Central cord syndrome: clinical features, etiological diagnosis, and outcome in 74 dogs

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https://doi.org/10.2460/javma.21.08.0389

OBJECTIVE
To describe the clinical and neurologic signs, diagnostic investigations, definitive or presumptive diagnosis, treatment, and outcome of dogs presented with acute onset central cord syndrome (CCS).

ANIMALS
74 client-owned dogs evaluated for CCS at 5 referral hospitals between January 2016 and March 2021.

PROCEDURES
Data were collected from the medical records of each dog, including patient signalment, physical and neurologic examination results, presence of signs of respiratory failure, diagnostic imaging findings, definitive or presumptive diagnosis, treatment and follow-up information. Descriptive statistics were calculated and bivariable analysis was performed to identify associations between selected variables.

RESULTS
2 neuroanatomic locations for the CCS were identified: C1-C5 spinal cord segments in 65 of 74 (88%) dogs and C6-T2 in 9 (12%) dogs. Neurolocalization did not correlate with the imaging findings in 43 (58%) dogs. Different diseases were associated with CCS. The most common condition was Hansen type I disk herniation in 27 (36%) dogs and hydrated nucleus pulposus extrusion in 16 (22%) dogs. Main lesion locations within the vertebral column associated with CCS were C3-C4 and C4-C5 intervertebral disk spaces in 21 (28%) and 18 (24%) dogs, respectively. Outcome was favorable in 69 (93%) dogs. Patients presenting with hypoventilation were 14.7 times more likely to have a poor outcome.

CLINICAL RELEVANCE
CCS in dogs may be seen with lesions in the C1-C5 and C6-T2 spinal cord segments. Etiologies are variable. Total or partial improvement was achieved in most dogs with the appropriate treatment. Hypoventilation was associated with death.
matter and spares the more superficial tracts. These are UMN pathways to the cervical intumescence. In humans, it has been suggested that spinal cord edema and hematoma formation following a mechanical lesion of the cervical spinal cord produce CCS, secondary to the dysfunction of the medial portion of the lateral corticospinal tract. Recent autopsy findings suggest that the injuries to the white matter of the lateral corticospinal tract, with sparing of the gray matter, are the responsible for CCS signs.

To the authors’ knowledge, there are no previous studies describing the clinicopathological findings and etiologies of acute CCS in veterinary medicine. The aim of this study was to describe the clinical and neurologic signs, investigation test results, definitive or presumptive diagnosis, treatment, and outcome of dogs presenting with acute onset of CCS as part of their neurologic signs.

Materials and Methods

Medical records of dogs presented to the Neurology and Neurosurgery Service of 5 referral hospitals were retrospectively reviewed from January 2016 to March 2021. Owner consent was obtained for all clinically indicated investigations. Dogs with acute onset of CCS as their neurologic signs were included. A patient was considered to present with CCS when paresis was more severe in the TLs than PLs or when paresis only involved the TLs. Patients were excluded from the study if records were incomplete or clinical signs were chronic (> 7 days).

Information obtained from medical records included signalment (breed, age, sex, and body weight), clinical history, physical and neurologic examination findings, complete blood analysis results, diagnostic imaging data, definitive diagnosis (or presumptive diagnosis following a complete diagnostic workup), treatment, and follow-up information. If the patient had signs consistent with respiratory compromise, results of blood gas analysis and arterial partial pressure of carbon dioxide (PaCO2) measurement were recorded when available.

All included dogs had a full neurologic examination performed by a board-certified neurologist or a neurology resident under supervision. Based on neurologic examination records, the patients’ neurologic status was graded as follows: grade 1, minimally decreased proprioceptive and motor function in both TLs with normal PLs; grade 2, severe paresis in both TLs and minimally decreased proprioceptive and motor function in both PLs; and grade 3, absence of motor function in both TLs and paresis in both PLs.grade 3, absence of motor function in both TLs and paresis in both PLs; and grade 3, absence of motor function in both TLs and minimally decreased proprioceptive and motor function in both PLs. Spinal hyperesthesia was determined based on palpation and manipulation of the spine at admission as well as information provided by the owner. The presence of partial or complete sympathetic denervation of the eye (Horner syndrome) was also recorded.

