Cerebellar Cortical Degeneration in Beagle Dogs

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Cerebellar disorders characterized by degeneration or loss of Purkinje cells have been reported in many species. In the dog, they have occurred in Airedales, Gordon setters, rough coated collies, border collies, beagles, Samoyeds, and Irish setters.

An 18-month-old female and a 9-month-old male were mated in our beagle colony. The female was purchased from Marshall Farms, North Rose, New York. The male was bred in our colony. Both had been on a complete vaccination program and were clinically normal. The dam delivered eight pups—three males and five females—on June 13, 1985. Two males and one female died within a day after birth. Of the remaining five pups, one male (case 1) and two females (cases 2 and 3) developed neurological signs first noted as frequent falling when the dogs became ambulatory at about 3 weeks of age. Signs slowly progressed without improvement until euthanasia at 14 weeks of age. The other two female littermates grew normally without neurological deficits.

At necropsy, tissues were fixed in 10% phosphate buffered formalin. Cerebrum and brain stem were sectioned coronally; cerebellum was sectioned sagittally through the vermis and transversely through the left hemisphere. Tissues were embedded in paraffin, sectioned, and stained with hematoxylin and eosin (HE). In the cerebellum, the following stains were also applied: Bodian, luxol fast blue (LFB), and, for glial fibrillary acidic protein (GFAP), an avidin-biotin immuno-

Fig. 1. Cerebellar vermis, case 2. Folia are thin, sulci widened. HE.
Fig. 2. Higher magnification of Fig. 1. Most Purkinje cells are lost, granular cells decreased in number.
Fig. 3. Cerebellar vermis, case 2. Purkinje cells are lost, leaving empty baskets. Bodian.
Fig. 4. Cerebellar hemisphere, case 2. Bergmann astrocytes with stained glial fibers increased in Purkinje cell layer. Immunohistochemical staining for glial fibrillary acidic protein (GFAP). Counter-stained with hematoxylin.
Fig. 5. Cerebellar vermis, case 2. Purkinje cells, degeneration with chromatolysis and marginal displacement of nuclei. HE.
Fig. 6. Cerebellar vermis, case 2. Purkinje cells decreased in number, granular cells relatively well preserved. Axonal torpedoes in granular layer. Bodian.

Fig. 7. Cerebellar hemisphere, case 2. Purkinje cells totally absent, considerable loss of basket fibers. Granular layer sparsely populated, molecular layer reduced in thickness. Bodian.

peroxidase staining kit (BioGenex Laboratories, Dublin, CA). Cerebellar sections from a normal male and female of corresponding ages were similarly prepared (controls).

Macroscopically, the cerebellum was smaller than normal and somewhat flattened in all three cases. No abnormalities were seen in other organs. Microscopical lesions were confined to the cerebellum and not detected in other parts of the central nervous system, peripheral nerves, and visceral organs.

Cerebellar lesions were consistent in three dogs, though varying in intensity. The folia were thin and the sulci widened (Fig. 1). The molecular layer was reduced in thickness with marked rarefaction of the neuropil. Purkinje cells were reduced in number (Fig. 2) and almost totally lost in the severely affected folium. The granular layer was also reduced in thickness with decreased granular cell population (Fig. 2). In sections stained with Bodian, empty baskets were in the Purkinje cell layer lacking Purkinje cell bodies (Fig. 3). Tangential fibers were generally well preserved. In severely involved areas, however, tangential and basket fibers as well as Purkinje cells also disappeared. Bergmann astrocytes, having pale, round to oval nuclei, were increased in number where Purkinje cell loss was advanced (Fig. 4). In sections stained immunohistochemically for GFAP, positively stained glial fibers were increased (Fig. 4). Occasionally, proliferating glial fibers surrounded necrotic Purkinje cells. The remaining Purkinje cells were atrophic or showed chromatolysis and marginal displacement of nuclei (Fig. 5). Some were necrotic, with shrinkage, pyknosis of nuclei, and eosinophilic cytoplasm. Purkinje cell dendrites radiating to the molecular layer were swollen and more prominent than those in age-matched controls. Some swollen dendrites were found as fusiform or spheroidal bodies in the molecular layer. Axonal torpedoes were in the granular layer. They were eosinophilic in HE and argentophilic in Bodian staining. Some were found to arise from axon hillocks of Purkinje cells.

