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Case Report

Algal Meningoencephalitis due to *Prototheca* spp. in a Dog

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A 6-year-old Boxer was examined because of progressive neurologic signs, with severe hindlimb ataxia and head tilt on presentation. There was no history of diarrhea or vomiting. MRI of the brain revealed multifocal ill-defined T1-enhancing lesions affecting the cerebrum, brainstem, and cervical meninges, without associated mass effect. Meningoencephalitis was considered the most likely diagnosis. Multiple algae were observed on the cytology of the CSF and were most consistent with *Prototheca* spp. Antiprotozoal treatment was denied by the owners, and 5 weeks after diagnosis, the dog was euthanized due to progression of the neurologic deficits, and a necropsy was performed. Histological changes in the brain were compatible with severe multifocal protothecal meningoencephalitis. The specific *Prototheca* species was not identified. The gastrointestinal tract was unremarkable on histology. According to this report, *Prototheca* spp. should be included in the differentials for neurological deficits even in the absence of gastrointestinal signs.

1. Introduction

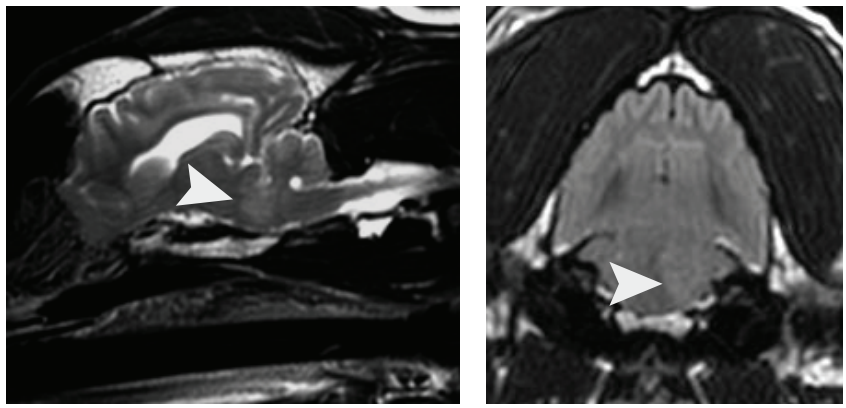
Protothecosis is a rare disease described in many species, caused by a green alga, *Prototheca* spp. In the cases reported in dogs [1–3], the algae are usually disseminated within the organism, and the affected dogs commonly present large intestine diarrhea. Ocular and neurologic symptoms are also described with protothecosis, but these signs usually appear in a later stage of the disease. To the authors' knowledge, this is the first case report describing cerebral protothecosis without evidence of dissemination of the alga within the other organs, and more particularly within the gastrointestinal tract.

2. Case Presentation

A 6-year-old spayed female Boxer was referred for progressive ataxia of the hindlimbs of 3-week duration. The dog was previously diagnosed with bilateral cranial cruciate ligament rupture, treated surgically 4 months prior to presentation.

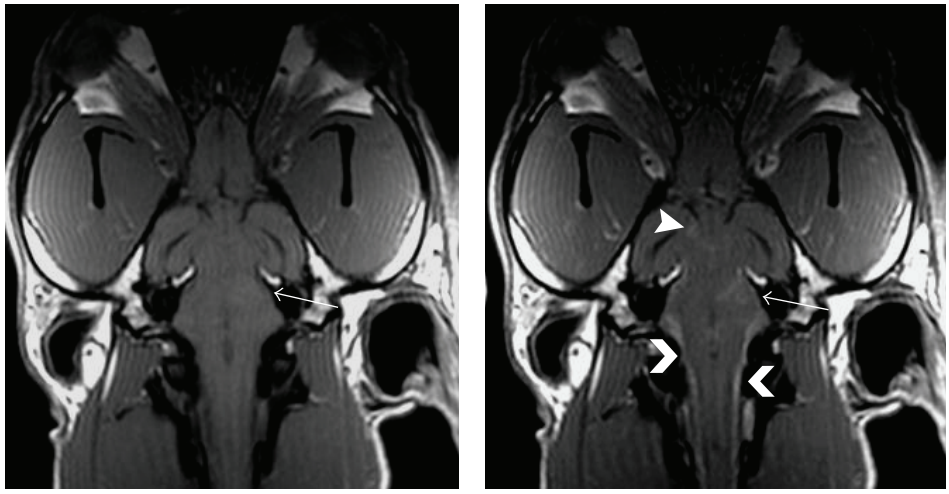
Physical examination was unremarkable. Neurologic examination revealed a severe hindlimb ataxia, worse on the left, and a left head tilt. Delayed hopping tests were noted in the forelimbs, and the dog fell when hopped in the rear. Crossing over and dragging of the hind feet were also observed. Cranial nerve examination was unremarkable, and there were no conscious proprioceptive deficits. Neurologic examination was consistent with brainstem and/or cerebellar localization. Based on the age, breed, and progressive neurological deficits, the following differentials were considered most likely causes of the clinical findings: neoplasia, such as meningioma or glioma, and an inflammatory lesion, such as an abscess or granuloma. Complete blood count was within normal reference range, and a mild hypercholesterolemia was noted on the chemistry panel.

