



# What Is Your Neurologic Diagnosis?

**A** 3-year-old 5.9-kg (12.98-lb) neutered male domestic shorthair cat was referred to the University of Florida College of Veterinary Medicine Neurology Service for evaluation of sudden-onset blindness and a nasopharyngeal mass. Previously noted findings included bilateral mydriasis, absent pupillary light reflexes, absent menace response and dazzle reflex in the right eye, decreased menace response and dazzle reflex in the left eye, and dendritic ulcers in the left eye.

Electroretinographic findings for both eyes were considered normal. Results of prior abdominal ultraso-

nography, thoracic radiography, ventrodorsal skull radiography, a CBC, and a serum biochemical panel were also normal. Pharyngeal examination and rhinoscopy revealed a mass dorsal to the distal portion of the soft palate. Findings of an examination of a biopsy specimen of the mass were interpreted as normal nasopharyngeal tissue.

On physical examination, the cat was bright, alert, and responsive. Abnormalities included severe bilateral mydriasis and intermittent stertor. There was no ocular or nasal discharge, and fundic examination findings for both eyes were considered normal.

## 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										

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

### Postural reactions

	LF	RF	LR	RR
Wheelbarrow	2	2		
Hopping	2	2	2	2
Ext postural thrust			NE	NE
Proprioceptive pos	2	2	2	2
Hemistand/walk	NE	NE		
Placing-tactile	2	2		
Placing-visual	NE	NE		

### Spinal reflexes

	LF	RF	LR	RR
Quadriceps			2	2
Extensor carpi	NE	NE		
Flexion	2	2	2	2
Crossed extensor	0	0	0	0
Perineal			NE	NE

### Cranial nerves

	L	R		L	R	Comments CN
II, VII-Vision menace	0	0	VIII-Nystagmus, resting	0	0	Pupils were fixed and dilated. Menace response and dazzle reflex were absent in both eyes. Direct and indirect pupillary light reflexes and physiologic nystagmus were absent bilaterally.
II, III-Pupils resting	2	2	VIII-Nystagmus, change	0	0	
Stim L	0	0	V-Sensation	2	2	
Stim R	0	0	VII-Facial mm	2	2	
II-Fundus	2	2	V, VII-Palpebral flex	2	2	
III, IV, VI-Strabismus, resting	0	0	IX, X-Gag	2	2	
III, IV, VI, VIII-Strabismus, position	0	0	XII-Tongue	2	2	

### Sensation (Locate and describe abnormal)

Hyperesthesia	0	
Superficial pain	2	
Cutaneous reflex	2	
Deep pain	NE	

**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
Sudden-onset blindness (bilateral)	Retina, cranial nerve II, midbrain, or cerebral cortex
Absent pupillary light reflex (bilateral)	Retina, cranial nerve II, or cranial nerve III
Absent menace response (bilateral)	Retina, cranial nerve II, forebrain, or cerebellum
Absent physiologic nystagmus	Cranial nerves III, IV, VI, or VIII; midbrain; cerebellum; or medial longitudinal fasciculus
Stertor	Nasal cavity or nasopharynx

### Likely location of I lesion

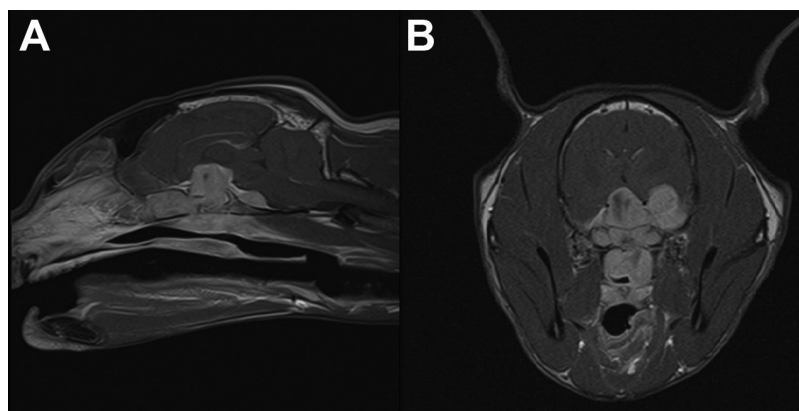
Disease of the CNS involving or affecting cranial nerves II, III, IV, or VI. Involvement of the nasal cavity or nasopharynx was suspected.

**Etiologic diagnosis**—On the assumption that the neurologic findings and nasopharyngeal mass were related, differential diagnoses included an infectious granuloma, cyst, or neoplasia such as lymphoma, squamous cell carcinoma, undifferentiated carcinoma, or craniopharyngioma.<sup>1</sup> The diagnostic plan included MRI of the entire head (to further evaluate the previously diagnosed nasopharyngeal mass and assess pathological changes to or around the optic nerves), repeated biopsies via retroflex nasopharyngeal endoscopy of the previously diagnosed nasopharyngeal mass (to get deeper samples for examination), and submission of a serum sample to determine the *Cryptococcus* antigen latex agglutination titer.

