.001**	**<.001**
Neurological abnormalities	Weakness		25	**<.001**	**.01**	**<.001**
	Muscle atrophy		4	.42*	.99	.16
	Postural responses decreased		10	**.05***	.367	**.004**
	Hypermetria		10	.69*	.99	.99
	Scoliosis/cervicothoracic torticollis		18	**.002**	.07	**<.001**
	Any neurological abnormality		35	**<.001**	**.01**	**<.001**

(Continues)

TABLE 5 (Continued)

Category	Sub category	Dogs (%)	Presence and size of SM (p value)		
			Size	Presence <0.5 mm/ ≥0.5 mm	SM-S < 4 mm/ ≥4 mm
OME/PSOMS	Any/both ears	45	.59	.11	.27
	Left	33	.35	.09	.19
	Right	35	.89	.42	.20
	Bilateral	25	.46	.36	.14

The percentage of the total cohort of 130 CKCS with each behavioral or clinical sign and the potential differences between the groups as follows: Size—the difference among all 4 groups; Presence—the difference between dogs without SM and dogs with a CCD/SM transverse diameter ≥0.5 mm, that is, group 1 versus groups 2–4; SM-S: the difference between dogs with SM-S and other dogs, that is, group 4 versus groups 1–3. Significant *P*-values are in bold.
Abbreviations: CKCS, Cavalier King Charles spaniel; CCD, central canal dilatation; OME, otitis media with effusion; PSOM, primary secretary otitis media; SM, syringomyelia; SM-S, severe syringomyelia with a maximum transverse syrinx diameter ≥4 mm.
*Test not robust due to small frequencies.

4 | DISCUSSION

As acknowledged in previous studies,[4,18] CM-P and SM are painful; however, this study showed that the signs of pain are not SM dependent suggesting CM-P causality or an epiphenomenon. Signs common in all groups were vocalization; reduced activity; reduced stairs/jumping ability; spinal pain; change in emotional state; sleep disturbance; aversion to touch and scratching; and rubbing head or ears. Signs specific to SM were only seen with large syringes, consistent with the neurolocalization of the cavity, and included phantom scratching, scoliosis with motor and sensory deficits. Our study aimed to determine common clinical and behavioral signs associated with CM-P and SM for further prospective studies, and we particularly wanted to ascertain what signs might indicate CM-P as diagnosis of this is challenging and made by excluding other causes of pain and head rubbing together with appropriate MRI changes.[5] We made a comprehensive analysis of the owner reported signs and clinical findings in a comparatively large cohort of 130 client owned dogs with rigorous inclusion and exclusion criteria and without the bias created by active recruitment of cases. However, the reader is recommended to be cautious in making conclusions, as the findings are the observations of 1 individual and reports from the owner and therefore subject to bias. A decision was made to limit the study to animals under the care of single veterinary surgeon who had over 20 years' experience of CM/SM as it was more likely that the history taking, clinical examination, and medical note annotation were detailed and consistent among dogs. However, the authors' acknowledge that this does introduce a bias of the opinion of that individual especially as the same individual analyzed the MRI, albeit separately to and after analysis of the clinical records. There could be a bias in the exclusion, for example, removing the dogs with scratching that had both SM and skin disease. In addition, including so many covariates in 1 study might have influenced the significance levels. Therefore, the findings in this study should be verified by other independent studies and perhaps concentrate on more specific covariates.

The most common sign reported by owners of CM-P and SM affected dogs is vocalization. More than 1 in 2 dogs were reported to yelp, described as being spontaneous or following/during movement especially when recumbent and during the night. Classically, human patients with the analogous condition Chiari type I malformation (CM1) have an occipital or suboccipital headache exacerbated by cough and other Valsalva maneuvers or exertion.[22] However, many patients report worse headaches when supine because fluid redistributes towards the head.[23-25] A similar headache is reported with benign intracranial hypertension[24,25] and is a possible explanation for the signs suggesting pain reported in CM-P-affected dogs. Vocalization when lifted by the sternum in CM-P-/SM-affected dogs has been reported anecdotally for many years[26] and is hypothesized to be a failure to equilibrate intracranial pressure due to obstruction of CSF pathways and the microgravitational effects when being lifted rapidly. More recently, this clinical sign was documented as occurring in 1 in 3 dogs with CM and SM,[4] which is a similar proportion to this study (29.2% postural pain). Neither study found an association with the presence or severity of a syrinx. In this study, this sign was more common in a CKCS with no or mild SM suggesting that this sign might be associated with CM-P.

