“Feisty Cait’s Erratic Mishap”

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Class of 2021

Clinicopathologic Conference

April 30, 2021

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Introduction

Fibrocartilaginous embolic myelopathy (FCEM) is more common in large and giant breed dogs. However it has also been reported in small breed dogs, especially miniature schnauzers.[1-3] Although rare, some studies report FCEM development in chondrodystrophic dog breeds.[4,5] Most dogs diagnosed with FCEM have body weights greater than 20 kg, the male-to-female ratio ranges from 1:1 to 2.5:1 and the age of diagnosis ranges from 2 months to 11 years and 11 months with a median of 5 or 6 years.[1,6]

FCEM's typical presentation is a peracute onset (less than 6 hours) of nonprogressive and nonpainful (after the first 24 hours), and often asymmetric myelopathy.[1,3] Maximal neurologic deterioration occurs in the first 6 to 24 hours after onset followed by stabilization of signs or gradual improvement depending on the extent of ischemic injury. Neurologic deficits depend on the location and severity of the injury and are asymmetric in 53% to 86% of dogs. The most commonly affected spinal cord segments with antemortem diagnosis are L4-S3 and T3-L3 whereas the most commonly affected spinal cord segments with histologic postmortem diagnosis of FCEM are L4-S3 and C6- T2.[6]

History and Presentation

Cait is a 14-year-old female spayed Border Collie who was found by her owner acutely laterally recumbent and unable to rise or ambulate on December 27, 2020. Cait was taken to her primary care veterinarian where she was diagnosed with tetraparesis, obesity, elevated liver enzymes, IRIS Stage I chronic kidney disease and pituitary dependent hyperadrenocorticism. Cait also had a history of hip dysplasia which had been treated with tramadol (50 mg tablets, 2 tablets orally) as needed for pain. Cait was started on Ursodiol (300 mg capsules, 1 capsule

orally every 24 hours) and she was referred to Mississippi State University College of Veterinary Medicine (MSU-CVM) for further work-up. Cait presented to the MSU-CVM Neurology Department on January 7, 2021. She had normal appetite, urination, and bowel movements.

Upon presentation, Cait was laterally recumbent, bright, alert and responsive. She was obese weighing 33.3 kg and had a body condition score of 8/9. She was mildly tachycardic at 160 beats per minute, had a normal respiratory rate of 36 breaths per minute with normal effort, and she was normothermic at 101.6° F. She was estimated 5% dehydrated. Noninvasive blood pressure readings revealed hypertension at 201/121 (148), 171/129 (143) and 171/105 (127). On physical examination moderate dental tartar, bilateral mild ceruminous debris, bilateral lenticular sclerosis and mild mucoid ocular discharge, as well as a cranial organomegaly with a soft-nonpainful abdomen were noted. Neurologic examination revealed a non-ambulatory tetraparesis with overriding right hemiparesis. There was strong motor movements and normal muscle tone on all limbs and she was attempting to place them. Conscious proprioception was absent in the right thoracic and pelvic limbs, mildly delayed in the left thoracic limb and delayed to intermittently absent in the left pelvic limb. There was a weak patellar reflex on the left. Mental status, cranial nerves, and cutaneous trunci stimulation were all within normal limits. No hyperpathia was noted. Based on her neurologic examination, her lesion was localized to the C1-C5 spinal cord segments.