Imaging diagnosis was performed with advanced imaging techniques, including myelography, CT (Somatron 16-slice or Somatrom Spirit; Siemens), CT with myelography and/or MRI (Magnetom Avanto 1.5 MRI; Siemens AG; Magnetom Essenza 1.5 MRI; Siemens AG; Vantage Elan high-field 1.5-T scan; Canon Medical Systems; Vet-MR 0.25-T scanner; Esote SpA). When possible, the specific etiology was recorded; for patients in which a definitive diagnosis was not achieved, presumptive diagnosis was recorded.

Lesions located cranial to the C5 vertebral body were considered cranial to the cervical intumescence. The reliability of the neuroanatomic diagnosis following examination, with the anatomic location of the lesion observed in diagnostic imaging.

For cases in which CSF was collected, the results were recorded. Infectious disease testing varied depending on the geographic area and included assays for Toxoplasma gondii, Neospora caninum, Erlichia canis, Leishmania infantum, and canine distemper virus.

Treatment options (surgical or medical) were recorded. Outcome was considered successful when the patient improved in neurologic grade or was clinically normal after treatment. Within this group, time to improve 1 neurologic grade, time to completely recover in days, or both were recorded when available. Outcome was considered unsuccessful when dogs did not neurologically improve or were euthanized due to lack of improvement or worsening of their clinical signs.

Statistical analysis

Data obtained were analyzed with commercially available statistical software (SPSS Statistics version 20; IBM Corp). Descriptive statistics were calculated, and categorical variables were summarized in frequencies and percentages, parametric data as mean and SD, and nonparametric data as median and interquartile (25th to 75th percentile) range and minimum and maximum when appropriate. Normality of distribution was evaluated by the Shapiro-Wilk test and histogram inspection.

Bivariant analysis was undertaken to evaluate the association of categorical variables with the outcome, neurologic grade at presentation, and partial or complete sympathetic denervation of the eye by use of the χ² or Fisher exact test for categorical data and Mann–Whitney U test for quantitative data. Odds ratios and 95% CIs were calculated by standard methods. Statistical significance was set at P < 0.05.

Results

Seventy-four dogs met the inclusion criteria. Median (range) age at the time of diagnosis was 6 years (0.3 to 14 years), and median body weight was 13.9 kg (0.6 to 58.7 kg). There were 32 female dogs (15 spayed and 17 sexually intact) and 42 males (22 neutered and 20 sexually intact). Breeds included 13 mixed-breed dogs (17%), 11 French Bulldogs (14%), 7 Yorkshire Terriers (9%), 4 Chihuahuas and Cocker Spaniels (5%), 3 Beagles and Miniature Pinschers (4%), and 22 other breeds represented by 2 or fewer dogs. Results of hematology and serum biochemistry were unremarkable in all dogs. Of the 74 dogs with CCS, 6 were considered grade 1 (8%), 26 grade 2 (35%), and 42 grade 3 (57%).
Based on the neurologic examination, the lesion was localized to the C1-C5 spinal cord segments in 21 (28%) dogs and C6-T2 segments in 53 (72%) dogs. Spinal hyperesthesia was reported in 47 (63%) dogs and partial or complete Horner syndrome in 5 (7%) dogs. Signs of impaired ventilation, consisting of inability to expand the thorax, were detected in 5 (7%) dogs, and all 5 dogs were regarded as neurologic grade 3. Blood gas analysis was performed in 3 dogs, and the median Paco₂ was 53.1 mm Hg (range, 39.4 to 63 mm Hg).

