Neuronal Ceroid-Lipofuscinosis in a Mature Dog

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The neuronal ceroid-lipofuscinoses are a group of diseases characterized by progressive accumulation of autofluorescent lipopigments within neurons with associated neuronal damage. Variations of these diseases occur which include accumulations of lipopigments in viscera. The diseases long have been recognized in man where earlier studies of the pathogenesis suggested an increased rate of peroxidation of unsaturated fats with accumulation of lipopigments in secondary lysosomes. Recent work, however, suggests that at least some forms of the human diseases involve disorders in the metabolism of dolichols. Ceroid-lipofuscinosis has been described in the dog, cat, cattle, and sheep. We describe a case of ceroid-lipofuscinosis in a mature dog associated with behavioral disturbance.

The affected terrier-cross breed male dog had progressively increasing aggressive tendencies from about four months of age. The dog was killed at nine years of age when circling and a head tilt developed and aggressive tendencies were severe.

The dog was necropsied and histologic examination was done on liver, spleen, kidney, and a series of sections of brain. Lesions were limited to the brain with slight yellow discoloration grossly. The cerebral cortex had prominent gyri and sulci suggesting some brain atrophy. Histologically there was accumulation of periodic acid-Schiff (PAS)-positive, autofluorescent granular material in neurons throughout the brain. Neuronal deposits varied in different anatomic areas. The most pronounced lesions were in the hippocampus and the temporal cortex where the lesion was general and focally severe (table I). With hematoxylin and eosin (HE) stain, severely affected neurons were swollen with the perikaryon containing cosinophilic, slightly golden brown, distinct or coalescing granules which displaced the nucleus peripherally (fig. 1). Neuronal loss, astrocytosis, and aggregation of gitter cells were prominent in severely affected areas. Gitter cells typically had rounded cell outlines, eccentrically flattened nuclei, and large amounts of cosinophilic cytoplasm that contained PAS-positive, autofluorescent material similar to that in neurons. These cells occurred sporadically throughout the neuropil and formed perivascular cuffs, one to several cells thick, in the gray matter.

Formalin-fixed tissue from the frontal cortex, temporal cortex, hippocampus, cerebellum, and the brain stem from the area of the vestibular nucleus was examined by transmission electron microscopy. Ultrastructurally, affected neurons had cytosomes of varying number, size, and morphology (fig. 2). Irregular cytosomes with a pleomorphic content were most

Table I. Severity of lesions of neuronal ceroid-lipofuscinosis in selected areas of central nervous system

<table>
<thead>
<tr>
<th>Area</th>
<th>Neurons</th>
<th>Macrophages</th>
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<tbody>
<tr>
<td>Frontal cortex</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Temporal cortex</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Thalamus</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Posterior colliculus</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Medulla-vestibular nucleus</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>+++*</td>
<td>++</td>
</tr>
</tbody>
</table>

+ = minimal; ++ = mild; +++ = moderate; and ++++ = marked.
* Purkinje's cells.

Fig. 1: Swollen neurons with peripherally displaced nuclei. Inset: Gitter cells forming perivascular cuff. Hippocampus. HE.
Fig. 2: Neuron with numerous cytosomes in cytoplasm. *Inset:* Cytosomes with laminated membranous material at higher magnification. Hippocampus.

frequent. This included membranous structures layered in irregular configurations, electron-dense lipofuscin, and aggregates of granular material. Some cytosomes contained only laminated membranous material while others had only lipofuscin. Gitter cells had cytosol engorged with vacuoles containing membranous figures and amorphous electron-dense material.

The diagnosis of neuronal ceroid-lipofuscinosis was made on the basis of histologic staining, autofluorescence of the pigment, and ultrastructural morphology of the neuronal cytosomes. The histologic appearance of the cytoplasmic deposits in neurons was similar to aging pigment. The progressive clinical disease, the large amount of pigment and the degenerative changes which were focally severe separate this case from simple senile lipofuscinosis as commonly seen in aged dogs in our experience. In addition, the cytoplasmic material in neurons of this dog was similar ultrastructurally to that described in other cases of ceroid-lipofuscinosis in dogs.3,6

This case is unusual because of the advanced age of the dog, the nature of the clinical signs, and the interesting anatomical correlation of lesions to behavioral signs in the dog. At nine years of age this dog was considerably older than the reported canine cases, which were two years of age or less1,6,8 with the exception of one 4½-year-old dachshund.3

Progressively increasing aggressive tendencies associated with ceroid-lipofuscinosis appear to be unique to this case. Aggressive tendencies in dogs previously have been reported in association with specific neurologic lesions which primarily affected the limbic system.2 The lesions in this dog also have this neuroanatomical correlation.

References

Lymphocytic Leukemia in a Ferret (*Mustela furo*)

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Tumors appear to be relatively rare in the ferret (*Mustela furo*).\(^1\) - \(^8\) Single cases of a squamous cell carcinoma,\(^9\) mammary cystadenocarcinoma,\(^2\) an ovarian carcinoma,\(^4\) and recently a megakaryocytic myelosis\(^5\) have been reported. Lymphocytic leukemia in a ferret has been reported only once in the literature.\(^1\) This report adds to the limited literature on neoplasms of the ferret.

Fig. 1: Neoplastic lymphocytes massively infiltrating hepatic sinusoids and causing atrophy of hepatic cords. HE.

Fig. 2: Neoplastic lymphocytes in hepatic sinusoid. Round nuclei with clumped chromatin, prominent nucleoli, and scanty cytoplasm. HE.