Title

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Journal

Journal of veterinary internal medicine, 37(2)

ISSN

0891-6640

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Publication Date

2023-03-01

DOI

10.1111/jvim.16588

Peer reviewed

Received: 6 July 2022 | Accepted: 11 November 2022

DOI: 10.1111/jvim.16588

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

Horner syndrome as a physiological biomarker of disease in canine cervical myelopathy

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Abstract

Background: Horner syndrome often occurs with cervical myelopathies and might provide insight into the underlying disease and prognosis.

Objectives: To describe the clinical and imaging features of dogs with cervical myelopathy and concurrent Horner syndrome and to determine association of Horner syndrome with diseases or magnetic resonance images (MRI).

Animals: Ninety-three client-owned dogs with cervical myelopathy and concurrent Horner syndrome and 99 randomly selected client-owned dogs with cervical myelopathy without Horner syndrome (control cases).

Methods: Retrospective study. Medical records were reviewed to identify Horner and control cases and clinical findings recorded. MRI were reviewed, and lesions characterized and recorded. Descriptive and comparative statistics were performed.

Results: Non-compressive disease occurred more frequently in the Horner group compared with controls (58%; 95% CI: 48-68 vs 9%; 95% CI: 5-16; $P < .0001$). The most common diseases were fibrocartilaginous embolism in the Horner group (44/93; 47%) and intervertebral disc extrusion (76/99; 77%) amongst controls. On MRI, parenchymal hyperintensity was seen more commonly in the Horner group (95%; 95% CI: 88-98) compared with controls (51%; 95% CI: 41-60; $P < .0001$). In the Horner group, dogs that did not survive to discharge ($N = 13$) had more extensive MRI lesions relative to the adjacent vertebral length (200%; IQR 110%-575%) compared with survivors ($N = 80$; 110%; IQR 40%-250%; $P = .02$). Lateralization of Horner signs and MRI changes matched in 54% of cases. The overall survival rate was high in both Horner (80/93; 86%) and control (95/99; 96%) groups.

Conclusions and Clinical Importance: Horner syndrome in cervical myelopathy is commonly associated with noncompressive intraparenchymal disease.

KEYWORDS

autonomic, fibrocartilaginous embolic myelopathy, hypothalamospinal, intervertebral disc disease, oculosympathetic, tectotegmental

Abbreviations: ANNPE, acute noncompressive nucleus pulposus extrusion; CI, confidence interval; FCEM, fibrocartilaginous embolic myelopathy; HNPE, hydrated nucleus pulposus extrusion; IQR, interquartile range; IVDE, intervertebral disc extrusion; MUO, meningoencephalitis(myelitis) of unknown origin; PNST, peripheral nerve sheath tumor.

1 | INTRODUCTION

Disruption of the oculosympathetic pathway manifests as Horner syndrome (Horner's syndrome).[1,2] Injury to any of the components of the neural pathway results in miosis, often also ptosis, enophthalmos, and protrusion of the nictitating membrane, and in non-equids, anhidrosis.[1-5] Partial Horner syndrome, characterized by miosis alone, is reported, but its existence is debated.[2,6]

Previous studies have looked at Horner syndrome in dogs, documenting cases with damage of each neuron of the pathway.[3-5] Cervical myelopathy is a common neurological presentation in dogs that can cause Horner syndrome through damage of the first-order neuron, but it remains unclear whether Horner syndrome in cervical myelopathy provides any insight into the underlying disease.

Based on clinical observations, we hypothesized that Horner syndrome in dogs with cervical myelopathy was more commonly seen with noncompressive intraparenchymal lesions than compressive extraparenchymal lesions. The goals of this study were to: (a) describe the clinical and imaging features of dogs with Horner syndrome believed to be secondary to cervical myelopathy; (b) investigate whether these dogs had different rates of noncompressive intraparenchymal disease compared with dogs with cervical myelopathy without Horner syndrome; (c) evaluate the clinical outcomes of dogs with Horner syndrome and cervical myelopathy.

