In cooperation with

What Is Your Neurologic Diagnosis?

A 12-year-old 14-kg spayed female mixed-breed dog was evaluated because of behavior changes of a few months' duration characterized by lethargy and short episodes of head tremors with irregular blinking of the eyes. A few weeks prior to presentation, the dog also began pacing more, developed a tendency to become stuck in corners, and began defecating inappropriately in the house. At the evaluation, notable general physical examination findings included a grade 4/6 left systolic heart murmur, strong femoral pulses that were occasionally asynchronous with the heartbeat, a body condition score of 4/9, muscle condition score of 2/3, and multiple subcutaneous masses consistent with lipomas. A neurologic examination was performed.

Neurologic examination

Observation

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

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

Postural reactions	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Wheelbarrow	NE	NE		
Hopping	NE	NE	NE	NE
Extensor postural thrust			NE	NE
Proprioceptive positioning	2	1	2	1
Hemistand/walk	NE	NE	NE	NE
Placing–tactile	NE	NE		
Placing–visual	NE	NE		

Spinal reflexes	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Quadriceps			3	3
Extensor carpi	NE	NE		
Flexion	2	2	3	3
Crossed extensor	0	0	3	3
Perineal			2	2

Cranial nerves

	L	R
II, VII–Vision menace	2	1
II, III–Pupils resting	2	2
Stim L	1	1
Stim R	1	1
II–Fundus	2	2
III, IV, VI–Strabismus, resting	0	0
III, IV, VI, VIII–Strabismus, position	0	0

	L	R
VIII–Nystagmus, resting	0	0
VIII–Nystagmus, change	0	0
V–Sensation	2	2
VII–Facial mm	2	2
V, VII–Palpebral flex	2	2
IX, X–Gag	2	2
XII–Tongue	2	2

Comments

Fundic examination findings were unremarkable.

Sensation (Locate and describe any abnormality)

Hyperesthesia	0	
Superficial pain	NE	
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
Tendency to circle right	Prosencephalon or diencephalon, right side more affected than the left side
Tendency to pace and get stuck in corners	Prosencephalon or diencephalon
Reduced pupillary light reflex (bilateral)	Bilateral iris sphincters, bilateral cranial nerve III, Edinger-Westphal nuclei, or pretectal nuclei
Reduced menace response (right)	Right cranial nerve II, optic tract, left lateral geniculate nucleus, visual cortex, pontine nucleus, or cerebellum; the right cranial nerve VII was considered less likely because complete menace response was evident intermittently
Mild head tilt (right)	Right caudal fossa (vestibular nuclei of medulla and cerebellum) or right cranial nerve VIII
Delayed hopping right side (thoracic and pelvic limbs)	Left side of the prosencephalon, left side of the diencephalon, right caudal fossa, or right side of C1-5
Increased pelvic limb reflexes with crossed extensor reflex	T3-L3 spinal segments

Likely location of 1 lesion

Midline region of the prosencephalon or of the diencephalon or multifocal disease

Etiologic diagnosis—The dog had a progressive disease that had caused nonlateralizing signs localized largely to the prosencephalon or diencephalon. Differential diagnoses included neoplasia (considered most likely) and infectious, inflammatory, or degenerative disease. Although the dog had a heart murmur, a vascular event was considered far less likely given the progression rather than resolution of clinical signs. The initial diagnostic plan consisted of a CBC, serum biochemical analysis, and 3-view thoracic radiography prior to anesthesia for further assessments. Brain MRI and collection of a CSF sample for analysis would then be pursued if nothing important was identified by the preanesthetic evaluations.

Diagnostic test findings—Results of the CBC were unremarkable. The serum biochemical analysis revealed mildly high total protein and albumin concentrations consistent with hemoconcentration and mildly high bilirubin concentration consistent with the sample being moderately hemolyzed. Serum alanine aminotransferase activity was also mildly high and was considered an age-related finding. Three-view thoracic radiography revealed mild sternal lymphadenopathy (reactive or neoplastic) and left atrial enlargement consistent with suspected myxomatous mitral valve degeneration. There was no evidence of metastatic disease.

The dog was anesthetized and MRI of the brain was performed with a 1.5-T scanner.[a] Sagittal (T2-weighted), transverse (T2-weighted, FLAIR, T1-weighted, T2*-gradient echo, diffusion-weighted imaging, and apparent diffusion coefficient), and dorsal (T1-weighted) images were acquired. In addition, T1-weighted images were obtained after contrast[b] administration.