Magnetic resonance imaging (MRI) of the brain was performed using a 1.5 T magnet (Echelon, Hitachi Medical Systems). Fast spin-echo T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and gradient-echo (GRE) pulse sequences were acquired in a transverse plane. A T2-weighted pulse sequence was also acquired in a sagittal plane, and a T1-weighted pulse sequence was acquired in



(a) (b)

Figure 1: (a) T2-weighted sagittal and (b) FLAIR transverse pulse sequences of the brain, at the level of the pons. There is a broadbased ill-defined homogeneous hyperintense lesion (arrowhead) along the sphenoid bone, encompassing approximately fifty percent of the left side of the pons and extending dorsal to the fourth ventricle, which appears slightly displaced to the right.



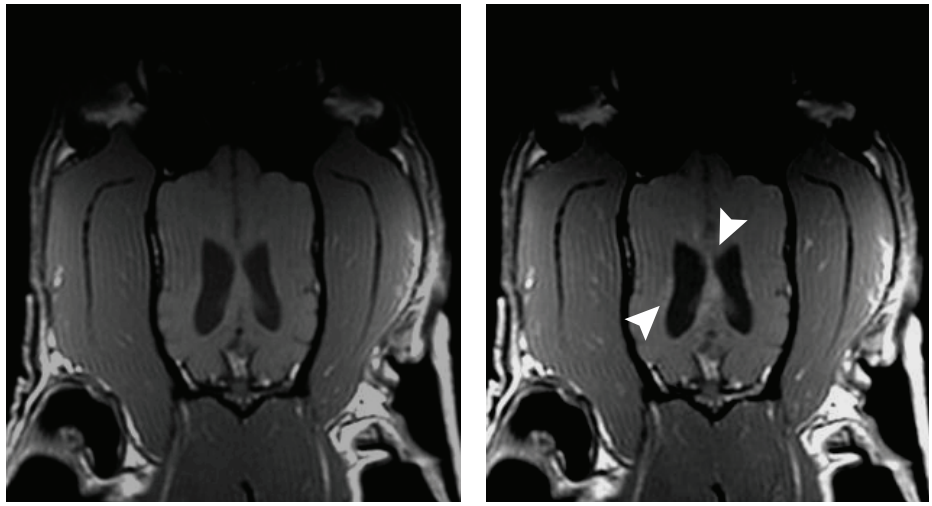
(a) (b)

Figure 2: T1-weighted dorsal pulse sequences before (a) and after contrast (b), at the level of the brainstem. (a) On the T1-weighted precontrast images, a faint ill-defined hyperintense signal was visible in the left pons (long arrow). (b) On the T1-weighted postcontrast sequence, meningeal enhancement was observed around the pons, *medulla oblongata*, and cranial cervical spine (arrowheads). A broadbased enhancement was visible in the left aspect of the pons (long arrow). Faint ill-defined enhancing lesions were also observed in the right frontal lobe (solid arrowhead).

a dorsal plane. Postcontrast T1-weighted pulse sequences were acquired in dorsal and transverse planes, after intravenous administration of gadopentetate dimeglumine (Magnevist, Berlex Imaging; 0.1 mmol/kg intravenously).

