Cerebellar Cortical Atrophy in a Kitten


Key words: Cats; cerebellar atrophy.

Cerebellar ataxia characterized histologically by degeneration or disappearance of Purkinje cells has been frequently reported in humans and several other species of animals. In the cat, cerebellar ataxia is frequently caused by congenital or postnatal infection with feline panleukopenia virus. In addition, a few hereditary diseases of neuroaxonal dystrophy and olivopontocerebellar atrophy have been reported. In this report, we describe the histopathology of primary cerebellar cortical atrophy in a cat and discuss the histogenesis of cerebellar lesions.

A 3-month-old mixed-breed female cat was clinically diagnosed as having progressive cerebellar ataxia. After the age of 6 weeks, the cat gradually developed neurologic signs characterized by unsteady hind legs, motor incoordination, dis-equilibrium, and tremors. Her mother and three littermates were normal. In the serologic hemagglutination inhibition (HI) tests for feline panleukopenia virus (FPV), feline infectious peritonitis virus (FIPV), and feline leukemia virus (FeLV), the antibody titers were less than 1:4. The clinical condition slowly worsened. At 3 months of age, the cat was euthanatized under anesthesia and immediately necropsied. Tissue samples were collected from the liver, spleen, kidneys, heart, lungs, pancreas, digestive tracts, urogenital tracts, eyes, spinal cord, and peripheral nervous system and fixed in 10% neutral buffered formalin. The brain was fixed by intracarotid injection of a 4% phosphate-buffered paraformaldehyde solution.

At necropsy, the cerebellum was slightly atrophied. There were no significant gross changes in the brain, spinal cord, or other visceral organs. Histologically, no significant changes were detected in the central and peripheral nervous systems or visceral organs except the cerebellum.

The most characteristic lesions in the cerebellum were the symmetrical degeneration or disappearance of Purkinje cells (Fig. 1) and proliferation of Bergmann glia in the Purkinje cell layer (Fig. 3). These lesions involved the entire cerebellum. The degeneration of Purkinje cells was evident from atrophy, central or marginal chromatolysis, shrinkage and increased eosinophilia of cytoplasm, and pyknotic nuclei (Fig. 2). Some cells showed fragmentation of cytoplasm and karyorrhexis indicative of neuronal necrosis. Proliferating Bergmann glia had clear round or oval nuclei. In the most severely affected area of the culmen and declive of the cerebellar hemisphere, folia had become very thin because of the almost complete disappearance of Purkinje cells. Basket cells in the deep molecular layer had pale and swollen nuclei. The granular layer was reduced in thickness with a diminished granular cell population. Diminution of the cellular population in the granular layer closely correlated with the severity of disappearance of Purkinje cells.

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Fig. 1. Cerebellar hemisphere; cat. Folium with absence of Purkinje cells and diminution of internal granular layer. HE. Bar = 100 μm.

Fig. 2. Cerebellar hemisphere; cat. Degeneration of this Purkinje cell is represented by shrinkage of the strongly eosinophilic cytoplasm and a pyknotic nucleus (arrow). HE. Bar = 20 μm.

Fig. 3. Cerebellar vermis; cat. Higher magnification of the cortex shows the disappearance of Purkinje cells and proliferation of Bergmann glia (between two arrows). HE. Bar = 20 μm.
Fig. 4. Cerebellar vermis, cat. Section from same area as in Fig. 3. Isomorphic gliosis in the molecular layer is characterized by glial fibers extending vertically from the layer of Bergmann glia to the cerebellar surface. Holzer's method. Bar = 20 μm.

Fig. 5. Cerebellar hemisphere, cat. Formation of empty baskets (arrows) lacking Purkinje cells. Note a residual Purkinje cell (arrowhead). Methenamine silver impregnation method for nerve fibers. Bar = 20 μm.

Fig. 6. Cerebellar hemisphere, cat. A few intact Purkinje cells (arrows) are left without the proliferation of Bergmann glia in dorsal paraflocculus. HE. Bar = 20 μm.

