In cooperation with

What Is Your Neurologic Diagnosis?

A 10-week-old 11.9-kg (26.2-lb) sexually intact female English Labrador Retriever was referred for neurologic evaluation because of episodic ataxia of 1 month's duration. During these episodes, which typically lasted several minutes, the dog would stumble through the house, listing from side to side with a kyphotic posture; its mentation appeared slightly altered, but the dog did not urinate or defecate during these episodes. The owners perceived that the episodes occurred more often when the dog was apparently nervous. The owners also reported that the dog was overall more lethargic. The referring veterinarian performed serologic testing for antibodies against *Neospora caninum* and *Toxoplasma* spp and prescribed clindamycin (9.4 mg/kg [4.3 mg/lb], PO, q 12 h) for 5 days, and then prescribed trimethoprim-sulfamethoxazole (10.1 mg/kg [4.6 mg/lb], PO, q 12 h) to be given in addition to clindamycin for 18 days. No improvement was noted in clinical signs as a result of treatment. At the referral evaluation, the dog was bright and physical examination findings were unremarkable. A neurologic examination was performed.

Neurologic examination

Observation

Mental	Alert	X	Depressed		Disoriented		Stupor		Coma		
Posture	Normal	X	Head tilt		Tremor		Falling				
Gait	Normal	X	Ataxia		Pelvic limbs		All 4		Circling		
Paresis	Pelvic limbs		Tetra		Hemi		Mono				
Other											

Postural reactions

Key: 4 = Exaggerated, clonus; 3 = Exaggerated; 2 = Normal; 1 = Diminished; 0 = None; NE = Not evaluated.

	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Wheelbarrow	2	2		
Hopping	2	2	2	2
Extensor postural thrust			2	2
Proprioceptive pos	2	2	2	2
Hemistand/walk	2	2	2	2
Placing–tactile	2	2		
Placing–visual	2	2		

Spinal reflexes

	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Quadriceps			2	2
Extensor carpi	2	2		
Flexion	2	2	2	2
Crossed extensor	0	0	0	0
Perineal			2	2

Cranial nerves

	L	R		L	R	Comments
II,VII–Vision menace	2	2	VIII–Nystagmus, resting	2	2	
II, III–Pupils resting	2	2	VIII–Nystagmus, change	2	2	
Stim L	2	2	V–Sensation	2	2	
Stim R	2	2	VII–Facial mm	2	2	
II–Fundus	2	2	V,VII–Palpebral flex	2	2	
III, IV,VI–Strabismus, resting	2	0	IX, X–Gag	2	2	
III, IV,VI,VIII–Strabismus, position	2	0	XII–Tongue	2	2	

Sensation (Locate and describe any abnormality)

Hyperesthesia	3	Signs of pain in response to direct palpation of the lumbar region of the vertebral column
Superficial pain	NE	Not examined because of apparently normal ambulation and proprioception
Cutaneous reflex	2	
Deep pain	NE	Not examined because of apparently normal ambulation and proprioception

What is the problem? Where is the lesion? What are the most probable causes of this problem? What is your plan to establish a diagnosis? Please turn the page.

Assessment

Anatomic diagnosis

Problem	Rule out location
Episodic ataxia with altered mentation, possible atypical seizure activity	Cerebrum
Signs of lumbar region pain	Lumbar portion of the spinal cord or lumbar muscles; less likely related to the vertebrae

Likely location of 1 lesion

Forebrain or multifocal lesion of the CNS, including the lumbar portion of the spinal cord, or separate cause of lumbar spinal cord, muscle, or vertebral column hyperesthesia

Etiologic diagnosis—The differential diagnoses for multifocal neurologic disease in this 10-week-old dog included infectious disease, intracranial congenital malformation with secondary changes to CSF flow with or without syringohydromyelia, and multifocal trauma. The initial diagnostic plan included a CBC, serum biochemical analysis, and assessment of plasma total thyroxine concentration to evaluate general wellness. Magnetic resonance imaging[a] of the brain was recommended to detect potential structural abnormalities within the brain, peripheral nerves, skull, or surrounding tissues. Cerebrospinal fluid sample collection via cerebellomedullary cisternal puncture following MRI with subsequent fluid analysis and microbial culture was recommended to detect inflammation or infectious organisms. Given the dog's lack of response to treatment, additional serologic testing to detect fungal and respiratory diseases was considered, depending on imaging findings.