2 | MATERIALS AND METHODS

The medical record database at the University of California, Davis Veterinary Medical Teaching Hospital was searched retrospectively for canine cases of cervical myelopathy with concurrent signs of Horner syndrome. Cases from 2007 to 2018 were included if cervical MRI was performed and available for review. Dogs were excluded if the Horner syndrome preceded the myelopathy, developed after anesthesia, or could be attributed to, or was suspected to be attributed to a nonmyelopathic cause like cervical soft tissue trauma, otitis media, or ocular or brain disease. Dogs were considered to have complete Horner syndrome if the record documented miosis along with ptosis, enophthalmos, and protrusion of the third eyelid. Dogs were considered to have partial Horner syndrome if the record only documented miosis. A comparison control group of dogs was generated by randomly selecting 100 dogs from a list of 882 retrospectively identified cases of canine cervical myelopathy without Horner syndrome from the same period.

Data collected included signalment, neurological grade, duration of clinical signs, lateralization of signs, lumbar CSF analysis (protein, cell count, cytology findings), outcome (survival to discharge), necropsy or biopsy findings, and final clinical diagnosis. Breeds were grouped as chondrodystrophic and nonchondrodystrophic breeds based on previously reported genetic data.[7-9] A modified Frankel scoring system was used to grade dogs as having tetraplegia with respiratory compromise or lacking deep nociception (grade 0), tetraplegia with intact deep but absent superficial nociception (grade 1), tetraplegia with intact nociception (grade 2), nonambulatory tetraparesis (grade 3), ambulatory tetraparesis (grade 4), spinal hyperesthesia, or nerve root signature only (grade 5).[10-12] All MRI images were acquired using a 1.5 T Signa LX MRI scanner (GE, Milwaukee, Wisconsin). MRIs of all cases were reviewed by a board-certified radiologist (KP) and board-certified neurologist (CFL), both blinded to the original diagnosis, for number, location, etiology of lesions, degree of parenchymal involvement, severity, length, and lateralization of lesions. The length of lesion was calculated as a percentage of the length of the adjacent cervical vertebra the lesion was centered over.

3 | STATISTICAL ANALYSIS

Data was analyzed using a commercially available statistical analysis software (GraphPad Prism v9.0. 2021, GraphPad Software, La Jolla, California). Descriptive statistics were calculated, including percentages of group total and 95% confidence intervals (CI) for categorical or ordinal data. Results are presented as total number (percentage) unless stated otherwise. Categorical variables were compared using Fisher's exact test. Proportions of categorical variables were compared using a chi-square test. Continuous variables (weight, length of lesion, CSF protein, CSF cell count) were tested for normality using the Shapiro-Wilk test. Non-normally distributed data were compared using the Mann-Whitney U test and results are presented as median (interquartile range IQR). A P-value of <.05 was considered statistically significant.

4 | RESULTS

4.1 | Clinical data: Horner cases

A total of 102 dogs met initial inclusion criteria for the Horner group out of a total of 984 dogs with cervical myelopathy and MRI from a 11-year period (incidence of 10%). Of these, 9 involved disease of the T1-T3 nerve roots—8 cases with suspected or confirmed peripheral nerve sheath tumor (PNST) and 1 brachial plexus avulsion. These cases of peripheral nerve disease were excluded from the analyses below in an attempt to specifically evaluate Horner syndrome arising from cervical myelopathy (first-order or second-order).

Dogs had a median age of 6.0 years (IQR 4.0-9.0 years) and weighed a median of 11.8 kg (IQR 6.9-29.0 kg). Body weight was unavailable in 9 dogs, but these were grouped based on reported breed. The proportion of large breed (>20 kg) and small breed (≤20 kg) dogs was 39/93 (42%) and 54/93 (58%), respectively. There were 9 intact males, 37 neutered males, 8 intact females, and 39 spayed females (Table 1). Breed type, duration of clinical signs, and neurological grade at admission are summarized in Table 1. Complete Horner syndrome was documented in 36/93 (39%) cases whereas 57/93 (61%) showed partial Horner syndrome. Unilateral Horner syndrome was identified in 84/93 (90%) dogs, with 40/93 (43%) involving the right eye and 44/93 (47%) involving the left eye. Bilateral ocular sympathetic dysfunction was seen in 9/93 (9%) dogs. Lumbar CSF was collected in

TABLE 1 Comparison of clinical features of the Horner group and Control group.

