What Is Your Diagnosis?

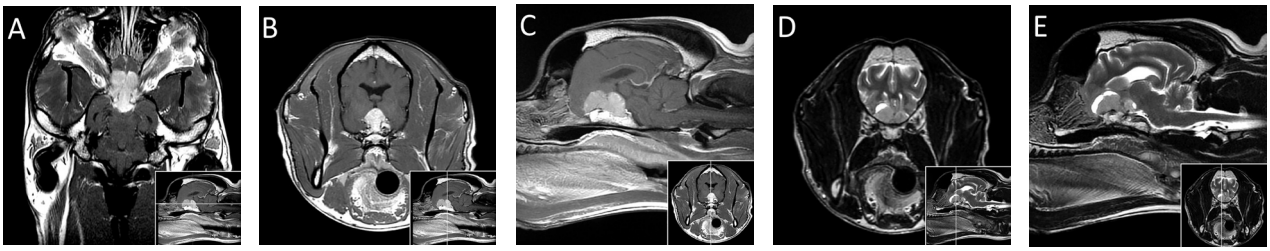

Figure 1—Postcontrast T1-weighted (A through C) and T2-weighted (D and E) MRI images in dorsal (A), transverse (B and D), and sagittal (C and E) planes at the level of the pituitary gland in a 7-year-old 28.0-kg (61.6-lb) castrated male Boxer evaluated because of a sudden onset of apparent blindness. In each panel, the anatomic location of the larger image is indicated by the white line transecting the smaller inset orthogonal image. A, B, and D—The dog's left is to the right of the image. C and E—Rostral is to the left of the image.

History

A 7-year-old 28.0-kg (61.6-lb) castrated male Boxer was referred to the Veterinary Referral Center of Colorado Specialty and Emergency Hospital because of a sudden onset of vision deficits followed by signs of complete blindness. One day earlier, the referring veterinarian had prescribed amlodipine besylate (0.4 mg/kg [0.2 mg/lb], PO, q 24 h) and maropitant citrate (1.8 mg/kg [0.8 mg/lb], PO, q 12 h) for suspected systemic hypertension and retinal detachment. Findings on initial neurologic and ophthalmologic examinations included bilaterally absent menace responses, mydriatic pupils, and sluggish, incomplete direct and consensual pupillary light reflexes (PLRs). Examination of the adnexa and the anterior and posterior segments of both eyes revealed no abnormalities, and results of a Schirmer tear test and tonometry were within reference limits for each eye. Results of fluorescein staining indicated no corneal ulceration in either eye, and electroretinography[a] revealed appropriate retinal function bilaterally. However, evaluation of colorimetric PLRs[b] revealed that neither eye had pupillary constriction in response to red light, but that both eyes had nearly complete pupillary constriction in response to blue light. Therefore, an immune-mediated retinitis (IMR) was suspected, and treatment with prednisolone (0.56 mg/kg [0.25 mg/lb], PO, q 12 h) and famotidine (0.71 mg/kg [0.32 mg/lb], PO, q 12 h) was initiated. The dog's vision improved within 48 hours after treatment was started, but then waxed and waned. Because the dog developed polyuria, the frequency of prednisolone (0.56 mg/kg, PO) administration was reduced to once every 24 hours, and treatment with mycophenolate mofetil (8.9 mg/kg [4.0 mg/lb], PO, q 12 h) was initiated. Treatment with amlodipine and maropitant was discontinued.

