Progressive Ataxia of Charolais Cattle

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Clinical Pathology Conference

August 18, 2017

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Introduction:

Over the past one hundred years, multiple nervous system abiotrophies have been described in many domestic species. Those animals include horses, cats, dogs, sheep, goats, and cattle. According to Merriam-Webster, an abiotrophy is the degeneration or loss of function or vitality in an organism or in cells or tissues not due to any apparent injury. This definition can be applied to any body system and further sub-classified by anatomical location or structure involved. In the case of progressive ataxia of Charolais cattle, lesions typically occur in the cerebellar medulla and peduncles, and cerebral peduncles.

Progressive ataxia of Charolais cattle was first described in 1972 by Palmer *et al.* in Britain, but has been identified worldwide. Documented cases involve purebred or at least three-quarters Charolais, with both males and females affected (3).

History and presentation:

Clinical signs can begin from six to thirty-six months of age, with signs typically occurring between twelve and twenty-four months (3, 4). Signs vary from hind limb weakness and ataxia leading to subsequent recumbency, or collapse of one hind limb with a tendency to fall to one side. Head bobbing, intention tremors, and irregular, pulsatile micturition in females (3, 6). All signs are commonly exacerbated by excitement of the individuals. However, animals remain bright and alert (5).

On December 16, 2016, a twenty month old, Charolais bull (ear tag #22) was referred to the MSU food animal unit for progressive ataxia. The bull started showing clinical signs two months prior. When stressed or excited, clinical signs started as muscle fasciculations around the face and head which progressed to head and body tremors, abnormal gait, and sometimes sternal

recumbency. The owner reports at least one bull a year in his herd around the same age exhibiting these clinical signs. Previous bulls have been euthanized, but no necropsies or clinical tests were performed. The bull was up to date on routine vaccines (respiratory pathogens, Leptospira, Clostridial). The bull had not previously received any medical treatment.

Physical examination of Bull #22 revealed normal rectal temperature, respiration, and heart rate and rhythm. He was alert and responsive to sights and sounds, although a horizontal nystagmus was present. When encouraged to walk, Bull #22 would take wide, swinging steps with the greatest limb abduction occurring in the hind limbs. Continued pressure to walk or move resulted in head tremoring that was most noticeable when the bull would stop walking. It is important to note that while being unloaded from the trailer the bull fell and became laterally recumbent, but was able to rise on his own.

Diagnostic Approach/Considerations:

Neurologic disease can manifest as a result of diet, toxins, trauma, neoplasia, infectious organisms, and many other etiologies (7). When presented with a neurologic patient, it is best to be systematic and thorough when obtaining a history, physical exam, and neurologic exam. Samples such as cerebrospinal fluid (CSF) and blood are helpful when ruling out infectious or metabolic causes. However, many neurologic disorders are difficult to definitively diagnosis with laboratory testing alone. This is also the case for cattle with suspect progressive ataxia. A presumptive diagnosis of progressive ataxia is made by signalment, clinical signs, and process of elimination. It can only be definitively diagnosed by histopathology as no gross lesions are seen in affected animals (3, 6).

In the case of Bull #22, the presence of nystagmus without a head tilt and normal mentation made the possibility of central vestibular disease less likely on the differential diagnoses list (7). Incoordination and intention tremors exhibited by the patient were indicative of a cerebellar disorder.

With the history provided by the owner and physical exam findings, humane euthanasia was elected and the body sent for necropsy and tissue collection. Pentobarbital was administered intravenously for humane euthanasia to preserve brain tissue pathology. CSF was obtained immediately postmortem and sent for analysis to rule out the possibility of an infectious component.

Gross necropsy of Bull #22 was unremarkable. Sections of brain and spinal cord tissue from Bull #22 were examined by MSU CVM diagnostic laboratory services. There were numerous discrete and occasional coalescing pale, finely granular, eosinophilic, acellular plaques. The plaques had marginal vacuolation of the neuropil, with the most extensive plaques being located in the cerebellar white matter, peduncles, optic tract, cerebral corona radiate, and internal capsule. In the affected tissue, oligodendrocytes were hypertrophic and thin axons that lacked myelin traversed the plaques. No macrophage response was associated with any of the widely distributed white matter plaques. CSF from Bull #22 was within normal limits.

Pathophysiology:

Progressive ataxia is a gradual disorder of oligodendrocyte dysplasia that is restricted to the white matter of the central nervous system, but the inciting cause and mechanism(s) of the condition are unknown (2, 5). The lesions and their locations, however, are well described.

Lesions consist of focal areas of demyelination referred to as plaques (3, 4). These focal areas are comprised of paranodal clumps where myelin sheaths originating from glial cells are distended. Unmyelinated axons traverse these plaques which are frequently located throughout the spinal cord ventral and lateral funiculi, cerebellar medulla and peduncles, transverse fibers of pons, cerebral internal capsule, and the corpus callosum (3, 4, 5). Based on cases seen elsewhere, lesions are less frequently found in the optic tracts, pontile decussation, and medial longitudinal fasciculus (3). Severely affected areas are said to be arranged like a string of beads. Plaques are pale, eosinophilic, and faintly granular often with a central clump of Luxol fast blue granules, and traversed by axons bearing little or no myelin even though there tend to be areas well myelinated nearby (3, 5).

In the case of Bull #22, plaques were most prominently seen in the cerebral internal capsule, optic tract, and cerebellar medulla. Plaques in the cerebellar white matter and peduncles were often coalescent resulting in very large areas being affected. The medial longitudinal fasciculus in the brainstem was moderately affected. However, significant plaques were in the corona radiata of the cerebrum and the internal capsule. The plaques were traversed by axons devoid of myelin. The nodes of Ranvier were expanded by abnormally formed paranodes.

Blakemore et al. demonstrated that the foci consists of several axons whose paranodal sheaths are distended by hypertrophied oligodendrocytic lateral tongues. There is a widening of nodes and a failure to ensheath adnodal axons as they extend longitudinally. It is thought that this ensheathment failure and widening of nodes of Ranvier interferes with normal tight junctions (2, 3). Progressive widening of nodes disrupts saltatory conduction, which likely results in the delayed or uncoordinated nerve impulses.

The dysplasia does not appear to be a primary defect in myelin synthesis. The hypertrophic oligodendrocytes resemble immature oligodendrocytes of active myelination (2, 3, 6). It has been purposed that an inability to switch off the proliferation of fine processes leads to continual activity, due to the high metabolic activity demonstrated by these cells (2). This would explain the late onset and progressive nature of the disease.

Treatment/management:

Currently, there is no cure for progressive ataxia. Any treatments that exist are palliative. It is recommended that affected animals be euthanized or culled as the prognosis is poor to grave (1).

Due to the potential heritability of progressive ataxia in Charolais cattle, herd breeding and calving records should be kept to allow for identification of dams and/or sires that produce offspring that develop this condition.

Case Outcome:

Histopathology provided confirmation of progressive ataxia.

References:

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