	Horner group, n = 93 N; % (95% CI)	Control group, n = 99 N; % (95% CI)	*P*-value
Sex			.002
Male	46; 49 (40-59)%	71; 72 (62-80)%	
Female	47; 50 (41-60)%	28; 28 (20-38)%	
Breed			.47
Chondrodystrophic	54; 58 (48-68)%	52; 53 (43-62)%	
Modified Frankel score			<.0001
Grade 0	2; 2 (0–8)%	0 (0-4)%	
Grade 1	1; 1 (0-6)%	0 (0-4)%	
Grade 2	17; 18 (12-27)%	4; 4 (2-10)%	
Grade 3	50; 54 (44-64)%	27; 27 (19-37)%	
Grade 4	20; 22 (14-31)%	56; 57 (47-66)%	
Grade 5	3; 3 (1-9)%	12; 12 (7-20)%	
Duration of clinical signs			.001
<24 hours	28; 27 (19-36)%	14; 14 (9-22)%	
1-3 days	34; 33 (24-42)%	18; 18 (12-27)%	
4-7 days	12; 12 (8-19)%	17; 17 (11-26)%	
8 days to 4 weeks	23; 22 (15-31)%	27; 27 (19-37)%	
>1 month	7; 7 (3-13)%	23; 23 (16-32)%	
Surgery	31; 33 (25-43)%	69; 70 (60-78)%	<.0001
Survival to discharge	80; 86 (78-92)%	95; 96 (90-98)%	.024

47 dogs and revealed a median total nucleated cell count of 5 cells (IQR 2-16 cells). CSF protein concentration was available in 45 dogs with a median of 99.0 mg/dL (IQR 60.0-279.0 mg/dL). Surgery was performed in 31/93 (33%) cases. Among these dogs, the most common surgery was ventral slot surgery, performed in 24 cases, whereas dorsal laminectomies were performed in 6 dogs and 1 dog had a dorsal vertebral stabilization. Survival to discharge occurred in 80/93 (86%) cases. Necropsy data was available for 11 dogs. Histopathology of the spinal cord revealed progressive myelomalacia in 3/11 (27%) cases (secondary to HNPE in 1 case and with no identifiable underlying cause in 2 cases). Fibrocartilaginous embolic myelopathy (FCEM) with regional myelomalacia was confirmed in 2/11 (18%) cases. Tumors involving the spinal cord were identified in 6/11 (55%) cases—2/11 showed undifferentiated extraparenchymal sarcomas, 2/11 (18%) showed cervical meningiomas, and extraparenchymal plasmacytoma and intramedullary hemangiosarcoma were identified in 1/11 (9%) case each.

4.2 | MRI findings: Horner cases

On MRI, a single lesion was seen in 77/93 (83%) dogs whereas the rest had multiple lesions. Clinical lateralization of Horner signs matched the lateralization of MRI findings in 50/93 (54%; 95% CI: 44-64) dogs. Lesions at C1-C5 were identified in 34/93 (37%) dogs, whereas C6-T2 lesions were seen in 39/93 (42%) cases. Extensive lesions spanning both segments of the cervical spinal cord were seen in 20/93 (22%) cases. Lesion length in the Horner group varied greatly, with a median of 115% (IQR 53%-335%) of the length of the adjacent cervical vertebra. MRI lesions were lateralized on the left side in 32/93 (34%), the right side in 37/93 (40%), and located on the midline or diffusely affecting the spinal cord in 24/93 (26%) cases. Exclusively gray matter involvement was seen in 23/93 (25%) dogs, exclusively white matter involvement in 7/93 (7%) and both gray and white matter involvement in 58/93 (62%) of cases. The remaining 5/93 (5%) had no parenchymal hyperintensity. Parenchymal hyperintensity occurred in 32/36 (89%) compressive dogs and 56/57 (98%) noncompressive dogs, which did not differ significantly ($P = .07$).