Purkinje cell loss showed a regional predilection. The cerebellar hemisphere was most severely affected, followed by tip parts of the culmen and declive of the vermis in all cases. In the cerebellar hemisphere, the majority of Purkinje cells were absent from all folia with concomitant changes of molecular and granular layers in all cases. In the vermis, Purkinje cell loss was confined to the culmen and declive in case 1, while it spread rostrally and caudally to other lobules in cases 2 and 3. In an affected folium, Purkinje cell loss apparently started at the tip and extended to the depths.

There was a relationship between degree of Purkinje cell degeneration and severity of lesions in the molecular and granular layers. In the region where Purkinje cells degenerated but neuronal loss was not apparent, granular cells were relatively well preserved with numerous axonal torpedoes. In the region where Purkinje cells disappeared leaving empty baskets, granular cells were relatively well preserved and axonal torpedoes were less numerous (Fig. 6). In the severely affected region where basket and tangential fibers as well as Purkinje cells were lost, molecular and granular layers were markedly affected (Fig. 7). The granular layer was sparsely populated with distortion of the normal cluster arrangement of granular cells (Fig. 7). Occasionally, granular cells were karyopyknotic.

Stellate and basket cells in the molecular layer and Golgi cells in the granular layer appeared normal. There was no alteration in cellularity of the molecular layer. The external granular layer had entirely disappeared. No abnormalities were seen in the meninges or blood vessels.

In LFB-stained sections, the laminae medullares showed pallor of myelin, especially where the neighboring cortex revealed advanced degeneration. Cerebellar nuclei were entirely normal, except that some neurons showed acute swelling with swollen cell body and marginal displacement of nuclei indicating central chromatolysis.

Lesions characterizing the present beagles were extensive.
Degeneration to loss of Purkinje cells. In the Purkinje cell layer where neurons were lost, there were empty baskets. Degenerate Purkinje cells were accompanied by axonal torpedoes in the granular layer. The empty baskets indicate Purkinje cell loss normally developed, while axonal torpedoes are a nonspecific sign of Purkinje cell degeneration and not a consequence of developmental failure. Thus, Purkinje cell degeneration in the present cases may have occurred after they attained normal development and reached the proper location.

In the present cases, there was a relationship between degree of Purkinje cell degeneration and severity of granular cell diminution. This suggests that granular cell alteration was secondary to Purkinje cell degeneration.

Granular cells are formed from the external germinal layer later in gestation than Purkinje cells, and their formation is not complete until the postnatal period. Investigation of cerebellar mutant mice suggested that there was an interaction between Purkinje cells and the external granular layer, i.e., the number of granular cells formed was appropriate to the number of Purkinje cells nearby. In the present dogs, development of granular cells might have been disturbed by degeneration or loss of Purkinje cells. Thus, the hypoplastic process might have contributed to development of the present granular cell lesions.

Early regressive changes found in the cerebellar nucleus neurons are regarded as transsynaptic degeneration after the Purkinje cell damage. Involvement of the cerebellar nuclei has been described in Airedale dogs.

The pathological features of the present cases were degeneration or loss of normally developed Purkinje cells and ensuing granular cell lesion. Thus, cerebellar cortical degeneration seems appropriate descriptive terminology for the present beagles.

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References


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Cerebral Infarction with Associated Venous Thrombosis in a Dog

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Occlusive cerebrovascular diseases with infarction are rare in domestic animals when compared to their frequency in humans. Previously reported canine cases involved the cerebral arterial system and resulted from bacteria-associated thrombosis and embolism, marrow emboli after trauma and/or fractures of bones, microfilarial emboli, neoplastic emboli, and rarely, atherosclerosis. The present case is of spontaneous cerebral venous thrombosis in a dog with clinical signs and histologic lesions compatible with hemorrhagic infarction.

A 10-year-old mixed breed obese female crossbred dog with a history of peracute onset of seizures had left-sided hemiparesis and compulsive walking with circling to the right. There was no direct or consensual pupillary light reflex in the left eye. Reflexes of the right eye were slow, but vision appeared to be normal. The dog resisted having its head turned to the left. No head tilt was observed. There was no evidence of head trauma. Hematologic findings were consistent with a stress leukogram. Blood urea nitrogen, glucose, alkaline phosphatase, alanine aminotransferase, and am-