Hyperventilation on presentation was not associated with Horner syndrome in the bivariable analysis; however, it was associated with poor outcome (P = 0.03), and patients presenting with hyperventilation were 14.7 times as likely to have a poor outcome as dogs ventilating normally (OR, 14.7; 95% CI, 1.7 to 123.5). The diagnosis and anatomic location of the lesion in dogs with respiratory compromise at presentation were diffuse inflammatory cervical disease in 1 dog, Hansen type I disk herniation in 2 dogs (1 patient at the C2-C3 vertebral fractures and/or luxations in 10 (13%) dogs, inflammatory noninfectious meningomyelitis in 5 (7%) dogs, acute noncompressive nuclear pulposus extrusion in 4 (5%) dogs, ischemic myelopathy in 3 (4%) dogs, infectious meningomyelitis in 3 (4%) dogs, acute deterioration of cervical spondylomyelopathy in 3 (4%) dogs, acute on chronic disk herniation in 2 (3%) dogs, and neoplasia in 1 (1%) dog.

Based on the imaging findings, the anatomic location of the lesion was the C3-C4 IVDS in 21 (28%) dogs, C4-C5 IVDS in 18 (24%) dogs, C5-C6 IVDS in 11 (15%) dogs, C6-C7 IVDS in 8 (11%) dogs, C2-C3 IVDS in 6 (8%) dogs, a diffuse cervical lesion cranial to the intumescence in 5 (7%) dogs, C1-C2 junction in 3 (4%) dogs, and atlanto-occipital junction and a diffuse lesion involving the cervical intumescence in 1 (1%) dog. Based on the imaging findings, 65 (88%) dogs had a lesion located cranial to the cervical intumescence, whereas 9 (12%) patients showed a lesion in the cervical intumescence. In 31 (42%) patients, imaging findings correlated with the neurolocalization; however, in 43 (58%) dogs, clinical neurolocalization did not correspond with the imaging findings.

Cerebrospinal fluid was analyzed in 12 (16%) dogs, and the results were abnormal in 9 (75%). Of these, 8 dogs were diagnosed with inflammatory/infectious meningomyelitis and 1 with T-cell lymphoma. Assessment of infectious diseases in CSF was performed in 8 dogs, and a positive PCR result for Leishmania infantum was obtained in 3 cases, which were classified as infectious meningomyelitis.

Surgery was performed in 42 (57%) dogs, and surgical treatments included ventral slot, cervical hemilaminectomy, and vertebral fixation-stabilization, depending on the condition. Surgeries were performed by a board-certified neurologist, board-certified surgeon, or both. Medical treatment was performed in 32 (43%) dogs. In 9 (12%) patients, it consisted of steroids at variable doses, other immunosuppressive drugs, and antiprotozoal treatment, depending on the etiology. In the other 23 (31%) dogs, medical treatment consisted of cage rest, analgesia, and physiotherapy.

Follow-up examinations were performed by a board-certified neurologist or neurology resident under supervision. Outcome was successful in 69 (93%) dogs and unsuccessful in 5 (7%) dogs. Median (range) time to show an improvement of neurologic grade was recorded for 56 (76%) dogs and was 12.5 days (1 to 30 days) from presentation. Additionally, median (range) time to complete recovery was recorded for 42 dogs and was 25 days (2 to 90) from presentation.