Fig. 7. Cerebellar hemisphere, cat. Section from same area as in Fig. 6. There is no isomorphic gliosis in the molecular layer. Note intact Purkinje cells (arrows). Holzer's method. Bar = 20 μm.
Fig. 8. Cerebellar hemisphere; cat. Isomorphic gliosis in molecular layer. Immunohistochemical staining for glial fibrillary acidic protein with Mayer's hematoxylin counter-stain. Bar = 20 μm.

In the sections stained with Holzer's method for glial fibers and an avidin–biotin immunoperoxidase staining for glial fibrillary acidic protein (GFAP, Dako ABC kit, Dako Corp., Carpinteria, CA), the molecular layer showed marked isomorphic gliosis, which was evident from glial fibers vertically extended from the layer of Bergmann glia toward the surface of the cerebellar cortex. These glial fibers ran in parallel with each other (Figs. 4, 8). Mild proliferation of fibrous astrocytes was also found in the granular layer.

The methenamine silver impregnation method for nerve fibers revealed the formation of empty baskets lacking a Purkinje cell (Fig. 5) in regions where these cells had disappeared. Axonal torpedoes strongly stained with eosin and methenamine silver impregnation were occasionally observed in the granular layer. Climbing and parallel fibers preserved their normal structures. A few of the residual Purkinje cells in a part of the inferior vermis and dorsal paraflocculus of the cerebellar hemisphere showed almost normal structures with clearly observable Nissl bodies and axons (Fig. 6). In these areas, there was no proliferation of Bergmann glia, isomorphic gliosis in the molecular layer (Fig. 7), or reduction of cellularity in the granular layer.

The histologic study indicated that the cerebellar lesions in this cat differed from those of the congenital cerebellar hypoplasia caused by viral infection. The atrophy of the cerebellar cortex in this case was caused by the preferential degeneration and loss of Purkinje cells. The isomorphic gliosis in the molecular layer must be interpreted as a compensatory reaction to axonal loss following the disappearance of Purkinje cells. The diminishing population of granule cells and the presence of an empty basket are regarded as secondary changes due to the destruction of Purkinje cells.

Most previously reported cases of feline cerebellar ataxia were characterized histologically by degeneration and loss of granule cells of the external germinal layer and of developing Purkinje cells during the stage of cerebellar development. Epidemiologically, these changes were caused frequently by infection with FPV (a feline parvovirus) before birth or very early in life. Intranuclear inclusion bodies and infiltrations of mononuclear cells suggesting viral infection were observed. None of these lesions were observed in the present case, and serologic HI tests indicated no evidence of infection with FPV, FIPV, and FeLV.

In neuroaxonal dystrophy, olivopontocerebellar atrophy, Pick's disease, and Friedreich's ataxia, which are characterized by degeneration or atrophy of the cerebellar cortex in humans and other animals, lesions were regularly observed in other parts of the central nervous systems with known functional relations to the cerebellum. The lesions in this cat were restricted to the cerebellum and did not extend to other parts of the central nervous system. The histologic features and the distribution of lesions in this case are, however, similar to those in hereditary cerebellar abiotrophy reported in domestic animals and in the mouse. In Purkinje cell degeneration of the mutant mouse, the inferior vermis remains intact until late in the disease course, just as in the present case. In dogs and cattle, the lesions are restricted mainly to the cerebellar hemispheres. Reported simultaneous infiltrates of macrophages in the cerebellar nuclei and degeneration of the retina, olfactory bulbs, and thyroid gland were not detected in the present case. The etiology of abiotrophy in dogs and mice has been shown to be linked genetically to an autosomal recessive inheritance. It could not be determined whether the cerebellar lesions in the cat were caused by the dysfunctional regulation of genetic factors because the cat was of mixed breed and was the only one affected among four littermates, and the mother was normal.

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References

Chromophilic-eosinophilic (Onecyte-like) Renal Cell Carcinoma in a Dog with Nodular Dermatofibrosis

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Key words: Dogs; kidney; nodular dermatofibrosis; renal cell carcinoma.

