History

An outdoor 5-year-old sexually intact female domestic shorthair cat with a 4-day history of upper respiratory tract disease was referred to a private clinic in June 2008.

Clinical and Gross Findings

No abnormalities were detected during physical examination, but a few hours later, the cat developed bilateral blindness, progressive hind limb ataxia, and head tilt. Considering that the cat had no history of vaccination, the clinician suspected rabies and the cat was euthanized and submitted for necropsy. The carcass was in good body condition. The most important gross findings were restricted to the brain and consisted of a locally extensive area of subdural hemorrhage that extended over the temporal and frontal areas of the left cerebral hemisphere. After complete removal of the brain, a small, 5 × 2-mm, brown insect larva that was prominently segmented with multiple dark cuticular platelets was observed on the dura mater near the left olfactory bulb (Figure 1). Cross sections of brain revealed multifocal, unilateral hemorrhagic areas that extended from the caudate nucleus to the thalamic region. Nasal ethmoid turbinates were brown and granular, and frontal sinuses were filled with brown, catarrhal exudate. Other findings included pulmonary congestion, an enlarged heart with thickened left myocardial wall, and the presence of small, red, irregular, and raised areas on the mucosa at the trigone of the urinary bladder.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →
Histopathologic Findings

Microscopically, the brain had multifocal, well-demarcated areas of coagulative necrosis and hemorrhage (infarcts) within the subcortical white matter of the left frontal and temporal lobes (Figure 2). Surrounding these foci of infarct, blood vessels had prominent endothelial cells and the neuroparenchyma was rarefied as a result of edema. Changes extended into the cortex, where there were multiple laminar or segmental areas of vacuolation of the neuropil that contained multiple shrunken, eosinophilic, necrotic neurons with pyknotic nuclei. A mild to moderate, mostly eosinophilic perivascular inflammatory infiltrate was observed in the perivascular spaces surrounding affected areas in the brain and also in the leptomeningeal vessels (Figure 3). Some of these vessels were also surrounded by fibrin or areas of hemorrhage. A similar inflammatory infiltrate was present around leptomeningeal vessels in the brainstem and cerebellum. A mild submucosal eosinophilic inflammatory infiltrate and large amounts of intraluminal mucus were observed in the nasal turbinates.

Expanding the urinary bladder was a focally extensive, infiltrative urothelial neoplasm composed of multiple small tubules composed of polygonal epithelial cells supported by a scant fibrovascular stroma. Throughout the myocardium were small foci of myofiber atrophy and loss with fibrosis.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: severe, multifocal, hemorrhagic cerebral infarcts, laminar cortical necrosis, and mild to moderate eosinophilic meningoencephalitis; moderate, multifocal, eosinophilic and catarhal rhinitis; nonpapillary infiltrative transitional cell carcinoma of the urinary bladder trigone; and multifocal myocardial atrophy and loss with fibrosis.

Case summary: ischemic encephalopathy caused by aberrant migration of a Cuterebra larva in a cat.

Comments

The microscopic findings in the brain and nasal cavity of the cat of this report were consistent with feline ischemic encephalopathy (FIE) caused by aberrant migration of a Cuterebra larva.1–5 The condition, referred to as cerebrospinal cuterebrasis, was confirmed during removal of the cat’s brain and gross observation of an insect larva next to the left olfactory bulb within the calvarium that was morphologically consistent with a species of Cuterebra.6 The cardiac changes (consistent with hypertrophic cardiomyopathy) and the transitional cell carcinoma of the urinary bladder were considered incidental findings in this case.

