Neuronal Loss and Gliosis in Limbic System in an Epileptic Dog

H. YAMASAKI, H. FURUOKA, M. TAKECHI, AND C. ITAKURA

Key words: Dogs; epilepsy; gliosis; limbic system; neuronal loss.

Epilepsy is a clinical syndrome characterized by recurrent convulsive seizure and, based on the lesions, is classified into two main groups: symptomatic and idiopathic. The symptomatic type in dogs, as well as in human beings, is secondary to various organic brain damage, such as malformations, traumas, neoplasms, infections, and metabolic disorders. Occasionally, the idiopathic type in dogs is suspected to be inherited, and usually it has no evidence of brain abnormalities. A few cases have perivascular hemorrhage in the brain. Human patients affected with idiopathic (cycloptic) epilepsy, on the other hand, often have neuronal loss and gliosis in some portions of the brain. This report describes chronic brain lesions with a specific distribution in an epileptic dog.

A 2-year-old male Shetland sheepdog had clonic spasms that occurred once every 3 or 10 days and lasted for a few seconds to a minute. He was thus clinically diagnosed as epileptic and appropriately treated. His fits became temporarily less frequent during the use of an anticonvulsant (primidone: Mysoline, Dainippon, Japan) therapy, but the incidence and duration of seizures gradually increased, and incontinence was observed. At 4 years old, the dog’s fits continued for several days and appeared several times a day, resulting in status epilepticus. He did not recover despite treatment with another anticonvulsant (sodium valproate: Depakene, Kyowa Hakko, Japan). He was therefore euthanatized at 5 years of age. His family history was not available.

After necropsy, only the brain tissues were fixed in 10% neutral buffered formalin and embedded in paraffin and sections were stained with hematoxylin and eosin. Selected sections were stained with luxol fast blue counterstained with HE, cresyl violet, Holzer, modified Bielschowsky, and silver reticulum stains. Immunohistochemistry was carried out using monoclonal antibody for glial fibrillary acidic protein (GFAP, Dakopatts, Glostrup, Denmark) with avidin-biotinperoxidase complex method (Vectastain ABC kit, Vector Laboratories, Burlingame, CA, USA) and counterstained with hematoxylin.

Grossly, both hemispheres of cerebrum, the hippocampal ventral horn, and the anterior to posterior portions of the cingulate gyrus were reduced in size. The lateral ventricles were mildly dilated.

Histologically, the lesions consisted of neuronal loss, gemistocytic to fibillary astrocytosis, and vascular proliferation. They were distributed bilaterally and symmetrically, and located selectively in limbic parts of the cingulate gyrus, amygdaloid nucleus, dorsal and ventral parts of the hippocampus, and dorsomedial nucleus of the thalamus (Fig. 1). The most severely and extensively affected sites were the cingulate gyri and medial aspects of the frontal lobes. The cortex in these areas was about half as wide as normal, and there were decreased numbers of neuronal cells. Few normal neuronal cells remained in the rarefied neuropil. With silver reticulum stain of the affected gray matter, proliferation of blood vessels was conspicuous, showing fibrous thickening of the walls (Fig. 3). There was also a marked increase in the number of plump...
astrocytes, whose processes often surround the vascular walls and remaining neuronal cells (Fig. 2). This change in astrocytes was well demonstrated in the sections immunostained with anti-GFAP immunostaining, as well as those stained by hematoxylin and eosin. In the hippocampal formation stained with cresyl violet, the H, field and endofolium showed moderate neuronal loss and gliosis. The dentate gyrus and H, field were minimally affected (Fig. 4). Restricted only to a part of the posterior portion of the hippocampus, a small number of remaining pyramidal neurons showed central chromatolysis. Holzer stain disclosed fibrillary gliosis located in the fimbria and focal areas in the amygdaloid nucleus and paratenial nucleus of the thalamus. Edematous rarefaction of the neuropil occurred with mild neuronal loss in the dorsomedial nucleus of the thalamus. The cerebellum and lower brain stem were apparently normal. In the subcortical white matter and centrum semiovale, there were ovoid myelin formations in luxol fast blue-HE-stained sections, though axonal swelling was not prominent.