Concurrent imaging of the skull was available in 7 dogs and was reviewed to rule out other causes of Horner syndrome. The final diagnoses are presented in Table 2. Amongst dogs with Horner syndrome, noncompressive disease was seen most frequently, in 54/93 (58%) cases (Figure 1). Of these cases, the most common cause was suspected ischemic myelopathy (suspected FCEM; Table 2). In comparison, 39/93 (42%) dogs had a compressive myelopathy arising from extraparenchymal disease, of which the most common etiology was intervertebral disc extrusion (IVDE) in 24/93 (26%) cases (Figure 1). Dogs with compressive disease had a median age of 7.5 years (IQR 5.3-12.0 years) whereas dogs with noncompressive disease had a median age of 6 years (IQR 3.5-9 years; $P = .02$). Weight and proportion of chondrodystrophic breeds between dogs with compressive and noncompressive disease were not significantly different ($P = .47$ and $P = .2$, respectively).

TABLE 2 Etiology of underlying disease.

	Horner group, n = 93 N; %	Control group, n = 99 N; %
Compressive disease	39; 42%	90; 91%
IVDE (Type I and II)	24; 26%	76; 77%
HNPE	6; 6%	3; 3%
Compressive trauma	2; 2%	—
Caudal cervical spondylomyelopathy	—	5; 5%
Extramedullary neoplasia	7; 8%	6; 6%
Noncompressive disease	54; 58%	9; 9%
Suspected or confirmed	44; 47%	3; 3%
Ischemic myelopathy/ FCEM		
ANNPE	3; 3%	2; 2%
MUO	1; 1%	2; 2%
Bacterial myelitis	1; 1%	—
Noncompressive trauma	3; 3%	—
Syringomyelia	1; 1%	1; 1%
Intramedullary neoplasia	1; 1%	1; 1%

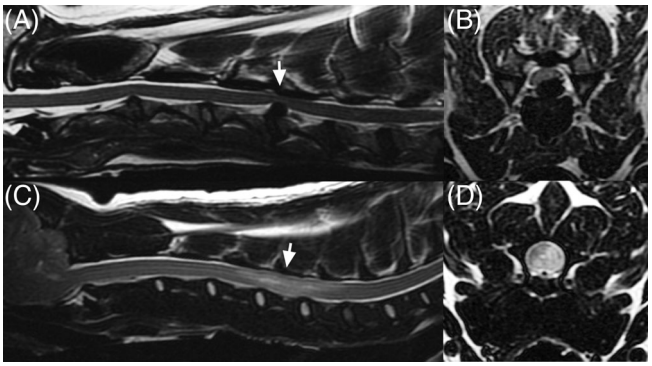

FIGURE 1 Representative T2W sagittal (A) and transverse (B) images from a 10-year-old male castrated Labrador Retriever presenting for ambulatory tetraparesis. The dog did not have Horner syndrome and was in the control group. The dog has a large T2 hypointense extruded compressive disc at C4-C5 (arrow) with minimal regional parenchymal hyperintensity. Representative T2W sagittal (C) and transverse (D) images from a 5-year-old Yorkshire Terrier presenting for non-ambulatory tetraparesis and right-sided Horner syndrome. The dog has severe intraparenchymal T2W hyperintensity, worse on the left side with no spinal cord compression (arrow). The intraparenchymal lesion spans over the length of 2.5 vertebral bodies (250% the length of the adjacent vertebra).

