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Congenital Cerebellar Cortical Degeneration in Holstein Cattle in Southern Brazil

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ABSTRACT

A congenital progressive cerebellar disorder is described in Holstein calves. The clinical signs were progressive and were characterized by ataxia, hypermetria, a wide stance and fine head tremors. When the affected cattle were forced to run, the signs were exacerbated, leading to epileptiform attacks. Histological lesions consisted of a very selective cerebellar cortical degeneration, almost exclusively affecting the Purkinje cells. The disease affected 6 out of 200 Holstein calves from the same bull. However, results of mating tests of the bull with his daughters and granddaughters suggested that it was not hereditary ($p = 0.0062$) although an environmental–genetic interaction could not be ruled out.

Keywords: cattle, cerebellar degeneration, cerebellum, genetics, histopathology, neurology, Purkinje cells

Abbreviations: BFCA, bovine familial convulsion and ataxia; BVDV, bovine viral diarrhoea virus; CNS, central nervous system; GFAP, glial fibrillary acidic protein; LFB, Luxol fast blue

INTRODUCTION

Cerebellar defects, including cerebellar degeneration and cerebellar abiotrophy are among the most common neurological disorders of domestic animals (Jubb and Huxtable, 1993; Whittington *et al.*, 1989). In Rio Grande do Sul, southern Brazil, cerebellar disorders in cattle include cerebellar hypoplasia, probably due to infection with BVDV (Riet-Correa *et al.*, 1998), hereditary hypermetria, a non-progressive condition characterized by cerebellar signs, with no recorded histological or ultrastructural abnormalities (Schild *et al.*, 1993), and intoxication with *Solanum fastigiatum*, which causes postnatal degeneration of Purkinje cells, mainly in adult cattle (Riet-Correa *et al.*, 1983). We describe an outbreak of a novel progressive cerebellar disease in calves, characterized by progressive Purkinje cell degeneration.

MATERIALS AND METHODS

Cerebellar cortical degeneration was observed in 6 out of 200 Holstein calves (2 males and 4 females) born in a 2-year period. The farm was located near a coal combustion electric power plant. All the cows in the herd were inseminated with semen from a Holstein bull (SS Bagda Remo) from an artificial insemination station. Semen from this source had previously been used in many Holstein herds in the state, apparently producing normal calves.

One affected 3-month-old calf was anaesthetized, killed by exsanguination and necropsied. Samples of all its organs and the CNS, including the cerebral cortex, internal capsule, caudate nucleus, thalamus, rostral and caudal colliculi, pons, medulla oblongata and cerebellum (caudal vermis, flocculus, nodulus, rostral vermis, hemispheres and regions of fastigial, interposital and lateral cerebellar nucleus), were fixed in buffered neutral 10% formalin, embedded in paraffin, sectioned at 6 μm, and stained with haematoxylin and eosin for histological study. Sections of CNS were also stained with LFB for myelin and with Sanvier–Munger for axons.

For genetic studies, the semen of the bull suspected of transmitting the disease was used to inseminate 8 of his daughters over a 3-year mating period. Twenty-three calves, 9 males and 14 females, were born from these matings. Seven of the females were later inseminated over two years with the same semen and 13 calves (6 males and 7 females) were born. These mating tests were performed at the experimental station of the Veterinary School. The probability of the birth of unaffected calves from a bull that carries a recessive trait was calculated, given that the probability of non-expression of a recessive trait in a mate with each daughter is 0.875 and in a mate with each granddaughter is 0.857.

RESULTS

All the calves were affected at birth and five of them died at about 6 months of age from misadventures related to the clinical signs, such as fractures and drowning, or from unrelated causes. The clinical signs were progressive and were characterized by ataxia, hypermetria (Figure 1), a wide stance and fine head tremors. When the affected calves were forced to run, the signs were exacerbated, leading to epileptiform attacks with ataxic gait and collapse with opisthotonus and spontaneous nystagmus, which lasted from one to several minutes.

Macroscopically, no abnormalities were detected in the CNS or other organs and there was no obvious gross reduction in the size of the cerebellum. Histological lesions consisted of a very selective cerebellar cortical degeneration, almost exclusively affecting Purkinje cells, without evidence of inflammation. The changes were widespread in the cerebellum and affected a proportion of the Purkinje cells in every folium. Degenerate Purkinje cells had pale-staining cytoplasm, or were vacuolated, swollen (Figure 2) and chromatolytic, with displaced nuclei. In Sanvier–Munger stained sections, empty baskets lacking Purkinje cell bodies were seen in the Purkinje cell layer. Axonal torpedoes were detected in the granular layer (Figure 3) and were

