Neuronal ceroid-lipofuscinosis and hydrocephalus in a chihuahua

A two-year-old, female chihuahua presented with a six-month history of visual dysfunction. Computed tomography revealed dilation of the lateral ventricles in the central nervous system (CNS). The dog was tentatively diagnosed as having hydrocephalus and a month later was euthanased at the owner's request. The skull was expanded and dome-like in shape and an open fontanelle was observed on postmortem examination. Histologically, swollen neurons possessing yellowish pigment granules in the cytoplasm were observed throughout the CNS. These storage materials stained positively with periodic acid Schiff, Schmorl method for lipofuscin and oil red O for lipid, and showed autofluorescence under fluorescence microscopy. Ultrastructurally, the storage materials consisted of dense lamellar structures. This case was unique in having ceroid-lipofuscinosis in association with hydrocephalus.
The skull of the dog was expanded like a dome (Fig 2). On postmortem examination, an open fontanelle and partial defect of the skull in the left occipital region were observed. The lateral and third ventricles were markedly dilated; in particular dilation of the right lateral ventricle was prominent (Fig 3). No macroscopic abnormalities were found in the visceral organs.

Histologically, swelling of neurons was observed throughout the central nervous system (CNS) and these neurons possessed yellowish pigment granules in the cytoplasm (Fig 4). Pigment deposition was marked in the neurons of the hippocampus and thalamus, and in the Purkinje cells in the cerebellum. Neurons in the retina also showed swelling with pigment storage. These pigments stained positively with periodic acid Schiff (Fig 5), Schmorl method for lipofuscin and oil red O for lipid. Fluorescence microscopy demonstrated yellow-green autofluorescent granules in the swollen cytoplasm of the affected neurons (Fig 6). Glial fibrillary acidic protein (GFAP) immunohistochemistry revealed prominent astrocytosis.
consisting of gemistocytes throughout the CNS, and a laminar pattern of gliosis was often found in the cerebral cortex. Loss of Purkinje cells, Bergmann glial proliferation and an attenuated molecular layer were noted in the cerebellum. GFAP immunohistochemistry clearly demonstrated Bergmann gliosis in the molecular layer of the cerebellum (Fig 7). No obstructive lesions were apparent in the ventricular system. No storage material was apparent outside the CNS.

Ultrastructurally, storage materials consisted of dense lamellar structures in the cytoplasm of the neurons (Fig 8). Occasionally, some lamellar structures were found in the cytoplasm of astrocytes.

FIG 7. Enhanced glial fibrillary acidic protein immunoreactivity in the Bergmann glia and astrocytes of the cerebellum. ×180

FIG 8. Electron microscopy of the storage materials, showing dense lamellar structures in the cytoplasm of the neuron. ×21,000

FIG 9. Infiltration of mononuclear cells around the ventricle in the cerebrum. H&E ×110

The parenchyma of the cerebrum adjacent to the dilated ventricles was compressed, and diffuse astrogliosis was noted in the corona radiata of the cerebrum. Minute foci of mononuclear cell infiltration were found around the lateral ventricles with perivascular to diffuse infiltrating patterns (Fig 9). Most of these cells were lymphocytes; a few macrophages were also involved. There were no inflammatory lesions around the third and fourth ventricles.

DISCUSSION

Frequent clinical signs of NCL include visual impairment, abnormal behaviour with aggression, tremor, ataxia and seizures (Jolly and others 1994b). Blindness was mostly reported as an early clinical change in dogs of several breeds affected with NCL (Jolly and others 1994b). The present case also showed visual dysfunction, which was similar to the previously reported cases of canine NCL in its onset and nature. Age at onset of canine NCL varies from six months to eight years; thus, it is clinically classified as prepubertal-protracted, early adult-acute course, and adult onset (Jolly and others 1994b). Reported cases of NCL in chihuahuas occur from 13 to 21 months of age (Rac and Giesecke 1975), similar to the present case. NCL affects the cerebral cortex, particularly the occipital pole. In addition, the cerebellum was severely involved in cases reported by Jolly and others (1994b), as in the present case.

The storage materials showed similar staining and fluorescent properties to those of ceroid and lipofuscin. The major constituent of storage pigment has been described as a lipid-binding protein, which is a component (subunit c) of mitochondrial ATP synthase (Jolly and others 1994b). The other storage material was identified as sphingolipid activator protein (or saposins) in the human infantile form and in miniature schnauzers with NCL (Palmer and others 1997). The precise nature of the storage materials in the present case remains to be investigated.
Generally, brain atrophy is the most common macroscopic finding in canine NCL (Jolly and others 1994b). Although slight dilation of the lateral ventricles associated with brain atrophy has been found, prominent hydrocephalus has not been recorded in previous cases of canine NCL (Jolly and others 1994b). Congenital hydrocephalus is more common in toy breeds of dogs, including the Maltese, Lhasa apso, Pug and Pekingese (Summers and others 1995). The present dog had an open fontanelle and a defect around the lateral ventricles, indicating a reaction associated with degenerative changes caused by the increased intraventricular pressure. Neurological dysfunction would have resulted from ceroid-lipofuscin deposition in the neurons, and physical compression of the brain by the hydrocephalus.

This dog may be unique in suffering from both NCL and hydrocephalus.

References