Diagnostic test findings—The CBC revealed mild lymphocytosis (6,460 lymphocytes/µL; reference interval, 690 to 4,500 lymphocytes/µL) with no other notable abnormalities. Results of serum biochemical analysis were considered normal. The plasma total thyroxine concentration was 0.7 µg/dL (reference interval, 1 to 4 µg/dL), which was assumed to be attributed to euthyroid sick syndrome. The dog was anesthetized, and MRI of the brain was performed. Image sequences included sagittal and transverse T2-weighted, transverse T2-weighted fluid-attenuated inversion recovery, transverse gradient echo T2*, and 3-plane pre- and postcontrast T1-weighted images of the brain. A sagittal T2-weighted sequence of the thoracolumbar portion of the vertebral column was also included. The MRI images were interpreted by a board-certified veterinary radiologist. On precontrast T1-weighted images, there was mild, diffuse widening of the sulci, most likely attributable to the dog's young age **(Figure 1)**. There was mild, bilateral symmetric periventricular hyperintensity on fluid-attenuated inversion recovery and T2-weighted images as well as mild fluid accumulation and thickening of the mucosa in the frontal sinuses bilaterally. Images of the thoracolumbar portion of the vertebral column appeared normal. Postcontrast T1-weighted images had faint contrast enhancement of the right caudal caudate nucleus, subtle multifocal meningeal enhancement surrounding the cerebral hemispheres (especially on the right side), and contrast enhancement of the thickened frontal sinus mucosa bilaterally. Findings were consistent with inflammatory disease of the brain and bilateral frontal sinusitis. Analysis of the CSF sample revealed

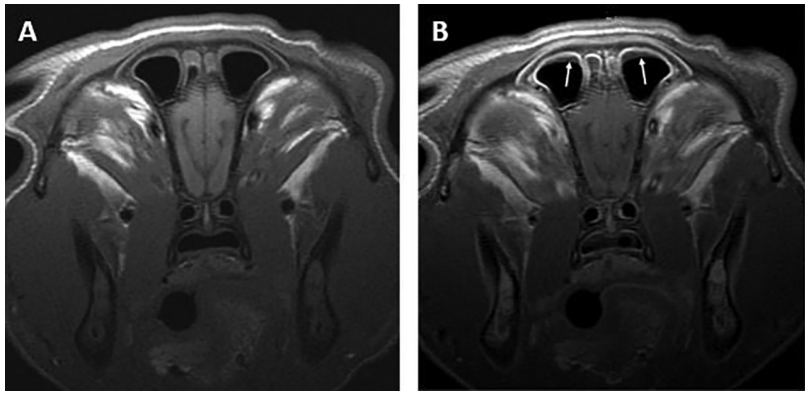

Figure 1—Transverse T1-weighted images (obtained before [A] and after [B] administration of contrast medium) of the brain and frontal sinuses of a 10-week-old female English Labrador Retriever that was examined for episodic ataxia of 1 month's duration. Notice thickening of the lining of the frontal sinuses and fluid accumulation along that lining (arrows).

a WBC count of 5 WBCs/µL (reference interval, 0 to 5 WBCs/µL) and an RBC count of 120 RBCs/µL (reference limit, 0 RBCs/µL), which were suggestive of mild inflammation and blood contamination, respectively. Although the reference interval for canine leukocyte cell counts is 0 to 5 WBCs/µL, results of analyses of CSF samples obtained from cerebellomedullary cisternal puncture from healthy dogs have indicated that CSF nucleated cell counts in healthy dogs typically range from 0 to 2 WBCs/µL (mean ± SD counts in 2 studies,[1,2] 1.4 ± 0.7 WBCs/µL and 1.5 ± 1.4 WBCs/µL). The CSF microprotein concentration for the dog of the present report was high (50 mg/dL; upper reference limit, 30 mg/dL), which was consistent with inflammation. Cytologic examination of the CSF sample revealed mild mononuclear pleocytosis comprised of well-differentiated lymphocytes and monocytes, with no evidence of infectious agents or neoplastic cells. The MRI and CSF analysis findings for this dog were considered most consistent with meningitis and frontal sinusitis.

Microbial culture of the CSF sample yielded no growth after 72 hours. While results of the CSF sample culture were pending, the dog was treated with clindamycin (12.6 mg/kg [5.7 mg/lb], PO, q 12 h), trimethoprim-sulfamethoxazole (20.2 mg/kg [9.2 mg/lb], PO, q 12 h), and metronidazole (15.8 mg/kg [7.2 mg/lb], PO, q 12 h) in addition to administration of anticonvulsants, extended-release levetiracetam (42.0 mg/kg [19.1 mg/lb], PO, q 12 h), and potassium bromide (42.0 mg/kg [19.1 mg/lb], PO, q 24 h). Results of serologic testing for antibodies against *N caninum* and *Toxoplasma* spp performed by the referring veterinarian were negative.