4.3 | Clinical outcomes: Horner cases

The median length of the lesion on MRI was greater in dogs with Horner that did not survive to discharge (200%; IQR 110%-575%) than dogs that did (110%; IQR 40%-250%; $P = .05$). There was no difference in rates of survival to discharge between dogs with lesions at C1-C5 and those with lesions at C6-T2 ($P = .5$), or when comparing neurological grade ($P = .48$), duration of clinical signs ($P = .2$) or affected eyes ($P = .16$). Completeness of Horner syndrome was not significantly different when compared with survival, neurological grade, lesion location (C1-C5 vs C6-T2), and duration of clinical signs ($P = .76$; $P = .62$; $P = .49$; $P = .33$, respectively).

4.4 | Clinical data: Control cases

A total of 100 dogs were selected for the control comparison group, but 1 dog was excluded for having a PNST involving the T1-T3 nerve roots. Control dogs had a median age of 8.0 years (IQR 5.0-10.0 years) and median weight of 14.5 kg (IQR 7.3-33.0 kg). Large breed (>20 kg) and small breed (≤20 kg) dogs accounted for 41/99 (41%) and 58/99 (59%) cases, respectively. There were 7 intact males, 64 neutered males, 4 intact females, and 24 spayed females (Table 1). Breed type, duration of clinical signs, and neurological grade at admission are summarized in Table 1. Lumbar CSF analysis was performed in 16 dogs and revealed a median total nucleated cell count of 3 cells (IQR 1-10 cells) and median protein concentration of 62.0 mg/dL (IQR 44.8-112.5 mg/dL). Surgical intervention was performed in 69/99 (70%) control dogs, with ventral slot surgery being the most common procedure in 65 cases. The remaining 4 cases underwent dorsal laminectomies. Overall, 95/99 (96%) cases survived. Necropsy data was available for 4/99 (4%) dogs in this group. Histopathology confirmed synovial cell sarcoma, hemangiosarcoma, IVDE and caudal cervical spondylomyelopathy in 1/4 (25%) dog each.

4.5 | MRI findings: Control cases

On MRI, a single lesion was seen in 80/99 (81%) dogs. The main lesion was identified within the C1-C5 segment in 44/99 (44%) and at C6-T2 in 51/99 (52%) cases. The remaining 4/99 (4%) dogs had lesions spanning both regions. Median lesion length was 28% (IQR 20%-85%) of the length of the adjacent cervical vertebra. MRI lesions were left lateralized in 24/99 (24%) and right lateralized in 16/99 (16%) cases. Midline or diffuse lesions predominated in 59/99 (60%) cases. Gray matter involvement was noted in 25/99 (25%) dogs, 3/99 (3%) had white matter involvement and 22/99 (22%) involved both gray and white matter. The remaining 49/99 (49%) had no parenchymal hyperintensity. The final diagnoses of control dogs are presented in Table 2. Compressive disease was seen in 90/99 (90%) cases with IVDE being the most common cause (Table 2).

4.6 | Comparison of Horner and control groups

The distribution of durations of clinical signs and distribution of neurological grades at admission were not significantly different between groups ($P = .65$ and $P = .89$, respectively).

Significantly fewer dogs in the Horner group (31/93; 33%) were treated surgically than in the control group (69/99; 70%; $P < .0001$; Figure 2). Rates of survival to discharge were lower in the Horner group (80/93; 86%) when compared with the control group (95/99; 96%; $P = .02$). The proportion of lesions at C1-C5 and C6-T2 outlined above were not significantly different between the Horner and control groups ($P > .99$; Figure 3). Non-compressive disease occurred more frequently in the Horner group compared with controls (58%, 95% CI: 48-68 vs 9, 95% CI: 5-16; $P < .0001$; Figure 4). Parenchymal hyperintensity was seen more commonly in the Horner group (88/93; 95% vs 50/99; 51%; $P < .0001$). Median lesion length on MRI was also longer amongst Horner cases (115%; IQR 52.5%-335%) than controls (28%; IQR 20%-85%; $P < .0001$).