**Diagnostic test findings**—The cat was anesthetized and MRI<sup>a</sup> of the head was performed. Sagittal and transverse T2-weighted images and transverse FLAIR, T2\*, and T1-weighted images were obtained. Following IV administration of gadodiamide<sup>b</sup> (71.75 mg/kg [32.61 mg/lb]), sagittal, transverse, and dorsal plane T1-weighted images were obtained. The MRI examination revealed a large, lobulated, contrast-enhancing

mass that was centered at the sella turcica. Caudally, the mass extended ventral to the pons; rostrally, it extended ventrally into the nasopharynx and into the right retrobulbar space. The mass also extended to the right side, compressing and dorsally displacing the right frontal and temporal lobes. Because of the mass, there was severe stenosis of the nasopharynx (**Figure 1**). Hyperintense material filled the lumen of both tympanic bullae on T2-weighted and fluid attenuated inversion recovery images.

The cat's *Cryptococcus* antigen latex agglutination titer was 1:256. During retroflex pharyngoscopy, a large sessile mass with indistinct borders was identified on the dorsal aspect of the nasopharynx. Biopsy specimens were collected with a flexible biopsy instrument. Cytologic examination of impression smears of the biopsy samples of the mass revealed pyogranulomatous and lymphoplasmacytic inflammation associated with yeasts consistent with *Cryptococcus* spp. The biopsy samples were submitted for histologic evaluation, and findings later confirmed an intracranial granulomatous mass secondary to cryptococcal infection.



**Figure 1**—Sagittal (A) and transverse (B) T1-weighted MRI images obtained after contrast agent administration from a 9-year-old cat that was evaluated because of sudden-onset blindness and a nasopharyngeal mass. Notice the expansive, lobulated, contrast-enhancing mass focused in the region of the sella turcica.

## Comments

The 2 pathogens that most commonly cause cryptococcal infection in cats are *Cryptococcus neoformans* and *Cryptococcus gattii*; infections with these pathogens are clinically indistinguishable.<sup>2</sup> Infection of the CNS by *Cryptococcus* organisms is uncommon and can affect solely the CNS or concurrently the CNS and other organ systems. Cats with cryptococcosis typically develop signs of nasal cavity disease and uncommonly have solely neurologic signs.<sup>3</sup>

The most useful diagnostic test for confirming cryptococcal infection is the *Cryptococcus* antigen latex agglutination test. The specificity of this test for detection of cryptococcal infection was 100% in study trials.<sup>4,5</sup> In the case described in the present report, the result of the *Cryptococcus* antigen latex agglutination test and the findings of microscopic examination of impression smears and biopsy specimens of the invasive mass were instrumental in determining that the mass was attributable to cryptococcosis and not to neoplasia. In humans, cryptococcosis can appear as tumor-like intraparenchymal masses containing yeast organisms and inflammatory cells (often termed cryptococcomas); these masses more frequently develop in immune-compromised patients.<sup>6,7</sup> The focal pathological changes and mass-like appearance in the cat of the present report were similar to those of cryptococcomas in humans.

The cat of the present report had neurologic signs consistent with descriptions of cavernous sinus syndrome in cats<sup>8-10</sup>; however, blindness is not considered a clinical sign of cavernous sinus syndrome because the optic nerves are not located in the cavernous sinus. The cat also had fluid within the tympanic bullae bilaterally. This may have been either a result of compression and physical obstruction of the auditory tubes by the mass or dysfunction of the tensor veli palatine muscle secondary to dysfunction of the mandibular branch of cranial nerve V.<sup>11</sup>

The cat was hospitalized for diuresis,<sup>c</sup> anti-inflammatory corticosteroid<sup>d</sup> treatment, and administration (as a constant rate infusion) of amphotericin B<sup>e</sup> (0.5 mg/kg [0.23 mg/lb]) diluted in 5% dextrose in water. The cat was discharged from the hospital, and the owner was to administer fluconazole<sup>f</sup> (50 mg [22.7 mg/lb], PO, q 12 h) and prednisolone<sup>g</sup> (2.5 mg [1.14 mg/lb], PO, q 24 h). At a recheck examination 9 days later, stertor was no longer present and the cat had vision with normal ophthalmic responses and anisocoria (the left eye was mydriatic, compared with the right eye). A serum biochemical panel was performed at that time, and renal variables were within reference ranges. Histologic examination of the biopsy specimens of the mass revealed severe, subacute, diffuse, necrotizing, and fibrinous rhinitis with intralesional yeasts consistent with *Cryptococcus* spp.