A large, rounded to lobular, 22 X 18-mm mass centered on the sella turcica was found **(Figure 1)**. On T2-weighted and FLAIR images, 3 distinctly different intensities within the mass were evident: compared with regional gray matter, the central portion was hypointense, the mid-portion was isointense, and the peripheral portion was hyperintense. The intensities had a similar gradient on the T2*-gradient echo, diffusion-weighted imaging, and apparent diffusion coefficient images. On T1-weighted images, the central region of the mass appeared hyperintense, whereas the intensities of the mid-portion and peripheral portion remained isointense and hyperintense, respectively. On T1-weighted images obtained after IV administration of contrast agent[b] to the dog, moderate contrast enhancement in the mid-portion of the mass was evident; there was no contrast enhancement of the central and peripheral portions. The mass caused moderate dorsal displacement of the lateral and third ventricles. A sample of CSF was collected from the cerebellomedullary cistern; cytologic examination of the sample revealed no abnormalities (0 nucleated cells/μL, 33 RBCs/μL, and 38 mg of protein/dL).

The MRI appearance of the suprasellar mass combined with a lack of CSF abnormalities were consistent with a neoplastic process. Given the anatomic location, pituitary macroadenoma, pituitary adenocarcinoma, craniopharyngioma, or a germ cell tumor were considered. Although craniopharyngioma and germ cell tumor are rarely reported, the imaging findings supported their inclusion among the differential diagnoses because of the suprasellar location of and multiple intensities within the mass.[1,2] A tentative diagnosis of a suprasellar neoplasia (type unknown) was made.

Following MRI, the dog had a prolonged recovery from anesthesia; it had a stuporous mentation

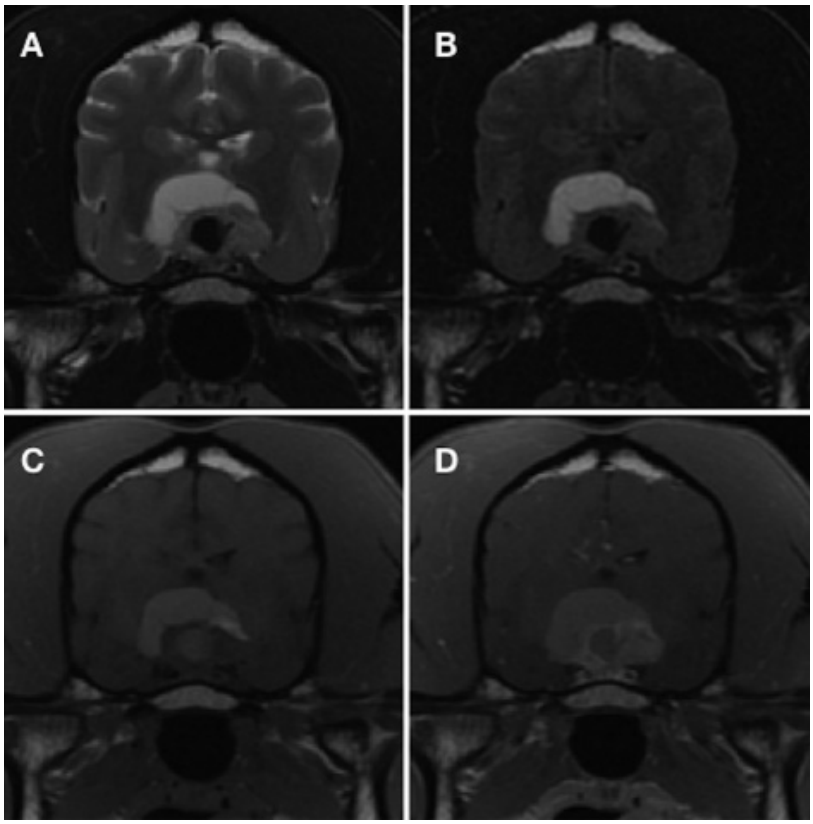

Figure 1—Magnetic resonance images obtained from a 12-year-old dog that was evaluated because of progressive neurologic signs of a few months' duration. The signs included lethargy, episodic head tremors with irregular blinking, pacing, getting stuck in corners, and inappropriate defecation. A—Transverse T2-weighted image at approximately the level of the mid-section of a suprasellar mass. Compared with the regional gray matter, the central region of the mass is hypointense, the mid-portion is isointense, and the peripheral portion is hyperintense. B—Transverse FLAIR image at the same level of the mass as in panel A. The mass appears similar as on the T2-weighted image, with the central region of the mass being hypointense, the mid-portion isointense, and the peripheral portion hyperintense compared to regional gray matter. C—Transverse T1-weighted image at the same level of the mass as in panel A. The central portion of the mass appears hyperintense when compared to regional gray matter, while the central portion and peripheral portion remain isointense and hyperintense respectively similar to the T2-weighted images. D—Transverse T1-weighted image at the same level of the mass as in panel A after IV administration of contrast medium. There is moderate contrast enhancement in the mid-portion of the mass, while the peripheral and central portions have no contrast enhancement.