Signs of blindness returned despite medical treatment, and the dog was referred to the Colorado State University's Veterinary Teaching Hospital Ophthalmology Service, where an ophthalmologic examination was performed 4 months after initial onset of clinical signs. Examination revealed severely diminished vision, weak and incomplete direct and consensual PLRs, and mildly tortuous retinal vessels, with an otherwise clinically normal–appearing fundus bilaterally. As before, tear production and intraocular pressures were within reference limits for each eye, and both eyes had negative results for fluorescein staining. In addition, serum biochemical analyses (including bile acids analysis after withholding of food), CBC, and urinalysis were performed, and indirect systemic blood pressure was measured. Findings were unremarkable, aside from mildly high activities of liver enzymes (alkaline phosphatase, 588 U/L [reference range, 15 to 140 U/L]; alanine transaminase, 196 U/L [reference range, 10 to 90 U/L]; and γ-glutamyltransferase 14 U/L [reference range, 0 to 9 U/L]) attributed to long-term systemic administration of glucocorticoids. Because of the combination of a clinical response to glucocorticoid administration, unremarkable findings on fundic examination, and a lack of retinal vascular attenuation or tapetal hyperreflectivity (indicative of progressive retinal degeneration associated with chronic IMR or sudden acquired retinal degeneration syndrome [SARDS]) despite the 4-month duration since onset of clinical signs, an intracranial abnormality was suspected as the underlying cause of the dog's clinical signs. Therefore, the dog was anesthetized, and MRI was performed **(Figure 1)**.

Determine whether additional imaging studies are required, or make your diagnosis from Figure 1—then turn the page →

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Diagnostic Imaging Findings and Interpretation

On postcontrast[c] MRI images, a large, round-to-lobular mass that was centered above the sella turcica in the area of the pituitary gland and extended rostrally along the ventral aspect of the calvarium to the level of the olfactory bulb was identified **(Figure 2)**. The mass was isointense on T1-weighted images and hyperintense on T2-weighted images and fluid-attenuated inversion recovery (FLAIR) images (not presented). Lateral to the right rostral aspect of the mass was a semilunar rim that was isointense on T1-weighted and FLAIR images and was hyperintense on T2-weighted images. The incomplete suppression of this rim on FLAIR image was consistent with the rim being a proteinaceous fluid-filled region. The mass, indistinguishable in areas from the pituitary gland itself, was approximately 2.8 X 2.4 X 1.5 cm. There was no evidence of intracranial hemorrhage when evaluated with a gradient recalled echo sequence (not presented). The primary differential diagnosis was a pituitary-origin neoplasia, such as a pituitary adenocarcinoma or atypical invasive pituitary adenoma. Owing to the rostral invasion and irregular shape of the mass, a pituitary adenoma was less likely because such tumors are generally round and confined to the region of the sella. An extra-axial neoplasm with compression of normal pituitary gland tissue, such as by a meningioma or round cell tumor (lymphoma or mast cell tumor), was also considered unlikely, as were germ cell tumor, craniopharyngioma, and ependymoma.[1] The mass was in an inoperable location, and thus a definitive diagnosis could not be determined without substantial risk to the dog.