A focal hyperintense lesion, 1 cm in diameter, was present on the T2-weighted, GRE, and FLAIR pulse sequences in the left pons and rostral medullary region (Figure 1), encompassing approximately 50% of the left side of the pons, extending dorsally to the fourth ventricle, mildly displacing it to the right. The lesion was broadbased along the sphenoid bone, in the region of the geniculate ganglion, and was faintly hyperintense on the T1-weighted sequences (Figure 2(a)). Additionally, faint ill-defined hyperintense lesions were also observed in the right frontal lobe and within the *corpus callosum* on the FLAIR images. On the T1-weighted postcontrast pulse sequences, mild contrast enhancement of the pons lesion was present (Figure 2(b)). Meningeal enhancement was observed surrounding the pons, *medulla oblongata,* and cranial cervical spine (Figure 2(b)), and ill-defined areas of enhancement were visible within the thalamus, right frontal lobe, and *corpus callosum* and surrounding the lateral ventricles (Figure 3). Multifocal, contrast-enhancing disease affecting the cerebrum, brainstem, and cervical meninges was diagnosed. Meningoencephalitis was considered the most likely diagnosis, with differential diagnoses of metastatic neoplasia and lymphoma.

Following the MRI examination, cerebrospinal fluid was collected from the cerebellomedullary cistern, and it revealed



(a) (b)

Figure 3: T1-weighted dorsal pulse sequences before (a) and after contrast (b), at the level of the lateral ventricles. (a) The T1-weighted precontrast images were unremarkable. (b) On the T1-weighted postcontrast sequence, multiple ill-defined mildly enhancing lesions were visible within the right frontal lobe, temporal lobe, and *corpus callosum* and surrounding the lateral ventricles (solid arrowheads).

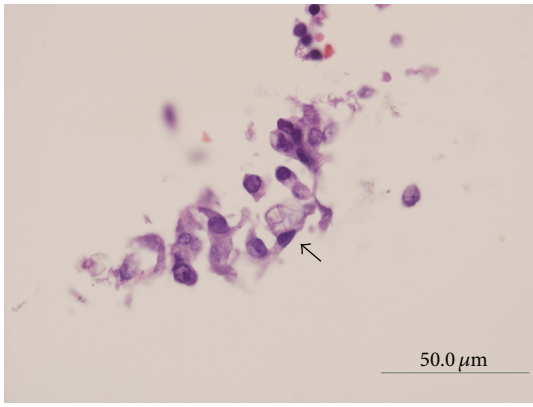


Figure 4: 1000x brain. A detached fragmented inflammatory focus of scattered histiocytes and few lymphocytes with extracellular, refractile, and round to oval thick-walled algal organism (arrow) which is 10–15 μm in diameter and composed of 2 to 3 wedge-shaped endospores is demonstrated. Hematoxylin and eosin stain: 1000x.

an eosinophilic pleocytosis with evidence of hemorrhage and intralesional yeast organisms, most consistent with *Prototheca* spp. Antiprotozoal treatment was denied by the owners, and 5 weeks after diagnosis, the dog was euthanized due to progression of the neurologic deficits. A postmortem examination was conducted. Macroscopically, the pons and *medulla oblongata* appeared slightly swollen with multifocal areas of dark brown to grey pinpoint foci in the hippocampus, thalamus, olfactory lobe, *medulla oblongata,* and pons. There was no other gross abnormality present.

Histopathologic examination of the brain revealed multiple random nodular aggregates of numerous lymphocytes, plasma cells, small numbers of histiocytes, and eosinophils centered on the blood vessels. Occasionally, few histiocytes contained refractile, round to oval algae, 10–15 μm in diameter (Figure 4), with a 2-3 μm thick cell wall, confirmed by special stain (Gomori's methenamine silver). Rarely, these algal cells had 2-3 wedge-shaped endospores. The meninges were sporadically infiltrated with similar inflammatory cells. In the hepatic parenchyma, few scattered granulomas, composed of moderate numbers of histiocytes admixed with lymphocytes and eosinophils, were observed, as well as a high number of macrophages containing golden brown pigment (hemosiderin/bile), predominately in the portal areas. Special staining for algal organisms did not reveal any algal cells. Histological changes in the brain were compatible with severe multifocal protothecal meningoencephalitis. The hepatic changes were suggestive of a chronic infectious process, but no organisms could be identified in the histopathologic sections. No significant microscopic changes were present in the other organs, including the gastrointestinal tract. Culture of the brain for *Prototheca* spp. did not grow any organism after 7 days, and a specific *Prototheca* species could not be identified.