5 | DISCUSSION

The oculosympathetic pathway is a 3-neuron pathway originating in the caudal hypothalamus, which receives visceral afferents from the cerebrum and thalamic nuclei.[13-17] The hypothalamus projects 2 sets of efferent first-order sympathetic fibers: a dorsal tract running through the periaqueductal gray and a ventrolateral tract running lateral to the substantia nigra.[13,14] Both converge caudolaterally along the lateral lemniscus, lateral to the pyramids, along the brainstem floor.[13,14] These tracts primarily project down the spinal cord in the dorsal lateral funiculi, close to the insertion of the dentate ligaments, via the hypothalamospinal tract (often referred to as the lateral tectotegmental tract in the veterinary literature, the origin of the latter name is unclear and is not in line with experimental literature) and

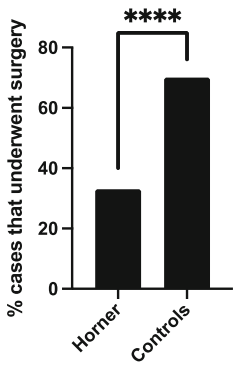

FIGURE 2 Bar graph comparing percentages of cases that received surgical intervention (* indicates statistical significance $P < .0001$).

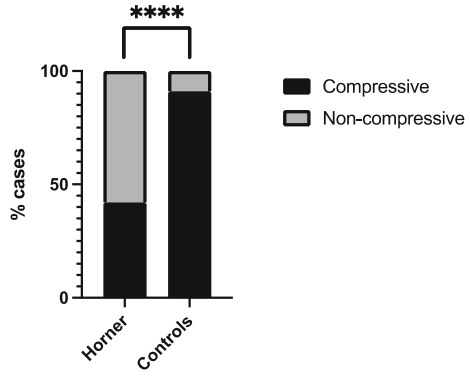

FIGURE 4 Stacked bar graph comparing percentages of compressive and noncompressive diseases between Horner and control groups (* indicates statistical significance $P < .0001$).

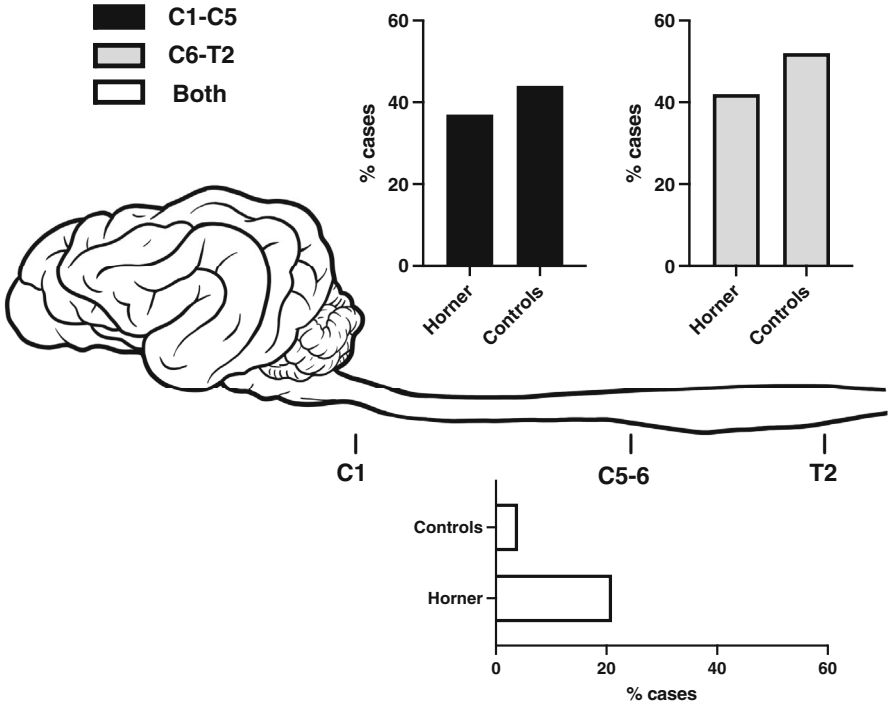

FIGURE 3 Bar graph showing distribution of lesions across cervical spinal cord segments. No significant difference was seen between groups based on location (C1-C5 vs C6-T2). However, disease affecting both segments was seen more commonly with Horner syndrome cases.