Nodular dermatofibrosis is a rare condition of German Shepherd Dogs characterized by fibromatous nodules in the skin associated with multifocal renal neoplasia. Pedigree analyses of affected dogs indicates that the disorder may be inherited in an autosomal dominant pattern. In this report, we describe an unusual variant of renal carcinoma in nodular dermatofibrosis.

A 9-year-old male German Shepherd Dog was referred to a veterinary teaching hospital for evaluation of multiple skin growths. Based on biopsy findings, a diagnosis of nodular dermatofibrosis was made. Radiologic and ultrasonographic evaluation of the kidneys revealed no abnormalities. The animal was discharged, and an oral treatment with antibiotics was prescribed. The dog was reexamined 8 months later because of progression of ulcerative skin nodules. Hemogram and ultrasonographic image of the kidneys remained unchanged. The dog was euthanatized because of poor physical condition, and a necropsy was done.

On gross examination, the dog had multiple skin lesions affecting the lower aspects of all four limbs that consisted of hyperpigmented, alopecic, firm nodules of various sizes (0.5-2 cm in diameter). Two firm, gray to white circular masses (0.5 and 3 mm in diameter) were detected. On histologic examination, the masses extended by a huge fibrous capsule and lined by cuboidal epithelium (Fig. 2). Neoplastic cell cytoplasm was abundant, highly eosinophilic, coarsely granulated, and distended by a huge vacuole in scattered cells (Fig. 1). In some areas of the neoplasm, the cells had intense pleomorphism and anisokaryosis and were multinucleate. The mitotic index was low. Cysts were demarcated from the surrounding tissue by a thin fibrous capsule and lined by cuboidal epithelium (Fig. 2). Neither cells lining cysts nor those forming the neoplasms stained with toluidine blue, and uranyl acetate and lead citrate, respectively. The peroxidase antiperoxidase method was used for visualizing the binding of the following antibodies on paraffin-embedded sections: cytokeratin (1:25) (MNF116, Dako Corp., Glostrup, Denmark), desmin (1:500) (Dako), vimentin (1:75) (Dako), glial fibrillary acidic protein (GFAP) (1:400) (Dako), lysozyme (1:130) (Dako), and α1-antichymotrypsin (1:200) (Dako).

Histologically, skin nodules consisted of dense, coarse collagen fibers arranged in irregular bundles and displaying a very low cellularity, which involved the entire dermal thickness. Adnexa within the lesions and subcutis appeared normal, and the inflammatory reaction was negligible. The overlying epidermis in these areas was variably ulcerated.

Renal masses consisted of neoplastic epithelial cell proliferation with a growth pattern ranging from solid to tubulopapillary. Neoplastic cell cytoplasmin was abundant, highly eosinophilic, coarsely granulated, and distended by a huge vacuole in scattered cells (Fig. 1). In some areas of the neoplasm, the cells had intense pleomorphism and anisokaryosis and were multinucleate. The mitotic index was low. Cysts were demarcated from the surrounding tissue by a thin fibrous capsule and lined by cuboidal epithelium (Fig. 2). Neither cells lining cysts nor those forming the neoplasms stained with PAS, Best’s carmine, alcian blue, and Hale’s colloidal iron reaction. Tissue samples for transmission electron microscopy were fixed in 2.5% sodium cacodylate-buffered glutaraldehyde solution (pH 7.4) and postfixed in 1% osmium tetroxide before Epon embedding. Semithin and ultrathin sections were stained with toluidine blue, and uranyl acetate and lead citrate, respectively. The peroxidase antiperoxidase method was used for visualizing the binding of the following antibodies on paraffin-embedded sections: cytokeratin (1:25) (MNF116, Dako Corp., Glostrup, Denmark), desmin (1:500) (Dako), vimentin (1:75) (Dako), glial fibrillary acidic protein (GFAP) (1:400) (Dako), lysozyme (1:130) (Dako), and α1-antichymotrypsin (1:200) (Dako).

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