Figure 1. Affected calf with ataxic gait and hypermetria

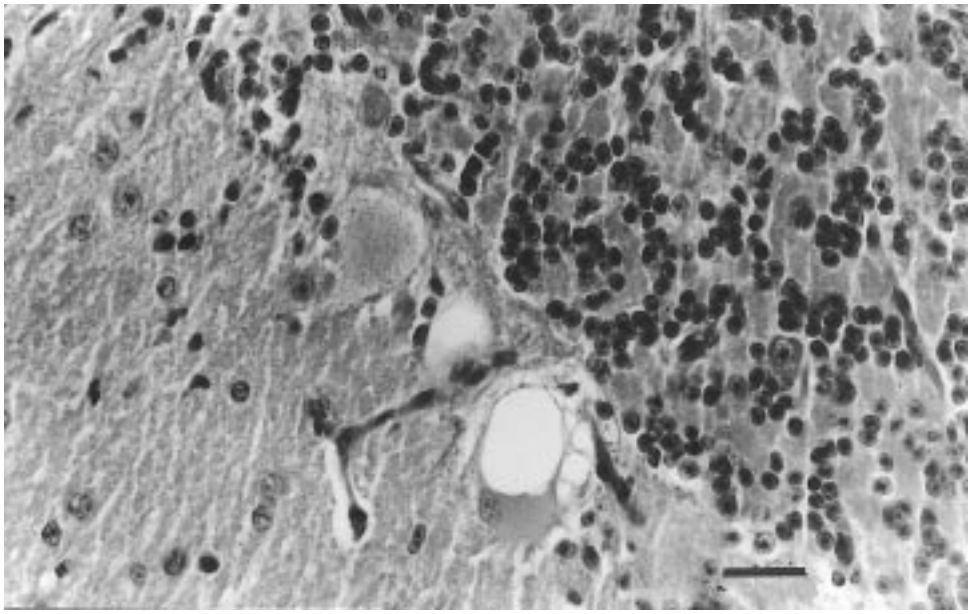

Figure 2. Cerebellum. Swollen and vacuolated Purkinje cell with displaced nucleus.
H&E; bar = 35 μm

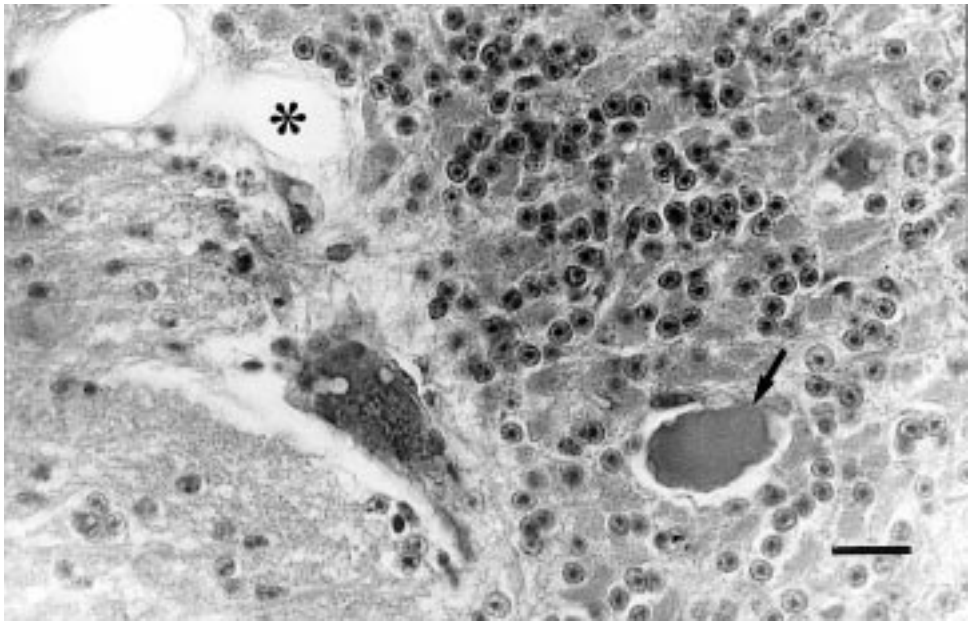

Figure 3. Cerebellum. Axonal torpedo (arrow) and empty basket of a degenerate Purkinje cell. (*) H&E ; bar = 35 μm

sometimes traced up to the axon hillocks of the Purkinje cells. Morphologically normal Purkinje cells were also observed. Mild vacuolation of the Purkinje cell dendrites in the molecular layer was observed (Figure 4). Mild Wallerian degeneration and occasional axonal spheroids were detected in the white matter of the cerebellar folia. In LFB-stained sections, the white matter was pale, indicating loss of myelin density. The stellate and basket cells in the molecular layer and the Golgi cells in the granular layer, cerebellar nuclei and other regions of the CNS were normal.

None of the 27 calves resulting from the test matings showed any clinical signs of the disease. Nine were stillborn or died soon after delivery but had no histological lesions in the cerebellum. The probability of the disease being hereditary was 0.0062 ($p = 0.875^{23} \times 0.857^{13}$).

DISCUSSION

The clinical signs in the affected calves in this report were similar to those described for BFCA in Angus cattle (Barlow *et al.*, 1968) and for cerebellar abiotrophy in Holstein, Charolais and Polled Herefords (White *et al.*, 1975; Cho and Leipold, 1978; Whittington *et al.*, 1989; Kemp *et al.*, 1995), although some differences were noted.