Pathophysiology

FCEM occurs when fibrocartilaginous material, that is identical to the nucleus pulposus from the intervertebral disk, occludes the spinal vasculature causing ischemic necrosis of dependent regions of the spinal cord parenchyma.[2-4] There are various hypotheses on the pathogenesis of FCEM including direct penetration of nucleus pulposus material into the spinal

cord or vertebral vasculature, chronic inflammatory neovascularization of degenerated intervertebral disc, embryonic remnant vessels within the nucleus pulposus, and mechanical herniation of the nucleus pulposus into the vertebral bone marrow sinusoidal venous channels.[6] The exact mechanism by which FCEM occurs is still unclear.[1]

Differential Diagnoses

The most common differential diagnosis for FCEM is acute noncompressive nucleus pulposus extrusion (ANNPE) which also causes a peracute onset of nonprogressive asymmetric myelopathy. This condition occurs under strenuous exercise or trauma where the nondegenerated nucleus pulposus extrudes causing contusion of the spinal cord but not compression. In addition to MRI, the main clinical findings that support a diagnosis of ANNPE over FCEM include an older age at disease onset (median age of 7 years), spinal hyperalgesia during the initial examination, and quicker improvement in neurologic signs with an increased chance of being ambulatory at hospital discharge. Moreover, several studies have reported lateralization of neurologic dysfunction of 53-87% in dogs with FCEM and 62-65% in dogs with ANNPE. [6,9,10]

Different types of emboli such as bacterial, parasitic, neoplastic, or fat can also occlude spinal blood vessels and cause ischemia and necrosis such as with FCEM, although less commonly. Some medical conditions that may predispose to embolization include cardiomyopathy, hypothyroidism, hyperthyroidism, hyperadrenocorticism, chronic renal failure, and hypertension.[6]

Other differential diagnoses include compressive intervertebral disc extrusion, infectious and immune-mediated focal myelitis, neoplasia, and intra- and extramedullary hemorrhage.[1] These conditions can be differentiated from FCEM by looking at the history, clinical signs, disease

progression, and diagnostic findings, especially MRI and cerebrospinal fluid (CSF) analysis. In patients where the history is incomplete or unknown, a traumatic spinal injury resulting in vertebral fracture, subluxation/luxation, spinal cord contusion, or hemorrhage need to be in the list of rule-outs. These patients generally present with severe spinal hyperesthesia and should be handled minimally and with extreme care until radiographs rule out an unstable lesion.[6]

Diagnostic Approach and Considerations

The antemortem diagnosis of FCEM can be reached by the typical presentation of clinical signs and exclusion of other causes of peracute/acute focal myelopathy.[6] Cait became acutely recumbent with no previous clinical signs, and her clinical signs did not progress following onset. Furthermore, Cait did not exhibit signs of pain upon becoming recumbent or following the incident. Cait's history indicates a peracute onset of nonprogressive and nonpainful myelopathy. Following examination, it was determined that Cait's myelopathy was asymmetric due to the lateralization of her neurologic dysfunction. Cait's clinical signs on presentation were characteristic of FCEM.

Cait's complete blood count revealed a mild thrombocytosis which is likely reactive and has no pathological significance, and a mild lymphopenia which is a common leukogram abnormality, most likely associated with stress. The chemistry panel revealed a mild hyperkalemia, mild acidosis, moderate azotemia, markedly elevated ALP, and mild hyperglobulinemia. These findings are consistent with Cait's chronic kidney disease and hyperadrenocorticism. A urinalysis revealed a urinary tract infection. Urine culture and sensitivity revealed that *Escherichia coli* was the causative organism. Thoracic radiographs revealed a mild hepatomegaly, esophageal gas, mild bilateral glenohumeral osteoarthrosis, and ruled out metastatic neoplasia. The mild hepatomegaly may have been due to nodular

regeneration, metabolic/endocrine etiologies, infectious inflammatory etiologies, or neoplasia. The esophageal gas was most likely due to aerophagia but esophagitis could not be entirely ruled out.