for over 4 hours before being moved to the intensive care unit. The following morning, the dog was still only minimally responsive to stimuli. Within 24 hours after anesthesia, the dog made a full recovery and was discharged from the hospital. The owner was instructed to administer the dog an anti-inflammatory dose of prednisone (0.7 mg/kg/d [0.31 mg/lb/d]) for potential tumor-associated edema and an anticonvulsant (levetiracetam, 26.8 mg/kg [12.18 mg/lb], q 8 h) because of the concern for possible seizure activity. Radiation therapy was recommended as the treatment of choice for a suprasellar neoplasm, but given the dog's poor recovery from anesthesia, the owner did not pursue this option. On the basis of the suspected progressive nature of the disease, the dog's long-term prognosis was considered poor with an estimated survival time of approximately 3 months.

At 3.5 months after discharge from the hospital, the dog had developed a painful subungual mass on digit III of the left forelimb along with neurologic deficits that made it difficult for the dog to ambulate. The owner had concerns for the dog's quality of life and elected euthanasia by IV injections of propofol and pentobarbital. Thereafter, diagnostic necropsy was performed. The brain had a round, soft mass with a 1.5 X 0.9-cm transverse area in the suprasellar cistern. The mass extended into the overlying hypothalamus and completely effaced the underlying pituitary. Most of the mass was tan with a dark red to black central region that extended into approximately 50% of the transverse area. Histologic examination of sections of the mass confirmed it was a pituitary chromophobe macroadenoma of the sinusoidal type. Regional compression, rarefaction, neuronal necrosis, and Wallerian degeneration in the surrounding area along with cholesterol granulomas were noted. Other notable necropsy findings included steroid-induced hepatopathy, subungual squamous cell carcinoma of digit III of the left forelimb, and mild membranous glomerulonephritis.

Comments

Although the mass in the case described in the present report was a pituitary macroadenoma, its MRI appearance was unusual. On the basis of the tumor's multiple regional intensities on MRI, other suprasellar neoplasms such as a craniopharyngioma or germ cell tumor were considered, despite being much less common. Those 2 rare tumor types are more likely to have a heterogeneous pattern with variable intensities on MRI, whereas pituitary macroadenomas are often isointense on T1-weighted images and hyperintense on T2-weighted images and have uniform contrast enhancement throughout the mass.[1–3] However, the presence of cystic, hemorrhagic, or necrotic foci in pituitary tumors can result in their heterogeneous MRI appearance,[3] which was suspected to be the case for the mass in the dog of the present report.

The central portion of the dog's mass was hyperintense on T1-weighted images and hypointense on T2-weighted images and did not enhance following contrast administration. There were a few possible explanations for the unusual appearance of the central portion of the mass. A likely possibility was that there was an accumulation of proteinaceous fluid

within a cystic structure. Typically, cystic intracranial masses have fluid that resembles CSF, which is hypointense on T1-weighted images and hyperintense on T2-weighted images and does not display contrast enhancement.[3] However, MRI findings similar to those for the central region of the dog's mass have been described for certain cases of Rathke cleft cysts in humans. The cyst forms or extends into the suprasellar region when CSF becomes trapped in a malformed Rathke pouch. The MRI appearance of the fluid in the cyst is often similar to that of CSF; however, in approximately 30% to 50% of cases, the fluid is hyperintense on T1-weighted images and hypointense on T2-weighted images and is not associated with contrast enhancement. The cause of this appearance is multifactorial, including the presence of mucopolysaccharides as a result of an increase in mucin-secreting cells along the cyst wall, elevated cholesterol concentration in the fluid, and the presence of cellular debris.[4,5] In the dog of the present report, it was suspected that a cyst formed within the pituitary macroadenoma and caused an increase in protein concentration within the central region, thereby resulting in its distinctive appearance.