**Discussion**

Central cord syndrome is a clinical presentation in which patients exhibit worse paresis in the TLs than the PLs secondary to a cervical spinal cord injury or lesion.² In the present study, CCS was detected in dogs with lesions in 2 neurolocalizations: C1-C5 and C6-T2 spinal cord segments. Lesions affecting the C6-T2 spinal cord segments may cause more paresis in the TLs and therefore are consistent with CCS signs due to involvement of the LMN of the TLs located in the gray matter of the cervical intumescence. In general, patients with a C6-T2 myelopathy have absent or delayed postural reactions in all 4 limbs with decreased or absent spinal reflexes and muscle tone in the TLs, consistent with LMN signs in the TLs and UMN signs in the PLs.³ In the present study, CCS was also associated with lesions affecting the C1-C5 spinal cord segments. These usually produce UMN signs causing absent or delayed postural reactions with normal spinal reflexes in all 4 limbs. In human medicine, it is becoming apparent that central spinal cord injuries are more complex than previously thought. Injuries affecting tracts closer to the gray matter and sparing more superficial tracts cause more severe damage to the UMN tracts of the TLs than to those of the PLs and therefore cause more paresis in the TLs than the PLs.² It is believed that damage to the lateral corticospinal tracts causes bilateral weakness of the upper body in humans, whereas patients retain strength in the lower limbs.² Both corticospinal and spinothalamic tracts have homunculi in which the upper body is located centrally, whereas the lower body is located more peripherally within the spinal cord.⁶ Axons of the lateral corticospinal tract terminating at the cervical spinal cord level are most medial in this tract, whereas those distributing to lumbosacral levels are more lateral.⁷ Clinical signs of CCS may be justified by a lesion affecting these descending pathways.

During the neurologic examination of patients with a cervical spinal cord lesion, spinal reflexes are
tested to classify the neurologic deficits to the TLs as either UMN (C1-C5 spinal cord segments) or LMN (C6-T2 spinal cord segments) signs. In both neurolocalizations, the patients have abnormal postural reactions in all 4 limbs; however, in cases of C6-T2 myelopathy, the spinal reflexes of the TLs are decreased or absent but are normal in patients with C1-C5 myelopathy. In the present study, based on the neurologic examination, 28% of patients with more severe paresis in the TLs and classified as CCS were localized as having a lesion in the C1-C5 spinal cord segments, while 72% were localized to C6-T2 spinal cord segments. However, diagnostic imaging demonstrated an anatomic location of the lesion cranial to the cervical intumescence in most (88%) dogs.

A discrepancy between clinical and imaging findings may have different explanations. Individual variation of the location of the cervical intumescence in the vertebral column in dogs could account for some of the cases. Additionally, the described reliability of the withdrawal reflex in dogs with cervical disk herniations for neurolocalization has been described as 65.8%. These may explain the inaccuracy between clinical neurolocalization and anatomic location based on the imaging findings for classifying it as an UMN or LMN paresis in the TLs; however, in the absence of histopathologic confirmation, microscopic nonobservable extension of the lesion into the cervical intumescence may be also considered. Due to the multicenter origin of the study, slight variation in the technique of the TL withdrawal reflex for neurolocalization in the cervical area may have influenced its assessment. Furthermore, suspected cervical spinal shock consisting of a transient hyporeflexia or areflexia caudal to a lesion in a patient with a normal anatomic reflex arc may also be considered; however, an absent or decreased withdrawal reflex in all limbs would be expected as described in the literature. Another hypothesis may be that the spinal shock could have an uneven improvement, with the recovery of the PLs being faster than recovery of the TLs.

In human medicine motor vehicle collisions, falls and diving are the most common causes of CCS. It is postulated that this syndrome results from a hyperextensive mechanism, spinal cord compression, and damage to the central area of the spinal cord and associated spinal tracts. Three affected groups of people are described. The younger population appears to be typically affected as a result of severe traumatic vertebral column lesions. The older population typically shows injuries as a result of hyperextensive movements in a spondylotic canal. The third group includes patients of any age who have no degenerative predisposing conditions but do have low velocity traumatic injuries resulting from acute central cervical disk herniations.