Magnetic resonance imaging (MRI) is the preferred imaging modality for diagnosis of FCEM because it shows signal intensity changes suggestive of ischemic infarction of the spinal cord. It excludes other important differentials for myelopathy, such as ANNPE.[4] Key MRI findings that help distinguish ANNPE from FCEM are T1W FS focal meningeal and epidural fat enhancement, nonlongitudinal directional pattern of intramedullary hyperintensity, cleft in the annulus fibrosus and reduced nucleus pulposus volume which are characteristic of ANNPE but are absent in FCEM. Furthermore, lesions overlying a vertebral body are more characteristic of FCEM, while lesions overlying an intervertebral disk are more indicative of ANNPE.[7,8,10] T-2 weighted FSE images indicative of FCEM show a focal, relatively sharply demarcated, and many times asymmetric intramedullary lesion, predominantly involving the gray matter that appears hyperintense to normal spinal cord gray matter.[3] On T1-weighted FSE images, these changes appear iso- or hypointense to normal spinal cord gray matter. Focal spinal cord swelling is a common finding on MRI.[4,6,10] Cait's MRI was consistent with FCEM revealing a smoothly marginated, ovoid to wedge-shaped, T1 isointense, T2 hyperintense, non-contrast enhancing region within the dorsal horn of the spinal cord at mid C4. Myelogram revealed thinning of the subarachnoid space in this region, and helped to exclude some of the differentials, particularly the ones that cause spinal cord compression such as intervertebral disk extrusion. The described intramedullary spinal cord lesion and thinning of the subarachnoid space at mid C4 is consistent with spinal cord edema in this region as with an ischemic infarct (fibrocartilaginous embolism or thromboembolism). This localization is in contrast with the localization of an ANNPE lesion,

which would be overlying an intervertebral disk. It should also be noted that this is the least commonly reported localization for an FCEM lesion (C1-C5), with L4-S3 and T3-L3 being the most commonly reported affected spinal cord segments in dogs with antemortem diagnosis of FCEM.[6,10]

Even though a presumptive diagnosis of FCEM was reached by exclusion for Cait, other diagnostics such as CT can also help rule out other causes if needed.[6] In addition, CSF abnormalities such as elevated protein concentration have been reported in 44% to 75% in dogs with antemortem diagnosis of FCEM.[1] Polymerase chain reaction (PCR) on CSF may help rule out infectious causes of meningomyelitis if it were a more plausible differential.[6]

The definitive diagnosis of FCEM is made by histologic examination of the affected spinal cord segments, although this is not typically performed due to common spontaneous neurologic recovery.[1,3,4] Histologic examination will show fibrocartilaginous material in spinal vessels within or near an area of focal myelomalacia. The gray matter is usually more severely affected than the white matter because it has a greater metabolic demand than the white matter.[6]

Treatment and Management

Treatment of FCEM consists of reducing secondary spinal cord injury, nursing care, and physiotherapy. Nursing care and physiotherapy are needed to promote recovery and help prevent complications. Nursing care consists of providing adequate bedding, regular turning, skin care, care of the respiratory system, bladder and bowel management, and adequate nutrition. Physiotherapy promotes functional recovery using the unaffected neural tissue and minimizes disuse and immobilization which are followed by muscle atrophy and muscle and joint contractures.[6]

During her stay in the hospital, Cait was placed on a well-padded and comfortable kennel, she was turned every 6 hours, her bladder was monitored via ultrasound to ensure she was able to empty it, her perineal region was clipped and Aquaphor Healing Ointment® was applied every 12 hours to avoid irritation in the area, she was offered food every 12 hours and water every 6 hours, and her bedding, skin and fur were kept clean and dry. Her blood pressures were closely monitored with Doppler. Immediately following her presumptive diagnosis of FCEM, Cait was enrolled on the MSU-CVM rehabilitation program for 5 days which included underwater treadmill, weight-shifting exercises, quad cart walks, assisted walks with Help'em up® harness and laser therapy. She was then sent home for the weekend and came back the next week for 5 more days of physical rehabilitation. Cait was started on enalapril (10 mg tabs, 1.5 tabs orally every 12 hours) and amlodipine (2.5 mg tabs, 1 tab orally every 24 hours) to control her hypertension, and cefpodoxime (200 mg tabs, 1.5 tablet orally every 24 hours) to clear her urinary tract infection. After 5 days, her enalapril was discontinued due to hyperkalemia, and her amlodipine dose was increased (5 mg tabs, 1 tab orally every 24 hours). She was also started on gabapentin (800 mg tabs, 0.5 tab orally every 12 hours) and galliprant (60 mg tabs, 1 tablet orally every 24 hours) for pain.

