History

A 15-month-old castrated male Labrador Retriever–Poodle crossbreed dog was referred for evaluation of a 6-day history of waxing and waning lethargy, ataxia, and signs of possible cervical region pain. Prior treatment included fluid therapy and administration of dextrose, antimicrobials, and corticosteroids. Results of a prereferral CBC, serum biochemical analysis, and ACTH stimulation test were within reference limits. A heartworm antigen test and ELISAs for tick-borne diseases yielded negative results. The dog had reportedly been healthy prior to the onset of clinical signs except for an episode of kennel cough 2 months earlier, which had resolved following treatment with antimicrobials. No vaccinations had been administered to the dog since puppyhood, and the dog had no history of travel outside of California.

Clinical and Gross Findings

At the referral evaluation, the dog was responsive at first but rapidly became severely obtunded by the end of the examination. Ataxia and tetraparesis were marked, and there was generalized muscle trembling and a lack of conscious proprioceptive reactions in all 4 limbs. The dog also had hypersalivation and positional nystagmus (horizontal movement in dorsal recumbency and vertical movement in lateral recumbency). Mild anisocoria developed by the end of the examination. A CBC, serum biochemical analysis, and coagulation panel revealed no abnormalities except mildly high calcium concentration (11.7 mg/dL; reference range, 9.7 to 11.5 mg/dL). Arterial blood pressure values were within reference limits. Despite treatment with fluids, 2 bolus IV injections of mannitol, and dexamethasone IV, the dog became agitated, disoriented, and eventually opisthotonic and comatose overnight. The anisocoria became marked and fixed. Because of the poor prognosis at this time, the owners elected euthanasia and necropsy.

Necropsy findings were limited to the brain and caudal portion of the nasal cavity. An irregular, soft to slightly firm, tan to gray gelatinous mass (approx 30 mm in diameter) effaced the ethmoid turbinates (A) and extended into the rostral cranial vault (brain removed) where it infiltrates an adhered portion of olfactory bulb (asterisk). The meninges and lining of the lateral ventricle on the left side (B) are multifocally expanded, and the cerebral parenchyma is compressed by pale tan gelatinous material (arrows). In each panel, scale = 1 cm.

Figure 1—Photographs of the left caudal portion of the nasal cavity (after sectioning of the head at midline [A]) and 2 formalin-fixed transverse sections of the cerebral hemispheres (B) of a dog that was evaluated because of a 6-day history of waxing and waning lethargy, ataxia, and signs of pain in the cervical region. Because of the rapidly deteriorating condition of the dog and poor prognosis, euthanasia and necropsy were performed. Notice that a pale tan solid gelatinous mass replaces the ethmoid turbinates (A) and extends into the rostral cranial vault (brain removed) where it infiltrates an adhered portion of olfactory bulb (asterisk). The meninges and lining of the lateral ventricle on the left side (B) are multifocally expanded, and the cerebral parenchyma is compressed by pale tan gelatinous material (arrows).
Figure 2—Photomicrograph of a gelatinous mass in the caudal portion of the nasal cavity in the dog in Figure 1. Sheets of yeast organisms with thick clear capsules (identified via fungal culture as Cryptococcus gattii) are mixed with numerous foamy macrophages and fewer lymphocytes and plasma cells. H&E stain; bar = 50 μm.

**Histopathologic Findings**

Histologically, all of the gelatinous masses were composed of sheets of fungal yeasts with a distinctive soap-bubble appearance (Figure 2). These organisms were 15 to 30 μm in diameter and characterized by a central, round to oval, thin-walled, 6- to 12-μm-diameter refractive yeast body that was surrounded by a 6- to 12-μm-thick clear capsule. Numerous foamy macrophages, many of which contained intracytoplasmic yeasts, were interspersed among the organisms along with frequent small perivascular aggregates of lymphocytes and plasma cells. The organisms and inflammatory changes caused expansion of the leptomeninges and ventricular system in all areas of the brain and spinal cord; the most severe infiltration of the brain parenchyma was in the olfactory bulbs and left rostroventral portion of the cerebral cortex. The remaining neuropil in infiltrated areas was vacuolated and had variable gliosis. Spinal nerve roots were multifocally infiltrated with organisms as far caudally as the cauda equina.

**Morphologic Diagnosis**

Severe chronic multifocal to coalescing granulomatous meningoencephalomyelitis, rhinitis, and sinusitis, with intraleSIONAL yeasts consistent with Cryptococcus spp.

**Comments**

The diagnosis of cryptococcosis was based on the characteristic gross and histologic appearance of the fungal masses. The organism was identified as Cryptococcus gattii (formerly Cryptococcus neoformans var gattii) on the basis of results of fungal cultures of pooled samples of CSF and the nasal mass collected during necropsy. Currently, C. gattii is the cause of a decade-long outbreak in the Pacific Northwest of North America that involves humans, dogs, and other animals; previously, this dimorphic, basidiomycetous fungus had been closely associated with eucalyptus trees in Australia and certain areas of California and was thought to be restricted to tropical and subtropical climates.\(^1\)\(^2\) Since recognition of the outbreak on Vancouver Island in British Columbia, Canada, \(C\) gattii has been cultured from the air and the bark and bases of a variety of trees in that region.\(^1\)\(^2\) The primary mode of infection is inhalation of the basidiospore stage or desiccated yeast cells from the environment. Risk factors for \(C\) gattii infection of dogs on Vancouver Island reflect potential increased exposure to the organism and include recent soil disturbance or logging near the animals' residences, high levels of activity outdoors, and travel on Vancouver Island.\(^3\) According to the owners, the dog of this report had not traveled outside of California, and the specific source of its infection is unknown. However, other factors similar to those associated with risk of \(C\) gattii infection in dogs on Vancouver Island may have been in effect or the dog may have been exposed to eucalyptus trees in California. Because genetic analysis was not performed, this \(C\) gattii isolate could not be compared with that involved in the Pacific Northwest outbreak, which has recently been detected as far south as western Oregon,\(^6\) or compared with other isolates from California.

The clinicopathologic features of this case were typical of those in dogs with \(C\) gattii infections associated with the North American outbreak. Young adult dogs (< 5 years old) are most commonly affected and develop multifocal CNS signs, including ataxia, blindness, nystagmus, upper motor neuron paresis, signs of pain in the cervical region, and seizures.\(^1\)\(^2\) Colonization of the nasal cavity probably precedes involvement of the CNS and may cause nasal discharge or facial distortion or swelling.\(^1\)\(^2\) As in the dog of this report, extension into the brain may be through the cribriform plate with subsequent spread along the meninges and via the CSF. Systemic dissemination of \(C\) gattii organisms can occur in apparently immunocompetent animals (including humans), but rapid progression of disease often follows administration of corticosteroids.\(^2\) The dog of this report was administered corticosteroids prior to referral and after it became obtunded at our institution. Changes in hematologic and serum biochemical variables are typically absent or non-specific, and antemortem diagnosis requires detection of the organism via cytologic or histologic evaluation of associated lesions or fungal culture or detection of capsular antigen in serum or CSF samples.\(^6\) The rapid deterioration of the condition of the dog of this report precluded performance of any of these diagnostic procedures.

**References**