In cats and dogs, *Cryptococcus* infection affecting the CNS has a more negative impact on outcome, compared with systemic infection, warranting prompt

and aggressive treatment.<sup>12</sup> Amphotericin B and fluconazole are the recommended treatments for CNS infections in cats.<sup>2</sup> In the case described in the present report, a liposomal formulation of amphotericin B was not available in a timely manner. To decrease the likelihood of nephrotoxic effects of amphotericin B, the cat received IV fluid therapy prior to drug treatment. The dose of 0.5 mg of amphotericin B/kg was substantially lower than the cumulative median dose of 16 mg/kg (7.27 mg/lb) used in cats with cryptococcosis that were cured on first attempt in a retrospective study of 59 cats.<sup>12</sup> At a recheck examination 10 days after the first dose of amphotericin B, the cat appeared almost normal; hence, administration of the drug was not continued. It was recommended that a recheck MRI examination of the cat's head and a repeated cryptococcal antigen latex agglutination test be performed in 3 to 4 months to evaluate the size of the mass and to direct ongoing treatment. Ten months after the initial MRI examination, the cat was neurologically normal with only very mild anisocoria (mild miosis of the left pupil); the cat's *Cryptococcus* antigen latex agglutination titer was 1:16.

The case described in the present report illustrated that the clinical appearance of *Cryptococcus* infection can be similar to that of an invasive tumor. It is important to consider cryptococcosis as a differential diagnosis in cats with neurologic signs, especially those with an expansive mass yet no evidence of systemic disease, and to perform the necessary diagnostic procedures to determine whether *Cryptococcus* infection is present.

## Acknowledgments

No funding was used for this report.

This material has not been previously presented.

## Footnotes

- a. Toshiba Titan, Toshiba America Medical Systems, Tustin, Calif.
- b. Gadodiamide injection, Omniscan, Daiichi Sankyo, Colorado Springs, Colo.
- c. Lactated Ringer Solution, Baxter Healthcare Corp, Marion, NC.
- d. Dexamethasone sodium phosphate, 4-mg injection, Bimed-MTC Animal Health Inc, Cambridge, ON, Canada.
- e. Amphotericin B for injection USP, X-Gen Pharmaceuticals Inc, Horseheads, NY.
- f. Fluconazole, 100-mg tablets, Teva Pharmaceuticals, Forest, Va.
- g. Prednisolone, PrednisTab, 5 mg, Lloyd Inc, Shenandoah, Iowa.

## References

1. Nagata T, Nakayama H, Uchida K, et al. Two cases of feline malignant craniopharyngioma. *Vet Pathol* 2005;42:663-665.
2. Pennisi MG, Hartman, K, Lloret A, et al. Cryptococcosis in cats: ABCD guidelines on prevention and management. *J Feline Med Surg* 2013;15:611-618
3. O'Brien CR, Krockenberger MB, Wigney DI, et al. Retrospective study of feline and canine cryptococcosis in Australia from 1981 to 2001: 195 cases. *Med Mycol* 2004;42:449-460
4. Medleau L, Marks MA, Brown J, et al. Clinical evaluation of a cryptococcal antigen latex agglutination test for diagnosis of

- cryptococcosis in cats. *J Am Vet Med Assoc* 1990;196:1470-1473.
5. Malik R, McPetrie R, Wigney DI, et al. A latex cryptococcal antigen agglutination test for diagnosis and monitoring of therapy for cryptococcosis. *Aust Vet J* 1996;74:358-364.
  6. Lee SC, Dickson DW, Casdevall A. Pathology of cryptococcal meningoencephalitis: analysis of 27 patients with pathogenetic implications. *Hum Pathol* 1996;27:839-847.
  7. Klock C, Cerski M, Goldani LZ. Histopathological aspects of neurocryptococcosis in HIV-infected patients: autopsy report of 45 patients. *Int J Surg Pathol* 2009;17:444-448.
  8. Theisen SK, Podell M, Schneider T, et al. A retrospective study of cavernous sinus syndrome in 4 dogs and 8 cats. *J Vet Intern Med* 1996;10:65-71.
  9. Guevar J, Gutierrez-Quintana R, Peplinski G, et al. Cavernous sinus syndrome secondary to intracranial lymphoma in a cat. *J Feline Med Surg* 2014;16:513-516.
  10. Perazzi A, Bernardini M, Mandara M, et al. Cavernous sinus syndrome due to osteochondromatosis in a cat. *J Feline Med Surg* 2013;15:1132-1136.
  11. Kent M, de Lahunta A, Platt SR, et al. Prevalence of effusion in the tympanic cavity in dogs with dysfunction of the trigeminal nerve: 18 cases (2004-2013). *J Vet Intern Med* 2013;27:1153-1158.
  12. O'Brien CR, Krockenberger MB, Martin P, et al. Long-term outcome of therapy for 59 cats and 11 dogs with cryptococcosis. *Aust Vet J* 2006;84:384-391.

---

This report was submitted by Kryssa L. Johnson, DVM; Michele D. James, DVM; and Sheila Carrera-Justiz, DVM; from the Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610.

Address correspondence to Dr. Carrera-Justiz (carrerajustiz.s@ufl.edu).

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 (800-248-2862, ext 6692) for case submission forms. Submissions will be sent to Dr. Karen Kline, DVM, DACVIM, for her review, except when Dr. Kline is an author.