Due to her obesity, Cait's daily energy requirement was calculated and adjusted for weight loss yielding 776 kcal/day as a result. She was started on Hills K/D + Mobility® dry food, taking into consideration her chronic kidney disease and osteoarthrosis, and other foods and treats were limited.

Prognosis and Outcome

The prognosis for recovery for patients with FCEM depends on the extent and severity of the ischemic injury. The reported negative prognostic indicators include loss of nociception,

lower motor neuron signs, symmetric neurologic deficits, severity of neurologic signs at initial examination, owner's reluctance to pursue nursing care and physiotherapy (particularly for giant and large breed dogs), and lack of improvement within the first 14 days.[6] However, many patients return to ambulatory status in 3 weeks.[1]

Historically, the outcome and prognosis has been associated with the extent of the ischemic injury measured on MRI as the ratio between the length of the intramedullary hyperintensity on mid-sagittal view and the length of the vertebral body of C6 (for cervical lesions) or L2 (for thoracolumbar lesions) as well as the cross-sectional area of the largest intramedullary hyperintensity on transverse images. Dogs with a ratio greater than 2.0 or a percent cross-sectional area of 67% had a significantly higher chance to have an unsuccessful outcome than those with lower values. [3,5,6] Cait's ratio was 0.6 and her percent cross sectional area was 33%.

One study revealed that MRI patterns in dogs with a presumptive diagnosis of ANNPE or FCEM with acute non-progressive T3-L3 myelopathy may help predict the risk of developing fecal incontinence. According to this study, fecal incontinence is five times more likely to develop in dogs with presumptive ANNPE in comparison to presumptive FCEM. A possible explanation for this is that FCEM primarily affects the gray matter, likely sparing upper motor neuron control and/or the ascending sensory pathways involved in defecation, while ANNPE is associated with a contusive lesion. The presumptive diagnosis is unrelated to motor function recovery, recovery times or urinary incontinence.[3] In comparison, a previous study suggested that dogs with FCEM had a higher prevalence of fecal incontinence in comparison to dogs with ANNPE.[3,9]

Case Outcome

At discharge on January 27, 2021 Cait was non-ambulatory tetraparetic with an overriding right hemiparesis, intact proprioception in the left limbs, delayed in the right thoracic limb and delayed to intermittently absent proprioception in the right pelvic limb. She had improved motor function compared to the time of presentation and was able to right herself to sternal from lateral recumbency. At this time Cait's systemic hypertension was under control. She was sent home with amlodipine (5 mg tabs, 1 tab orally every 24 hours), gabapentin (800 mg tabs, 0.5 tab orally every 12 hours) and galliprant (60 mg tabs, 1 tablet orally every 24 hours as needed for pain). The owner was instructed to have Cait continue physical rehabilitation exercises at-home such as assisted sling-walks with the Help'em up® harness for 2-5 minutes one to three times a day, passive range of motion and flexor exercises among other passive exercises and to continue nursing care. An appointment with Cait's primary veterinarian was recommended the next week to recheck her kidney values, electrolytes, and blood pressures and to formulate a treatment plan for her hyperadrenocorticism disease if indicated at that time. It was also recommended to enroll Cait in out-patient physical therapy a few days a week at the Animal Rehabilitation Center in Flowood, MS as well as following a strict weight loss plan in the hope that she will regain the ability to walk without assistance. It was acknowledged that due to the extent of her neurologic dysfunction, it is possible that she will always exhibit some weakness and incoordination.

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