Although cerebral cuterebrasis is most common in domestic cats,2,4,7 it has been described in dogs8 and an African lion.9 In cats, the condition usually affects adults, but there is no sex predilection.1,2,4 Cerebral cuterebrasis most commonly develops in cats that have access to the outdoors7 and most cases in cats have been reported in the eastern and Midwestern parts of United States.6 Cases are reported predominantly but not
exclusively in the summer months, which coincides with the activity of Cuterebra larvae in the United States. Many species of Cuterebra have been identified, and their typical hosts include wild rodents and rabbits. Instead of laying eggs directly on the host, female Cuterebra flies lay their eggs around the opening of host burrows and nests during the summer months. The host becomes infected after it passes through the contaminated area, when the eggs hatch in response to contact with body warmth. Once the larvae attach to the host, they enter the body through the oral cavity, nares, or eyes and less often through open wounds, then they migrate to several locations, most commonly subcutaneous tissue. A typical host, larvae evacuate after a few weeks, fall to the soil, and pupate. Infection in atypical hosts, such as cats and dogs, can develop after those animals access sites where the eggs have been laid. In these cases, aberrant larval migration to several body sites, including the brain, eyes, or respiratory tract, may occur. Before reaching the brain, presumably through the cribriform plate, larvae migrate through the nares and sinuses and may cause catarrhal rhinitis and sinusitis, similar to what was observed in the cat of this report. Aberrant migration in atypical hosts usually leads to death as a result of migration through the CNS. Affected cats may develop a wide range of nonspecific clinical signs that may include blindness, signs of depression, circling, and other abnormalities such as ataxia, seizures, and head tilt. Some cats may have a previous history of upper respiratory tract disease. In the cat of the present report, gross examination of nasal turbinates and frontal sinuses confirmed the history of upper respiratory tract infection and revealed marked accumulation of brown mucoid material in those sites. Additionally, the other observed gross findings in the brain were consistent with those described for cases of FIE, which included areas of necrosis with yellow discoloration involving mostly the rostral portions of the brain. The parasite may be observed within the brain and cribriform plate and also in the calvarium, spinal cord, meninges, and trigeminal ganglion or nerve. From 2006 to 2011, 20 cats with neurologic lesions consistent with FIE were submitted to the diagnostic service at the University of Georgia Department of Pathology. A review of these reports revealed that parasites were grossly observed within the calvarium in only 4 cases, including the one described in this report. The parasites were observed microscopically in only 1 of these 4 cases. The reason why the parasites are not commonly observed during necropsy is unknown, but the larvae are very small and therefore could be easily overlooked during gross examination. Thus, a close postmortem inspection of the calvarium, cribriform plate, and nasal passages is highly recommended in cases of suspected FIE. Reported gross findings in chronic cases of FIE may include atrophy of the frontal and parietal cerebral cortex, although these changes have been observed rarely at our institution. Microscopically, a constellation of findings may be detected in cases of FIE. As illustrated by the findings for the cat of this report, laminar neuronal necrosis, with rarefaction of the neuropil, and endothelial swelling seem to be consistent pathological changes that may be observed throughout the neocortex in affected individuals. Affected cats may also develop multifocal areas of cerebral necrosis and hemorrhage, which contain foamy macrophages and fewer eosinophils, neutrophils, lymphocytes, and plasma cells, that may extend to the perivascular spaces. These foci are surrounded by reactive astrocytes and develop predominantly in the olfactory bulbs, caudate nucleus, and thalamus. It is likely that the foci represent areas of active parasitic migration. In cats with chronic FIE, extensive areas of cerebral infarct and atrophy may develop predominantly in the frontal and parietal lobes. In these areas, there is collapse of the pachymenia and infiltration of large numbers of foamy macrophages. Less common changes include attenuation or loss of ependymal cells and inflammatory or degenerative lesions in the spinal cord. IntraleSIONAL larvae or larval remnants may also be detected. The necrotic foci observed in the cat of this report represented foci of coagulative necrosis with maintenance of the tissue architecture and were not consistent with the migration tracts described by other authors, which are characterized by areas of liquefactive necrosis with cavitation and hemorrhage. Thus, it is possible that the necrotic foci represented areas of necrosis secondary to vasospasm rather than areas of damage caused by the parasite.

The pathogenesis of FIE is complex. Migration of the parasite through the brain results in hemorrhage and necrosis and most likely causes secondary vasospasm through an unknown mechanism, presumably in response to a substance released either from the parasite or from the damaged host tissue. The vascular-associated changes observed in affected cats are usually localized in areas perfused by the middle cerebral artery, indicating a major role of this artery or its branches in the development of FIE. Clinically, FIE may be suspected following detection of areas of ischemia and infarction in the brain via MRI. However, because of the variety of clinical signs and lack of a specific antemortem method of diagnosis, the gross observation of larvae in the brain or tissues of the cranium appears to be crucial for the diagnostic confirmation of FIE. Gross and microscopic findings in the cat of this report were characteristic of FIE, and the diagnosis was confirmed by the presence of a Cuterebra larva within the calvarium.

References