synapse onto the ciliospinal center of the intermediolateral column at T1-T3.[1,13-19] The axon of the second-order neuron arises from the ventral horn at this level and runs along the ventral nerve root to exit the spinal nerve via the white segmental ramus communicans.[1,17,20] The fibers run over the stellate ganglion, through the ansa subclavia, over the middle cervical ganglion to join the vagosympathetic trunk, which runs longitudinally up the cervicothoracic region, terminating in the cranial cervical ganglion, caudomedial to the tympanic bulla.[1,17,20] The third-order neuron projects fibers out through the middle ear, along the wall of the cavernous sinus and through the orbital fissure to the eye, typically following the ophthalmic branch of the trigeminal nerve, innervating the muscles of the iris, eyelids, and orbit.[1,20] Whereas some species and individual variation of the third-order neuron pathway has been reported, the pathway of the first- and second-order neurons is highly conserved.[1,14,16,21,22] Whereas Horner syndrome secondary to injury of the first-order neuron has been documented, it has not been thoroughly investigated in the context of cervical myelopathy.[1,3,23,24] In this cohort of dogs with Horner syndrome suspected to arise from cervical myelopathy, most dogs had nonsurgical, noncompressive intraparenchymal diseases with extensive T2W hyperintense lesions on MRI. Additionally, dogs with Horner syndrome were much more likely to have noncompressive lesions when compared with the general population of dogs presenting with cervical myelopathy without Horner syndrome. Whereas the identification of Horner syndrome on neurological examination in dogs with cervical myelopathies may raise suspicion for possible underlying lesions and prognosis, advanced diagnostics are still warranted to provide a full clinical picture.

We found that both unilateral and bilateral Horner syndrome commonly occurs with both C1-C5 lesions as well as C6-T2 lesions and can occur with injuries of a range of neurological severities. This is different from previous reports from some sources that report a higher incidence of Horner syndrome with C6-T2 lesions, and in more severe cervical myelopathies, where there is concern for ventilatory compromise, especially if bilateral Horner syndrome is seen.[1,25] The lack of effect of lesion location (C1-C5 vs C6-T2) on survival to discharge was also notable as lower motor neuron injury from disease in the intumescence is typically thought to carry a worse prognosis. However, other outcome variables such as time to recovery or completeness of recovery were beyond the scope of the study.

The exact location of the hypothalamospinal tract remains unclear in the literature, with some evidence suggesting a more superficial location.[14] At first glance, our findings are suggestive of a more central location, close to the gray matter, given the types of diseases seen and low incidence of extradural compression, especially of the dorsolateral spinal cord. However, the hyperintensity seen on MRI often involved the entire cross-section of the spinal cord, limiting our ability to comment on this. This picture is further clouded by the lack of congruence between the lateralization of Horner signs and MRI changes. Further investigation is required to define the location of these tracts and assess whether this pathway simply shows significant resilience, or if any collateral compensation exists.

Amongst our cohort, dogs with Horner syndrome had a high frequency of parenchymal hyperintensity on MRI that was significantly more extensive than control cases. However, it is important to note that such parenchymal changes were seen with both compressive and noncompressive diseases, although they were more common in cases with noncompressive disease. Therefore, the presence of Horner syndrome did not accurately predict the underlying lesion for use as a clinical biomarker.

Similarly, given the high rate of noncompressive parenchymal diseases, dogs with concurrent Horner syndrome required surgery significantly less often than control dogs. Despite this, surgery was still performed in a third of cases, reflecting the heterogeneity of diseases within the Horner group. Thus, whereas the presence of Horner syndrome might suggest a nonsurgical disease process in most cases, the full clinical picture, including signalment, history, and advanced imaging are often necessary to evaluate the likelihood of surgical disease.