Human cadaveric research has revealed that in CCS, there is no axon loss at the level of the injury but rather Wallerian-like degeneration of the axons adjacent to the epicenter of the injury, which is likely the cause of the neurologic findings. In our study, the most common condition associated with CCS was Hansen type I disk herniation and HNPE. Main locations of the lesion were over the C3-C4 and C4-C5 IVDS. Spinal cord contusion and secondary intramedullary damage were suspected to be responsible for the clinical signs. In 1 case report a dog was presented for cranial cervical CCS secondary to an electrocution. Investigations revealed an ischemic myelopathy at the C2-C3 spinal cord segments, and the histopathologic analysis revealed a focal disruption of the C2-C3 gray matter and extensive loss of the parenchyma at the dorsal horn, an area where the lateral corticospinal tract is located. Other etiologies of CCS encountered in this study were cervical vertebral fractures and luxations, inflammatory-infectious meningomyelitis, acute noncompressive nucleus pulposus extrusion, ischemic myelopathy, acute deterioration of cervical spondylomyelopathy, acute on chronic disk herniation, and neoplasia.

Absence of spinal hyperesthesia associated with intramedullary lesions such as ischemic myelopathy, intramedullary neoplasia, or contusive damage secondary to a noncompressive disk extrusion has been commonly described in dogs. The primary concurrent painful conditions that present with the intramedullary contusive lesions may justify these findings. Furthermore, the remodeling or destruction of the dorsal horn secondary to the contusive event or a local mass effect that could cause some degree of meningeal stretching should also be considered as causes of spinal discomfort.

In human medicine, CCS has a good outcome; however, older age and more severe neurological injury at presentation are associated with poorer outcomes. In our study, there was no statistical association between older age and neurologic grade at presentation and poorer outcome, but this may be due to the low number of patients with poor outcome (only 5/74 dogs).

In the present study, 93% of the patients had a favorable outcome, including different etiologies and treatments. Ventilatory problems were associated with a poor outcome. Respiratory complications may occur secondary to cervical spinal cord injuries. It has been reported that approximately 5% of dogs with cervical spinal cord disorders may need ventilatory support. In our study, 7% of dogs with CCS had respiratory failure. This may have been caused by paresis or paralysis of the respiratory muscles via damage of the phrenic nuclei or due to a lesion of the sympathetic pathway and secondary cholinergic bronchoconstrictor activity.

In humans, CCS is also associated with some degree of sensory impairment below the level of the lesion and bladder dysfunction, usually urinary retention. No abnormalities were detected regarding urination in the dogs of the present study; however, further prospective studies are required to evaluate the relationship between CCS and urinary problems in dogs.

The limitations of this study were its retrospective nature, inclusion of dogs from multiple referral hospitals, use of different imaging techniques for the diagnosis of CCS, lack of histopathologic confirma-
tion of the extent of the lesion, and lack of follow-up diagnostic tests. Moreover, the small number of cases enrolled in the study made it impossible to perform multivariable analysis; therefore, the associations between putative risk factors and outcomes encountered in the bivariable analysis were likely to be preliminary. Future studies with a larger sample size are warranted as well as further studies comparing imaging findings and histopathology of dogs with CCS.

In conclusion, CCS is a clinical condition in patients with cervical myelopathy who have more paresis in the TLs than in the PLs. It can be associated with lesions in 2 neuroanatomic locations: the cervical intumescence and cranial cervical area. In the present study, main locations of the lesion associated with CCS were C3-C4 and C4-C5 IVDS. Although different etiologies may cause CCS, the most common conditions were Hansen type I intervertebral disk herniation and HNPE. Our findings suggest that, generally, CCS has a favorable outcome in dogs; however, hypoventilation at presentation seems associated with a poor outcome.

Acknowledgments

No external funding was used in this study. The authors declare that there were no conflicts of interest.

Dr. Ros contributed to the study design and execution, data collection, and preparation of the manuscript; Drs. José-López, Suñol, Montoliu, and Aige contributed to the data collection, preparation of the manuscript, and revision; Dr. Aige contributed to the study design, preparation of the manuscript, and revision; Dr. García de Carellán Mateo contributed to the study design, statistical analysis, and revision of the manuscript; and Dr. Font contributed to the study design and execution, data collection, and preparation of the manuscript, and revision.

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