Spinal pain at 1 or more sites was found in 54.6% of dogs; however, this was not related to syrinx size or presence. Indeed, for groups 1 and 2 (26 dogs with no syrinx or with CCD), 14 had cervical pain, 10 had thoracolumbar pain, and 3 dogs had caudal lumbar/lumbosacral pain. In the total cohort, thoracolumbar pain was more common than cervical pain (36.9% versus 32.3%) and caudal lumbar/lumbosacral pain was seen in a minority of patients (12.3%). This finding of more caudal spinal pain does not have a clear neuroanatomical explanation but has been documented previously.[4,26] This sign is difficult to be compared to CM1 as a significant number of human patients have comorbidities that could also result in back pain such as IVD disease, fibromyalgia, and Ehlers-Danlos syndrome.[27] Further studies are required to investigate this finding in dogs and what morphological changes predict it (if any). This study did not assess the spinal cord distribution of the syrinx (if present). Defining total involvement of the spinal cord by the syrinx is difficult, for example, it is challenging to quantify and compare varying diameter of the syrinx, CCD, and the presence of presyrinx along the spinal cord. However, this could be studied separately in prospective studies in a larger cohort. Other behavioral signs of pain were reported, with 43.1% of the cohort having signs suggesting head, limb, or flank pain of which the most common was aversion to touch of the ears, head, or neck. Signs of pain from stimuli that do not normally

cause pain have been previously associated with CM-P and SM and are thought to represent allodynia.[17,28]

Scratching, rubbing the head or ears, or both was 1 of the more common signs, seen in 28.5% of the cohort, and has been previously described in dogs affected by CM-P and SM.[4,26] Why this behavior might be seen is obviously speculative. One study showed that 81% of human patients with CM1 reported aural fullness and 81% reported tinnitus, symptoms usually attributed to ear disease.[29] We suggest this as 1 possible explanation for why dogs with CM-P might rub their ears. It was interesting that OME (PSOM), something that has been reported to cause ear discomfort,[30] was not significantly associated with head/ear rubbing or scratching in the CM-P/SM cohort. It can be difficult for veterinarians to know whether signs of ear discomfort are attributed to OME or CM-P and consequently unclear whether to advise myringotomy and/or placement of tympanostomy tube(s).[31] Otitis media with effusion is a sequel of brachycephalic conformation and poor drainage of the middle ear,[30,32,33] and although drainage of the material might improve signs, there is often recurrence because the predisposing factors are not addressed.[30] This study suggests that OME is common in CM-P- and SM-affected dogs, and caution should be observed before attributing signs of ear rubbing with OME (PSOM).

Other common signs that were not related to syrinx presence or size were changes in activity and behavior which suggested avoidance or pain when jumping or doing stairs. This could have a variety of explanations, but in comparison to CM1, 96.1% of patients report impact in 1 or more areas of daily living and physical activity[34] and activity headache is common.[35]

A behavioral change was reported in almost 1 in 3 dogs (28.5%). Again, this could have a variety of explanations, but pain can negatively affect a dog's emotional state and increase anxiety,[36] lower the threshold for aggressive behavior or increase the likelihood of a protective/defensive response,[37] or both. A questionnaire-based behavioral analysis found that CM-P/SM-affected CKCS were more likely than normal CKCS to show stranger-directed fear, nonsocial fear, separation-related behavior, attachment behavior, anxiety (described as excitability in the study), had poor ability to settle, and were more reluctant to exercise.[36]

Pain-related sleep disruption is important morbidity affecting quality of life and is recognized in other painful conditions in the dog such as osteoarthritis.[38] In this study, sleep disruption was reported in approximately 1 in 5 dogs. Pain sensitivity and sleep have a mutual deleterious influence; for example, in humans, insomnia significantly increases the risk for reduced pain tolerance.[39] It is recommended that human patients with neuropathic pain have assessment of sleep, mood, and functional capacity in addition to simple pain relief scales (eg, numerical rating scale or visual analog scales) especially when assessing treatment effects.[40] One comorbidity that was not fully investigated in this retrospective study was whether sleep apnea could be a complicating factor. Patients with CM1 are predisposed to sleep disorders and have a high prevalence of sleep apnea-hypopnea syndrome.[41] Cavalier King Charles spaniels are also predisposed to BOAS, and although an attempt was made to exclude these dogs, none of the dogs with sleep disruption had whole-body barometric plethysmography.[42]

The study suggested that the presence of SM per se might not be associated with certain signs of pain; however, no attempt was made to quantify the signs of discomfort or an individual dog's quality of life as this was beyond the scope of this retrospective study. In other words, it is possible that SM-affected dogs had similar signs to dogs with CM-P but that the signs in SM affected dogs were more frequent or severe. There was a suggestion that this might be so, for example, SM-S dogs were more likely to be withdrawn. A recommendation from this study is to use the clinical signs identified to develop a prospective quality-of-life scoring system.

