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Case Report

Cerebellar Abiotrophy in Nelore: First Report in Zebu Cattle (*Bos taurus indicus*)

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Abstract

Cerebellar abiotrophy (CA) is a degenerative disorder of the central nervous system (CNS) that has been reported in humans and animals. In cattle, CA had been reported in *Bos taurus taurus* and crossbreed cattle. CA is characterized by degeneration and loss of Purkinje cells and decrease in the population of granule cells. The pathogenesis of this process is unknown, but it is believed that there is an autosomal recessive heritable factor involved. A 15-month-old Nelore ox (*Bos taurus indicus*) was sent to a slaughterhouse, where it presented cerebellar ataxia, symmetrical hypermetria, spasticity, ptyalism, and incoordination. There were no macroscopic changes. CNS samples were negative for BSE, rabies, and other infectious pathogens. Microscopically, there was atrophy of the molecular, granular, and Purkinje cell layers of the cerebellar cortex, and a marked and diffuse loss of the Purkinje cells. No other microscopic lesions were observed in CNS. These findings were consistent with cerebellar abiotrophy. To the best of our knowledge, no cases of CA have ever been reported in *Bos taurus indicus*. Therefore, the present case of CA in Nelore is the first report of the disease in Zebu cattle.

Key Words: Cerebellar cortical abiotrophy, cerebellum, *Bos taurus indicus*.

Introduction

Cerebellar abiotrophy (CA) is a degenerative disorder of the central nervous system that has been reported in humans and animals. CA is the most common manifestation of abiotrophy in domestic animals, and it is also referred to as cerebellar cortical abiotrophy (8). In domestic animals, CA has been reported in cattle, horse, dog, cat, sheep and pig (1, 2, 3, 7, 9, 10, 11, 12, 13, 14, 15, 17, 19, 21, 24, 25, 26). In addition, CA has also been diagnosed in nonhuman primates, laboratory mice and exotic animals (18, 23). In cattle, CA has been described in Holstein, Angus, Ayrshire, Shorthorn, Hereford, Charolais, Aquitanica and *Bos taurus taurus* crossbred cattle (7, 14, 16, 17, 20, 25, 26), but not in Zebu cattle (*Bos taurus indicus*). CA is characterized by degeneration and loss of Purkinje cells and decrease in the population of granule cells (23). The integrity of the granule cell neurons is dependent on its synaptic relationship with the dendritic zone of the Purkinje neurons, therefore, loss of these neurons usually results in a secondary depletion of granule cells (6). The pathogenesis of this process is unknown, however it is believed that there is a autosomal recessive heritable factor involved (4, 5, 9, 10, 22).

Case Report

A 15-month-old ***Nelore ox* (Bos taurus indicus)** was sent to a slaughterhouse in Presidente Olegário (State of Minas Gerais, Brazil), where it presented cerebellar ataxia with head tremor, symmetrical hypermetria, spasticity, ptyalism, and

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incoordination. The ox was slaughtered and no macroscopic changes were observed in the central nervous system (CNS) or elsewhere. The CNS was collected by a veterinarian belonging to the official inspection service, and sent to the official diagnostic laboratory. CNS samples were negative for rabies by immunofluorescence and inoculation in mice; negative for BSE by histopathology and immunohistochemistry; and PCR (polymerase chain reaction) negative for bovine herpesvirus type-5, bovine herpesvirus type-1, ovine herpesvirus type-2, swine herpesvirus type-1, *Listeria monocytogenes*, and *Histophilus somni*. Microscopically, there was atrophy of the molecular, granular, and Purkinje cell layers of the cerebellar cortex. There was also a marked and diffuse loss of the Purkinje cells, with moderate attenuation and astrogliosis of the molecular cell layer, and depletion of granule cells, with marked thinning of granular cell layer, which contained degenerative Purkinje cells. The remaining Purkinje cells were either shrunken and hyperchromatic or swollen and pale with cytoplasmic vacuolization, often exhibiting central chromatolysis, with peripheral displacement of Nissl substance. No other lesions were observed in any other area of the CNS (i.e. cerebrum, thalamus and brainstem). These microscopic findings were consistent with cerebellar abiotrophy (Figure 1-3).