After 1 week of treatment, the dog's seizures were controlled but it continued to be lethargic. Because the results of all other testing for infectious agents had been negative and there was MRI evidence of meningitis and frontal sinusitis, a serum sample and swab specimens of the oropharynx were obtained to test for *Coccidioides* antigens[b] and *Aspergillus* antigens[c] by enzyme immunoassay and for canine respiratory tract diseases[d] (infection with *Bordetella bronchiseptica,* canine adenovirus type 2, canine distemper virus, canine parainfluenza virus, canine respiratory coronavirus, canine pneumovirus, or *Mycoplasma cynos)* by use of a PCR assay panel. Testing for infection with *Cryptococcus* sp was not performed because of the dog's young age and because that organism was regionally less common. Results of testing for circulating *Coccidioides* and *Aspergillus* antigens were negative. The respiratory disease panel yielded a positive result for *Bordetella* DNA and *M cynos* DNA.

Comments

Mycoplasma cynos is one of several opportunistic pathogens involved in cases of canine infectious respiratory tract disease. *Mycoplasma cynos* can be isolated from the lungs, trachea, conjunctiva, and tonsils and has been implicated as a cause of canine pneumonia.[3] In a recent study,[4] *Mycoplasma canis* was cultured from the brains of 4 of 5 dogs with granulomatous meningoencephalomyelitis and 4 of 8 dogs with necrotizing meningoencephalitis, although the clinical importance of these findings was unclear. *Mycoplasma edwardii* was cultured from the brain of a 6-week-old dog with suppurative and histiocytic meningoencephalitis.[5] *Mycoplasma hominis* has been identified as a rare cause of brain abscesses and meningitis in human neonates.[6,7] These facts suggest that *Mycoplasma* spp may be important as a cause of meningoencephalitis, but more studies would be required to determine the prognosis for dogs with clinical signs of mycoplasmal meningitis, predilection of mycoplasmas for certain ages or breeds of dogs, or propensity of mycoplasmas to cause a particular type of meningoencephalitis (eg, granulomatous vs necrotizing meningoencephalitis).

Infection with *Bordetella* spp may have contributed to this dog's sinusitis, but it was of questionable influence with regard to the dog's neurologic signs. To the authors' knowledge, there are no published reports of *Bordetella* infection causing neurologic disease or signs in any species. On the basis of the lack of other findings, positive result of the mycoplasma PCR assay, and subsequent response to treatment for the dog of the present report, a presumptive diagnosis of meningoencephalitis secondary to *M cynos* infection was made.

First-line treatment for *Mycoplasma* infection in cases of canine infectious respiratory tract disease is administration of doxycycline or amoxicillin–clavulanic acid.[8] After diagnosis of *M cynos* infection, the dog of the present report was treated with doxycycline (12.0 mg/kg [5.5 mg/lb], PO, q 12 h) and amoxicillin–clavulanic acid (15.1 mg/kg [6.9 mg/lb], PO, q 12 h). Administration of all other medications was discontinued with the exception of anticonvulsants. Prednisone was not administered at any time. The dog became seizure free, and all clinical signs of illness resolved. Six weeks after commencement of this treatment, PCR assays revealed that the dog was negative for *Mycoplasma* spp and *Bordetella* spp (*Bordetella* infection would also have been appropriately treated with doxycycline). Administration of antimicrobials to the dog was discontinued, and at a 12-month postreferral evaluation, the dog had had no breakthrough seizure events or return of any clinical signs. Regardless of the paucity of information regarding the diagnosis and management of intracranial disease caused by mycoplasmal infection, such infections should be considered as a differential diagnosis for dogs with inflammatory brain disease, especially when there is evidence of concurrent respiratory tract disease. Without doubt, further studies to explore the clinical importance of mycoplasmal meningoencephalitis are warranted.

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The authors declare that there were no conflicts of interest.

Footnotes

a. SIGNA MRI machine, 1.5T, GE Healthcare, Waukesha, Wis.
b. *Coccidioides* Antigen Quantitative EIA, MiraVista Diagnostics, Indianapolis, Ind.
c. *Aspergillus* Galactomannan Antigen EIA, MiraVista Diagnostics, Indianapolis, Ind.
d. Canine Respiratory Disease (CRD) RealPCR Panel (standard), Idexx Laboratories Inc, Westbrook, Me.

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This report was submitted by Olivia R. Shoup, MS, DVM; Jocelyn J. Cooper, DVM; Danielle L. D. Powers, DVM; and Matthew S. Cannon, DVM; from MissionVet Specialty & Emergency, San Antonio, TX 78249.

Address correspondence to Dr. Shoup (orshoup@gmail.com).

This feature is published in coordination with the American College of Veterinary Internal Medicine on behalf of the specialty of neurology. Contributors to this feature should contact Dr. Helen L. Simons (hsimons@avma.org) for case submission forms. Submissions will be sent to Dr. Karen Kline, DVM, DACVIM, for her review, except when Dr. Kline is an author.