The survival rate among Horner cases, though lower than controls, was still quite high. Of the cases with Horner syndrome that died or were euthanized, necropsy confirmed progressive hemorrhagic myelomalacia secondary to HNPE in 1 case, whereas an underlying etiology for myelomalacia was not found in 2 cases. Necropsy confirmed FCEM in 2 cases and neoplastic diseases resulting in cervical myelopathy in 6 cases. One case that was euthanized did not undergo necropsy and was suspected to have ischemic myelopathy (suspected FCEM) based on clinical and imaging diagnosis. Thus, a single disease process was not overrepresented in this group. Similarly, of these cases, neurological grade at presentation varied, with 1 case presenting with ventilatory compromise and 4 cases presenting apparently tetraplegic. Of the remaining 8 cases, 6 were nonambulatory tetraparetic and 2 were ambulatory. Thus, it appears that neurological grade did not affect survival in these cases. Neurological grade also did not appear to affect survival even when all cases (Horner and controls) were combined. This may be due to relatively low numbers of dogs with severe myelopathies (grade 1 or 0).

The duration of clinical signs and neurological grade at presentation are thought to be associated with prognosis, and often factor into clinical decision making. Whereas we did not specifically see an effect of these in our population, given the retrospective nature of this study, it is yet possible that such factors may have influenced clinician decision making and recommendations around surgery or otherwise influenced dog survival.

This study has limitations, including a lack of definitive diagnosis of Horner syndrome through pharmacological testing to confirm sympathetic dysfunction. However, tight adherence to testing protocols is needed, as the use of phenylephrine to diagnose Horner syndrome and localize the lesion can be unreliable.[3] As such, Horner syndrome is typically a clinical diagnosis, and all efforts were made to rule out other causes of miosis, as well as Horner syndrome of other causes, using the retrospective data available for each case. The lack of consistent diagnostic testing to rule out other causes of miosis and Horner syndrome of other causes remains a limitation of the retrospective nature of this study. Idiopathic Horner syndrome could not be completely ruled out but was considered unlikely as such dogs most likely would have met the exclusion criteria with the onset of their Horner syndrome not coinciding with the onset of their

myelopathy. Additionally, Horner syndrome only occurred in approximately 10% of cases of cervical myelopathy in this study population. It is possible that the true incidence may be higher, as we did not include cases that did not receive MRI or were not referred to our tertiary care center. Additionally, given the retrospective nature of this study, diagnoses of partial Horner syndrome may have been missed, if simply not assessed or recorded. As such, it is possible that our study underestimates the incidence of partial Horner syndrome.

This study characterizes dogs with Horner syndrome, believed to be due to damage of the first-order neuron, caused by cervical myelopathy. The presence of Horner syndrome was associated with non-compressive diseases, and as such, often did not require surgical intervention. Whereas cases with Horner syndrome had a lower survival rate compared with the control group, differences in disease etiology, severity of neurological grade, and other potential confounders between groups limit the comparisons in this retrospective data set. As such, the presence of Horner syndrome did not have a strong predictive value for prediction of disease, need for surgery or prognosis for survival. Future prospective research might consider incorporating the presence of Horner syndrome, and other similar physiological biomarkers as components of multifactorial diagnostic or prognostic algorithms.

ACKNOWLEDGMENT

No funding was received for this study. This work was presented in part at the 2019 ACVIM Forum, Phoenix, AZ, USA. The authors thank Peter Dickinson for his assistance in the review of the relevant neural pathways outlined in this paper.

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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How to cite this article: Murthy VD, Phillips K, Knipe M, Giuffrida M, Li C-F. Horner syndrome as a physiological biomarker of disease in canine cervical myelopathy. *J Vet Intern Med*. 2023;37(2):598-605. doi:10.1111/jvim.16588