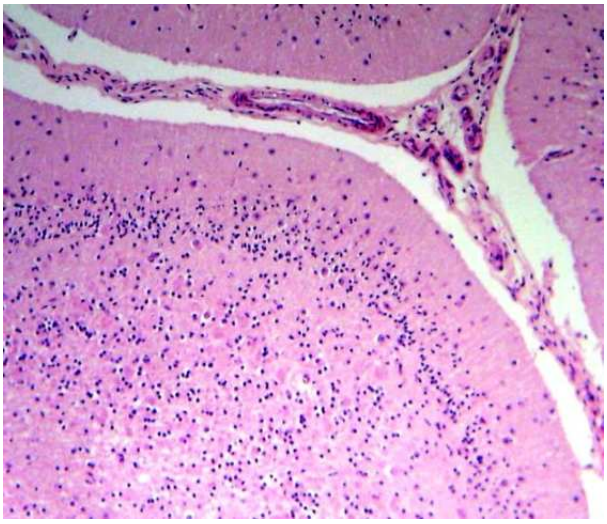


Figure 1. Cerebellum, ox. Cerebellar cortex with atrophy of molecular, granular, and Purkinje cell layers. Marked and diffuse loss of the Purkinje cell layer, with moderate attenuation and astrogliosis of the molecular cell layer (H&E, 10x).

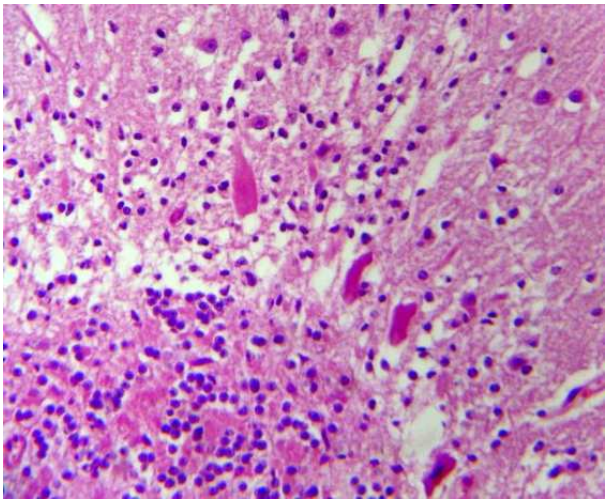


Figure 2. Cerebellum, ox. Remaining Purkinje cells are shrunken and hyperchromatic, with moderate attenuation and astrogliosis of the molecular cell layer. (H&E, 40x).

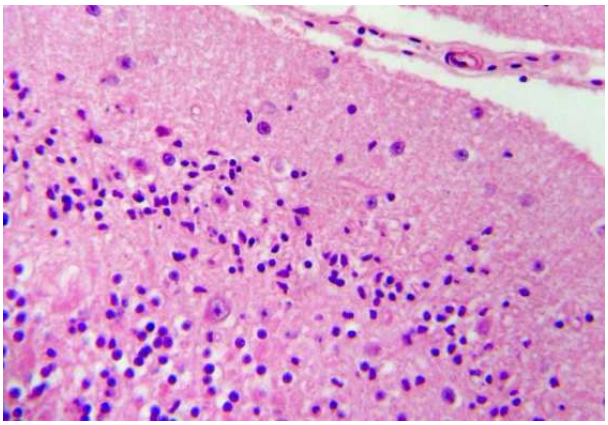


Figure 3. Cerebellum, ox. Depletion of granule cells, with marked thinning of the granular cell layer (H&E, 40x).

Discussion

The progressive degeneration and loss of cerebellar cortical neurons that occurs in CA usually results in clinical changes in young patients, i.e. during early stages of life. Therefore, the affected animal is normal at birth and develops progressive cerebellar deficits during the postnatal period (7). In this case, there was no record of clinical signs prior to slaughter. The clinical manifestations of CA are cerebellar ataxia characterized by head tremor, symmetrical hypermetria, spasticity, broad-based stance, and loss of balance, similar to that observed in this case. The cerebellum is grossly normal, and microscopic changes do not have an uniform distribution. These changes usually develop first in the vermis and paramedian lobules and then spread to the lateral lobules (23).

The cause of CA is unknown, however is presumed to be an intrinsic metabolic effect related to inherited recessive genetic defect (7). One hypothesis involves excytotoxic degeneration of neurons that have glutamate receptors and receive axon terminals with

glutamate as the excitatory transmitter (7). Excessive glutamate stimulation could cause degeneration of the neuron. Possible explanations for excessive glutamate stimulation include excessive glutamate release, decreased glutamate uptake and clearance, or increased glutamate receptor sensitivity (7).