The study found that wide (≥4 mm) SM results could result in a myelopathy with sensory and motor signs that localize to the level of the spinal cord affected by the syrinx. However, gait disturbances could be mild even with extensive SM. Specific signs that were suggestive of a wide cervical syringe was phantom scratching and cervicothoracic torticollis (scoliosis). Phantom scratching is described a rhythmic scratching action, without making contact with the skin, together with a curvature of the body and neck towards the foot.[16] It can be induced by lightly rubbing a defined area of skin, typically on the neck. This light touch–induced scratch reflex makes walking on a collar difficult. Phantom scratching also be triggered by excitement or anxiety. Although considered a specific sign of SM, this sign is not universal and is associated with large syrinx extending to the superficial dorsal horn in the C3-C6 spinal cord segments (C2-C5 vertebrae) ipsilateral to the scratching limb.[16] Originally thought to represent a paraesthesia, current thinking is that it is more similar to fictive scratch reported in spinalized animals[17,18] and hypothesized due to alteration of dorsal horn input to the scratching central pattern generator.[16] Our study also found that phantom scratching was associated with large syringes and ipsilateral extension of the syrinx to the region of the cervical cord dorsal horn. Phantom scratching was observed in approximately 2/3 of CKCS with SM-S and in all dogs where the syrinx was ≥6.4 mm. Our study findings further suggest that phantom scratching is highly unlikely with small syringes. A minority of the dogs (3) had a phantom scratching action to the sternum, and there was a suggestion that this might be involved with thoracic spinal cord dorsal horn involvement, a hypothesis which should be investigated in a larger cohort.

Cervicothoracic torticollis (scoliosis) was also a sign exclusive to and common in the SM-S group. This sign has previously been associated with wide syringes in the dorsal spinal cord, and our study supported an association to superficial dorsal horn involvement with a corkscrew deviation of the head and neck so that the head is twisted ventrally contralateral to and the shoulder twisted and pushed out ipsilateral to the side of dorsal horn involvement. Cervicothoracic torticollis is thought to be due to asymmetrical damage of the dorsal gray column, over a number of spinal cord segments, resulting in an imbalance of afferent proprioceptive information from the cervical neuromuscular spindles.[17,43]

Comorbidities were common and not unexpected given the breed disposition to MVD,[44] pancreatic disorders,[45] keratoconjunctivitis sicca,[46] and other neurological disorders.[6,21] Other than ascertaining that a group

was not predisposed to a certain comorbidities, detailed analysis was not preformed because of the retrospective and likely incomplete nature of the study, for example, MVD was the most common comorbidity present in approximately 1 in 5 CKCS but cannot be translated as the lifetime risk of a CM-/SM-affected dog having MVD because this disease is more common in older CKCS.[44] The study did suggest that myoclonus was more commonly seen within the SM-S group. However, caution is observed because numbers were small and a previous study of 40 CKCS with myoclonus did not suggest it was more common with SM-S.[21]

5 | CONCLUSION

Our results suggest any tool developed for ascertaining quality of life in CM-P and SM should have specific questions on signs suggesting discomfort, scratching/rubbing (including character/site), sensitivity to touch, activity, ability to jump and climb stairs, emotional state, and sleep. The study further suggests that SM-specific signs are phantom scratching, scoliosis, and sensory and motor signs that can be related to spinal cord damage by the syrinx and are associated with large syringes (transverse width ≥4 mm). Non-SM-specific signs include vocalization (described as without obvious trigger, when shifting position when recumbent and when being lifted under the sternum to a height), spinal pain, head and ear rubbing or scratching, aversion to touch, refusal or difficulty jumping or doing stairs, exercise intolerance/reduced activity, sleep disruption, or behavioral change described as becoming more anxious, timid, aggressive, or withdrawn. These non-SM-specific signs could reflect CM-P. Although possible variables for the tool have been identified, interrelationships between them would have to be taken into account in a multivariate sense when modeling.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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