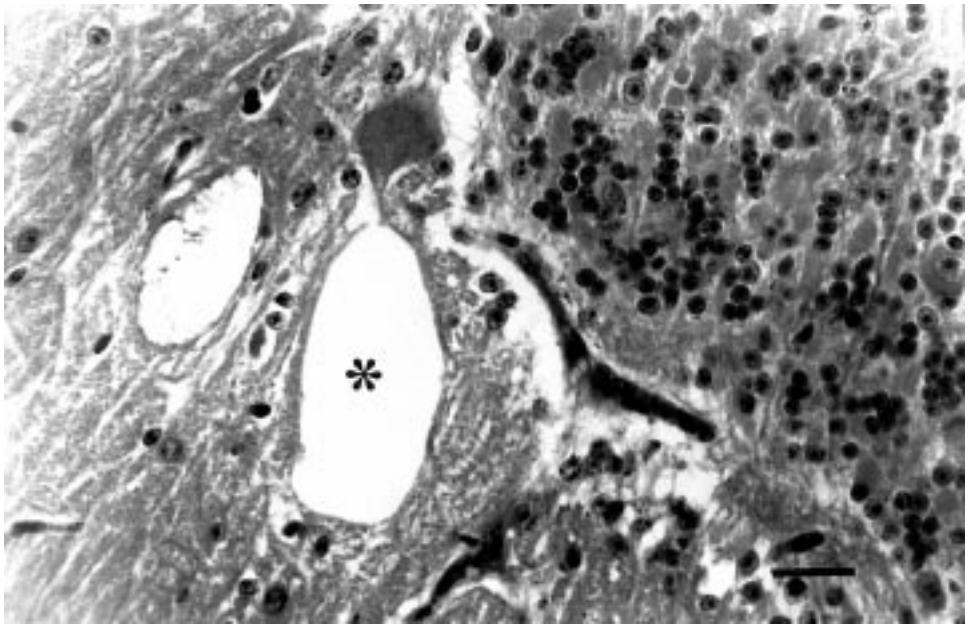

Figure 4. Cerebellum. Purkinje cell with dendrite vacuolation in the molecular layer. (*) H&E ; bar = 35 μm

The clinical signs were always observed at birth in the calves we studied, which is uncommon in most abiotrophies (de Lahunta, 1990; Summers *et al.*, 1995). Nevertheless, clinical signs presenting at birth or within the first 24 h have been described for some of the affected crossbred Polled Hereford calves (Whittington *et al.*, 1989), in BFCA of Angus cattle (Barlow, 1981) and in cerebellar abiotrophy of Holstein-Friesian calves (Kemp *et al.*, 1995). The epileptiform seizures that we observed are also uncommon in these diseases, but had been reported in BFCA in Angus cattle (Barlow, 1981), and in a Charolais calf (Cho and Leipold, 1978). Nevertheless, in these breeds, this clinical sign apparently waned, resulting in a residual ataxia.

A congenital progressive cerebellar disorder in calves raises several differential diagnoses. BVDV can affect the developing CNS, resulting in cerebellar hypoplasia and degeneration. Clinical signs are present at birth but, typically, the cerebellum is obviously small in size. Furthermore, BVDV infection produces white-matter cavitation (Brown *et al.*, 1974; Kahrs *et al.*, 1979), quite different from what was observed in the case concerned in this report. Cerebellar abiotrophies may be evident at or soon after birth and the deficits are progressive (de Lahunta, 1990; Summers *et al.*, 1995). However, the neuropathological features are characterized by the progressive loss of Purkinje neurons rather than the presence of numerous degenerate Purkinje cells, an associated loss of granule neurons and a narrowing of the molecular layer in some folia

of the cerebellum (Summers *et al.*, 1995). Typically, these changes are not widespread until the degeneration is advanced.

The cerebellar cortical degeneration in our calf is somewhat reminiscent of the cerebellar syndrome induced by *Solanum fastigiatum* (Riet-Correa *et al.*, 1983). Ingestion of this plant results in progressive Purkinje cell degeneration, torpedoes, spheroids in the cerebellar folial white matter and associated gliosis. Purkinje cell changes are distinguished by progressive cytoplasmic vacuolation (Riet-Correa *et al.*, 1983). It is possible that exposure to a toxic substance *in utero* produced the congenital lesion in our calves. In this regard, it may be relevant that the farm was located near a thermoelectric coal plant. However, the farm was also populated with Hereford cattle, which remained unaffected.

The aetiology of the disease described here is still uncertain. Affected calves were all from a Holstein herd on a farm where the population of Herefords was twice that of Holsteins and ataxic calves occurred only in the Holstein breed. The use of the semen from the SS Bagda Remo bull was discontinued on the affected farm after the birth of the calves of this report and no additional affected calves have been born since then. The mating tests were performed at the experimental station of the Veterinary School, away from the site where affected calves were born. Hence, although the results of mating tests suggest that a genetic malfunction is not involved, this cannot be totally excluded since an environmental–genetic interaction can be an important factor in the expression of undesirable genes, especially when there is incomplete penetrance (Leipold and Dennis, 1980).

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