CA must be differentiated from multisystemic neuronal abiotrophy and cerebellar hypoplasia. In multisystemic neuronal abiotrophy, neuropathological changes develop during early to middle adulthood. In this disease, there is usually a concurrent degeneration of other neuronal populations (cerebellar, brain stem, and spinal forms), and it is a rare condition in the veterinary medicine (23). Cerebellar hypoplasia is one of the most common congenital anomalies in cattle. It can occur sporadically or be caused by viral infections such as the bovine viral diarrhea virus (BVD), bluetongue virus, and Akabane virus. In the Shorthorn breed there is evidence that the disease is hereditary. Clinically, the disease is characterized by the birth of animals with tremors, incoordination and hypermetria, but in contrast to CA, clinical signs are not progressive (20).

CA have been described in most domestic animal species, including dog, cattle, sheep, horse, pig, and cat (7). It has also been reported in nonhuman primates, laboratory mice, and exotic animal species (18, 23). Most CA reports in domestic animals involve dogs. Canine CA was first reported in the Kerry Blue Terrier, in which it has been characterized as an autosomal recessive heritable disease (9). Other canine breeds also have heritable CA, including Gordon Setters (10), Rough-coated Collies (12), Border Collies (20) and Australian Kelpies (22, 24). CA has also been diagnosed in Boxers (11), Schnauzers (2), Beagles (15), Airedale Terriers, Finnish Harriers, Bernese Mountain Dogs, Miniature Poodles, Brittany Spaniels, Cocker Spaniels, Labrador Retrievers, Golden Retrievers, and Great Danes (7). CA is uncommon in cats when compared to dogs (1, 3, 7, 19). In horses, CA has been described in the Swedish Gotland Pony, and Arabian or Part-arabian foals. Equine CA has been characterized as an autosomal recessive heritable disease, a possible mutation (4) that is linked to the Arabian ancestry (5, 23). In Yorkshire pigs, CA has also been diagnosed, appearing between the fourth and fifth weeks of live (23). In sheep, a genetic cause for CA with putative inheritance as an autosomal recessive trait has been reported in Wiltshire sheep (13).

There are several reports of CA in cattle, especially in *Bos taurus taurus*, mainly affecting Aberdeen Angus and Holstein (14, 16, 17, 25, 20, 26). In cattle, it is presumed that CA is inherited as an autosomal dominant disorder with incomplete penetrance. In Brazil, CA has been described in Holstein (20) and Aquitanica (16). To the best of our knowledge, no cases of CA have ever been reported affecting *Bos taurus indicus*. Therefore, the present case of CA in Nelore is the first report of the disease in Zebu cattle. In this case, the ox belonged to a dealer, and there was no information available concerning its genetic background. Therefore, it was impossible to verify any pattern of genetic inheritance. Yet, this is an important report since it demonstrates for the first time that Zebu cattle are also affected by CA.

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References

1. BARONE G., FOUREMAN P., DELAHUNTA A. Adult-onset cerebellar cortical abiotrophy and retinal degeneration in a domestic shorthair cat. J. Am. Anim. Hosp. Assoc., 2002, 38(1), 51-54.

2. BERRY ML., BLAS-MACHADO U. Cerebellar abiotrophy in a miniature schnauzer. Can. Vet. J., 2003, 44(8), 657-659.

3. BIOLATTI C., GIANELLA P., CAPUCCHIO MT., BORRELLI A., D'ANGELO A. Late onset and rapid progression of cerebellar abiotrophy in a domestic shorthair cat. J. Small Anim. Pract., 2010, 51(2), 123-126.

4. BRAULT LS., COOPER CA., FAMULA TR., MURRAY JD., PENEDO MC. Mapping of equine cerebellar abiotrophy to ECA2 and identification of a potential causative mutation affecting expression of MUTYH. Genomics, 2011, 97(2), 121-129.

5. BRAULT LS., PENEDO MC. The frequency of the equine cerebellar abiotrophy mutation in non-Arabian horse breeds. Equine Vet. J., 2011. In press.