In canine epilepsy, there are only a few reports that refer to the specific distribution of the lesions as seen in the present dog.1, 4, 7 Associated with canine distemper virus infection, bilateral-symmetrical malacia in the olfactory and limbic system has been observed in dogs with convulsive seizures.4 The authors suggest that the virus entered in the olfactory pathways and created the epileptogenic focus resulting in further damage to the hippocampal areas.4 In our dog, the olfactory rhinencephalon was not involved, and there were neither inflammatory nor malacic (destructive) changes throughout the brain. Selective neuronal atrophy with gliosis has been described once in an epileptic Poodle dog; however, the lesions in that dog were restricted to the hippocampus,1 thus differing from those in the present dog. Acute brain lesions with a distribution similar to that in our case have been reported in 33 dogs, obtained from a colony of epileptic Beagles used for an irradiation effect study.1 In the present case, the extensive and chronic lesions may have resulted from recurrent seizures during the disease course. Acute lesions such as edematous neuropil found in the thalamus in our dog may have been related to violent seizures recorded in the short time prior to euthanasia.

Idiopathic epilepsy in human beings is well-documented, and the patients most often have an absence of lesions but patients with lesions have the following three types of pathologic changes: minor dysgenetic lesions, lesions secondary to trauma, and neuronal loss and gliosis.7 The latter is known as Ammon’s horn or hippocampal sclerosis, and in such a case, the H, field is the most vulnerable site, followed by the endofolium.3 The thalamus, amygdaloid nucleus, and cerebral cortex are also frequently affected with this type of lesion.3, 5 Identical lesions are produced in primates and rats with experimental epilepsy.3, 6 The nature and distribution of the lesions noted in this dog are similar to those in human and experimental animal cases.
The morphologic changes in idiopathic epilepsy are largely considered to be the result of epileptic attacks, but the lesions themselves may cause seizures. Similar lesions are also induced by hypoxic conditions. In some cases, the seizure activity and the consequent ischemic events may play a role in the development of lesions occurring in status epilepticus; however, in another study on experimental epilepsy, the strict control of blood pressure and oxygen tension has not been able to prevent the formation of brain lesions. Once produced, the lesions may become an epileptogenic focus, resulting in extensive brain damage.

References

Request reprints from Dr. H. Yamasaki, Department of Comparative Pathology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo, 060 (Japan).

Chronic Eosinophilic Enteritis Attributed to Pythium sp. in a Horse


Key words: Eosinophilic enteritis; horses; Pythium sp., pythiosis.

Pythiosis in the horse is usually a local subcutaneous infection, often accompanied by cutaneous ulceration and fistulous tracts. It is characterized by the presence of exuberant granulation tissue containing granular yellow or yellow-gray cores called “leeches” or “kunkers.” Eosinophils are the most common inflammatory cell, and the cores consist of degenerating or necrotic eosinophilic debris. A marked granulomatous reaction usually is present around the cores. Recently, two cases of equine enteric pythiosis were described. In both cases, there was a stenotic jejunal mass that consisted of dense fibrous connective tissue, containing granulomas or necrotic cores that were surrounded by granulomatous inflammation. In one case, variably intense infiltrates of eosinophils were present. We describe a case of equine enteric pythiosis in which eosinophils were the predominant inflammatory cell.

A 7-year-old Arabian gelding was presented to the University of Illinois Veterinary Teaching Hospital with a 36-hour history of colic that failed to respond to medical treatment. Rectal palpation revealed colonic impaction. Large bowel tympany developed, and the horse was taken to surgery. A ventral midline laparotomy revealed three abnormalities: an impaction of the diaphragmatic flexure, gastric and large bowel tympany, and a mid-jejunal intramural soft tissue mass. After correcting the tympany and colonic obstruction, approximately 42 cm of the jejunum, including the mass, were removed and an anastomosis performed. The horse recovered uneventfully and was doing well, with no further episodes of colic, 1.5 years after surgery.

The jejunal mass was nodular, intramural, measured $3 \times 4 \times 5$ cm, and occupied $320\degree$ of the intestinal circumference. The overlying mucosa was ulcerated with green-brown fibrillar material that adhered to the ulcerated surface. Histologically there was focally extensive mucosal ulceration overlying multiple irregularly shaped, 2- to 7-mm diameter intramucosal nodules. The nodules consisted of a central core of granular eosinophilic debris (predominantly necrotic eosinophils) surrounded by degenerating eosinophils and neutrophils with a few macrophages and an occasional multinucleated giant cell. Fragments of plant material were present within some of the eosinophilic cores. Colonies of coccobacilli were present at the peripheries of some nodules. Dense granulation tissue containing many eosinophils, lesser numbers of lymphocytes and plasma cells, and occasional...