Another possible explanation for the MRI appearance of the central portion of the mass was hemorrhage. Hemorrhage may result in same pattern of intensities seen in the central portion of the mass, and pituitary macroadenomas have the potential to be hemorrhagic.[2,3] Although blood typically has a variable MRI appearance, an area of hemorrhage that contains free methemoglobin (commonly seen with subacute bleeding) will appear hyperintense on T1-weighted images.[2,6] The intensity of hemorrhage containing free methemoglobin on T2-weighted images can be variable, influenced by factors such as duration (chronicity being associated with variation in the state [eg, free vs intracellular] of the methemoglobin), but it commonly appears hypointense on T2-weightted images.[6] Additionally, in the case described in the present report, the central region of the mass was grossly dark red to black, which could subjectively support chronic hemorrhage as an explanation; however, there was no histologic evidence of hemorrhage, making this explanation less likely.

Pituitary macroadenomas can either be functional (secreting ACTH) or nonfunctional. Clinical signs relating to functional pituitary macroadenomas can be hyperadrenocorticism secondary to ACTH secretion, neurologic signs relating to the tumor's occupation of space in the brain, or both. Nonfunctional pituitary macroadenomas are usually associated with clinical signs that solely relate to space-occupying effects.[7] The neurologic signs vary depending on the invasiveness of the mass and the extent of tumor-associated compression of the brain; such signs include behavior changes, mentation changes, seizures, inappetence, anisocoria, perceived or actual blindness, and pupillary light reflex abnormalities.[7,8] Given a lack of endocrine signs or serum biochemical findings supportive of hyperadrenocorticism and the presence of neurologic signs, a nonfunctional tumor was suspected and later confirmed in the case described in the present report.

For the dog of the present report, the signs of behavior change, suspected focal seizures, delayed postural reactions, reduced pupillary light reflexes, head tilt, and reduced menace response could be explained by a lesion in the suprasellar region extending into and compressing the surrounding structures. The increased pelvic limb reflexes with crossed-extensor reflex and normal muscle tone could have been caused by an unrelated subclinical myelopathy or may have been a normal variation for this dog. However, the clinical findings were consistent with a suprasellar pituitary macroadenoma, which was detected by MRI and later confirmed on the basis of necropsy and histopathologic findings. A suprasellar lesion should be considered in dogs with prosencephalic or diencephalic signs in combination with visual pathway deficits.

Footnotes

a. GE LX 1.5 Tesla MR Scanner, GE Healthcare, Chicago, Ill.
b. Magnevist (gandopentate dimeglumine), Bayer HealthCare Pharmaceuticals, Wayne, NJ.

References

1. Cook L, Tensley M, Drost WT, et al. MRI findings of suprasellar germ cell tumors in two dogs. *J Am Anim Hosp Assoc* 2018;54:167–172.
2. Bonneville F, Cattin F, Marsot-Dupuch K, et al. T1 signal hyperintensity in the sellar region: spectrum of findings. *Radiographics* 2006;26:93–113.
3. Dewey CW, da Costa RC. *Practical guide to canine and feline neurology.* 3rd ed. Wiley-Blackwell, 2015;98–114.
4. Shin JL, Asa SL, Woodhouse LJ, et al. Cystic lesions of the pituitary: clinicopathological features distinguishing craniopharyngioma, Rathke's cleft cyst, and arachnoid cyst. *J Clin Endocrinol Metab* 1999;84:3972–3982.
5. Naik VD, Thakore NR. A case of symptomatic Rathke's cyst. *BMJ Case Rep* 2013;2013:bcr2012006943.
6. Gomori JM, Grossman RI, Hackney DB, et al. Variable appearances of subacute intracranial hematomas on high-field spin-echo MR. *AJR Am J Roentgenol* 1988;150:171–178.
7. Kent MS, Bommarito D, Feldman E, et al. Survival, neurologic response, and prognostic factors in dogs with pituitary masses treated with radiation therapy and untreated dogs. *J Vet Intern Med* 2007;21:1027–1033.
8. DeLahunta A, Glass E. *Veterinary neuroanatomy and clinical neurology.* 3rd ed. St Louis: Penny Rudolph, 2009;487–501.

This report was submitted by Emily B. DuPont, VMD, and Scott C. Petesch, VMD; from the Matthew J. Ryan Veterinary Hospital, University of Pennsylvania, Philadelphia, PA 19104.

Please address correspondence to Dr. DuPont (edupont@tamu.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 (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.