6. CHEN S., HILLMAN DE. Regulation of granule cell number by predeterminant number of Purkinje cells in development. Dev. Brain. Res., 1989, 45, 137-147.

7. DE LAHUNTA A. Abiotrophy in domestic animals: A review. Can. J. Vet. Res., 1990, 54, 65-76.

8. DE LAHUNTA A. Comparative cerebellar disease in domestic animals. Compend. Contin. Educ., 1980, 2, 8-19.

9. DE LAHUNTA A., AVERILL DR. JR. Hereditary cerebellar cortical and extrapyramidal nuclear abiotrophy in Kerry Blue Terriers. J. Am. Vet. Med. Assoc., 1976, 168(12), 1119-1124.

10. DE LAHUNTA A., FENNER WR., INDRIERI RJ., MELLICK PW., GARDNER S., BELL JS. Hereditary cerebellar cortical abiotrophy in the Gordon setter. J Am. Vet. Med. Assoc., 1980, 177, 538-541.

11. GUMBER S., CHO DY., MORGAN TW. Late onset of cerebellar abiotrophy in a boxer dog. Vet. Med. Int., 2010. (in press)

12. HARTLEY WJ., BARKER JSF., WANNER RA., FARROW BR. Inherited cerebellar degeneration in the rough coated collie. Aust. Vet. Pract., 1978, 8, 79-85.

13. JOHNSTONE AC., JOHNSON CB., MALCOLM KE., JOLLY RD. Cerebellar cortical abiotrophy in Wiltshire sheep. N. Z. Vet. J., 2005, 53(4), 242-245.

14. KEMP J., MCORIST S., JEFFREY M. Cerebellar abiotrophy in Holstein Friesian calves. Vet. Rec., 1995, 136(8), 198.

15. KENT M., GLASS E., DELAHUNTA A. Cerebellar cortical abiotrophy in a beagle. J. Small Anim. Pract., 2000, 41(7), 321-323.

16. MACÊDO JTSA., LUCENA RB., GIARETTA PR., KOMMERS GD., FIGHERA RA., IRIGOYEN LF., BARROS CSL. Defeitos congênitos em bovinos da Região Central do Rio Grande do Sul. Pesq. Vet. Bras., 2011, 31(4), 297-306.

17. MITCHELL PJ., REILLY W., HARPER PA., MCCAUGHAN CJ. Cerebellar abiotrophy in Angus cattle. Aust. Vet. J., 1993, 70(2), 67-68.

18. MOUSER P., LÉVY M., SOJKA JE., RAMOS-VARA JA. Cerebellar abiotrophy in an alpaca (*Lama pacos*). Vet Pathol., 2009, 46(6), 1133-1137.

19. NEGRIN A., BERNARDINI M., BAUMGÄRTNER W., CASTAGNARO M. Late onset cerebellar degeneration in a middle-aged cat. J. Feline Med. Surg., 2006, 8(6), 424-429.

20. RIET-CORREA F., SCHILD AL., FERNANDES, CG. Enfermidades do sistema nervoso dos ruminantes no sul do Rio Grande do Sul. Cienc. Rural, 1998, 28(2), 341-348.

21. SANDY JR., SLOCOMBE RE., MITTEN RW., JEDWAB D. Cerebellar abiotrophy in a family of Border Collie dogs. Vet. Pathol., 2002, 39(6), 736-738.

22. SHEARMAN JR., LAU VM., WILTON AN. Elimination of SETX, SYNE1 and ATCAY as the cause of cerebellar abiotrophy in Australian Kelpies. Anim. Genet., 2008, 39(5), 573.

23. SUMMERS BA., CUMMINGS JF., DE LAHUNTA A. Degenerative diseases of the central nervous system. In: Veterinary Neuropathology. 1st Ed, St. Louis, Mosby-Year Book, 1994, 300-307.

24. THOMAS JB., ROBERTSON D. Hereditary cerebellar abiotrophy in Australian kelpie dogs. Aust. Vet. J., 1989, 66, 301-302.

25. WHITE ME., WHITLOCK RH., LAHUNTA A. A cerebellar abiotrophy of calves. Cornell Vet., 1975, 65(4), 476-491.

26. WHITTINGTON RJ., MORTON AG., KENNEDY DJ. Cerebellar abiotrophy in crossbred cattle. Aust. Vet. J., 1989, 66(1), 12-15.

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