3. Discussion

Protothecosis is a rare disease that has been reported in many species including dogs [1–3], cats [4], cattle [5], and humans [6, 7]. It is caused by unicellular, achlorophyllous algae which exist in the environment as ubiquitous detritus inhabitants and contaminants of various substrates: raw and treated sewage, trees, soil, mud, and feces [7, 8] which may contaminate aquatic systems or food and subsequently be ingested by man and animals. Protothecosis can also occur secondary to traumatic inoculation [8]. Three species are currently recognized, with the most common two being *Prototheca wickerhamii* and *Prototheca zopfii*. They have a worldwide distribution and are both described to cause disease in

dogs [2], while most human [6] and feline [4] cases are caused by *P. wickerhamii*.

The clinical signs of this disease are variable depending on the species affected. In humans and cats, it involves most commonly the skin, with vesiculobullous and granulomatous lesions observed, and it occurs more often in patients with underlying immunosuppression or concomitant disease [4, 7].

In dogs, there is currently no established breed, age, or sex predilections [9], but Collies [10–12] and Boxers [3] tend to be more frequently affected. The algae are usually widely disseminated throughout many organs including small intestines/colon, eyes, ears, skin, skeletal muscles, kidneys, liver, peritoneum, thyroid, heart, spinal cord, and brain [1–3]. The most common signs described are large bowel hemorrhagic diarrhea [1–3, 11–14] and ocular involvement [2, 10, 15–18] with retinal degeneration, chorioretinitis, or retinal detachment, potentially leading to blindness. Eventually, neurological signs can be observed in the form of lethargy, behavioral changes, paresis, head tilt, cervical pain, circling, ataxia, or seizures [2, 3, 19, 20]. In this case report, the neurological signs and histopathological results were similar to those of the previously published cases of canine central nervous system (CNS) protothecosis [19, 20]. However, the dog in this report presented only neurologic symptoms. This atypical clinical presentation of protothecosis has been previously described only in two instances [19, 21]. In our report, a few granulomas were observed in the liver during the necropsy, but no algal organisms were detected histopathologically. Microscopic examination of the eyes revealed only mild focal cataractous changes.

Only one report describing MR features of canine central protothecosis has been reported in the literature [22]. In both, that case [22] and the case reported here, the MR lesions observed were suggestive of an inflammatory or infectious process. However, the lesion observed in the pons in our case was broadbased, which may be suggestive of an extra-axial neoplastic disease [23, 24], but it was also ill defined and poorly marginated, with only minimal displacement of the fourth ventricle to the right and only mild T1 post-gadolinium enhancement, without dural tail sign observed, which is more suggestive of an inflammatory lesion. Primary brain tumors are often contrast enhancing compared with inflammatory lesions [23, 24]. The combination of meningeal enhancement and multifocal parenchymal lesions favored an inflammatory or infectious disease process. In a study [25] of 25 dogs with inflammatory cerebrospinal fluid (24 infectious/inflammatory diseases and 1 choroid plexus tumor), MRI lesions observed in 19 dogs (76%) were described as T1-weighted or T2-weighted multifocal or diffuse intracranial lesions. Meningeal enhancement was identified in 28% of these dogs. According to this study, meningeal enhancement is suggestive of inflammatory cerebrospinal fluid, but it is a nonspecific sign. To better assess meningeal enhancement, the use of chemical fat suppression as well as delayed imaging following gadolinium may help in identifying its presence with an increased level of confidence [26]. Multifocal MR lesions such as in our patient are suggestive of inflammatory or metastatic disease, while a single lesion is usually observed more frequently in patients with primary brain tumors [23]. Multifocal primary brain tumors or combinations of primary and secondary tumors have been reported, however, in the same patient [27].

Cerebrospinal fluid analysis was important for the diagnosis in this dog. Other methods to diagnose *Prototheca* spp. infection include bacteriological culture, using blood agar and common mycologic media, from colonic scrapping, cerebrospinal fluid, or any other infected tissue [7, 14]. The reason for a negative culture in the dog in this report is unclear, but it could have been due to delayed tissue sampling, which was performed at the time of necropsy.

4. Conclusion

Although rare in dogs, *Prototheca* spp. infection should be considered when MR examination is suggestive of meningoencephalitis, even if there is no evidence of gastrointestinal disease.

Abbreviations

CNS: Central nervous system
FLAIR: Fluid-attenuated inversion recovery
GRE: Gradient echo
MRI: Magnetic resonance imaging.

Conflict of Interests

The authors have no relevant affiliations or financial involvements with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in this paper.

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