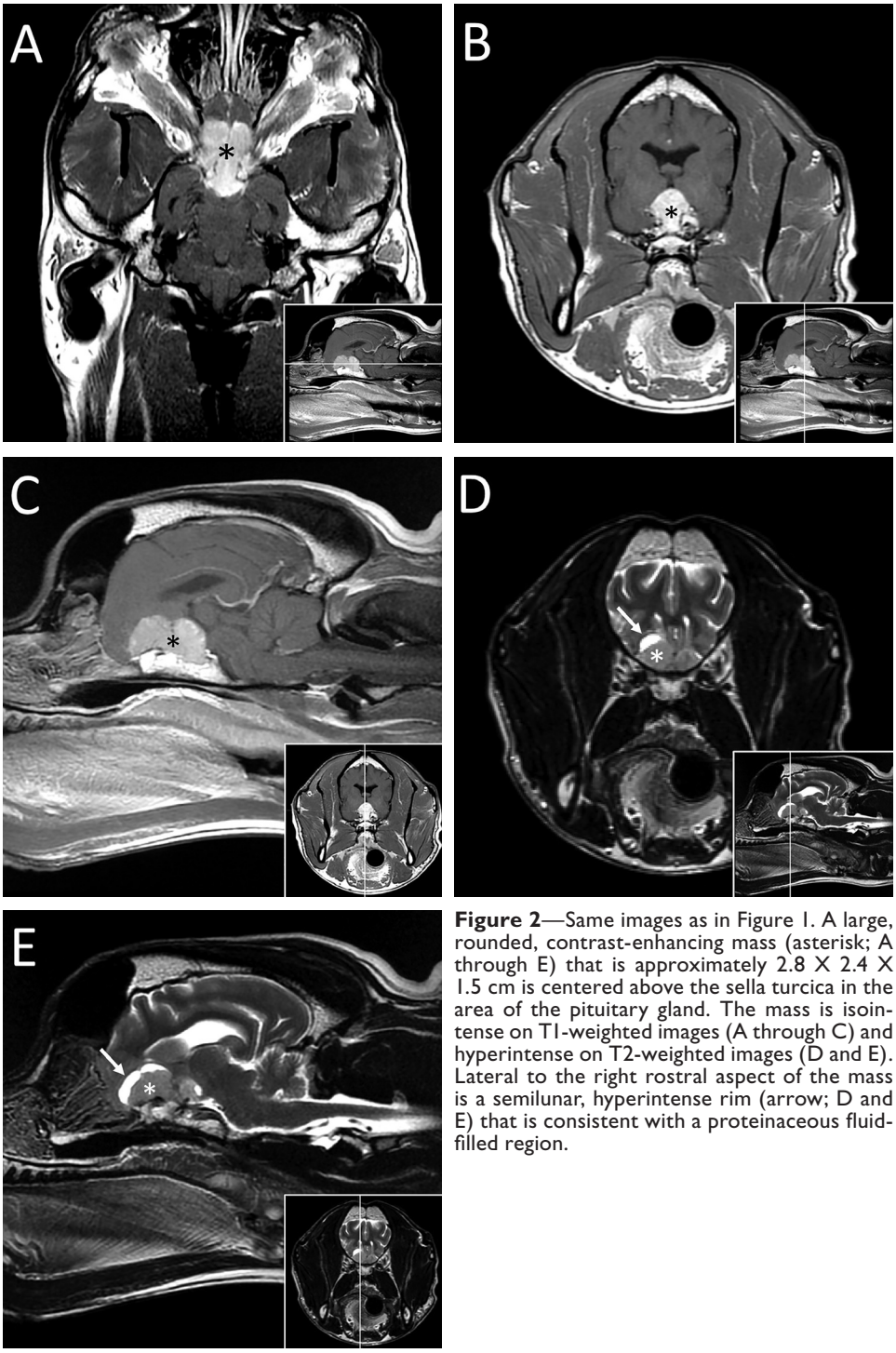

Figure 2—Same images as in Figure 1. A large, rounded, contrast-enhancing mass (asterisk; A through E) that is approximately 2.8 X 2.4 X 1.5 cm is centered above the sella turcica in the area of the pituitary gland. The mass is isointense on T1-weighted images (A through C) and hyperintense on T2-weighted images (D and E). Lateral to the right rostral aspect of the mass is a semilunar, hyperintense rim (arrow; D and E) that is consistent with a proteinaceous fluid-filled region.

Treatment and Outcome

Three days after MRI, the dog developed cluster seizures, and treatment with levetiracetam (26.8 mg/kg [12.2 mg/lb], PO, q 12 h) was initiated. Although no more seizures were observed, signs of apparent blindness remained. Recommended treatment options included intensity-modulated radiation therapy and stereotactic radiation therapy (SRT); surgery was not recommended because of the size and loca-

tion of the mass. Stereotactic radiation therapy was elected, and the dog received a total of 24 Gy administered in 3 fractions of 8 Gy each, once daily for 3 out of 4 consecutive days. Approximately 3 weeks following SRT, the dog appeared responsive to shadows and large-scale movements. Three months following SRT, the dog's visual improvement remained static. A recheck MRI in 1 to 3 months was recommended but declined by the owner.

Comments

Causes of blindness include true ocular disease (eg, corneal pigmentation, hyphema, cataract, retinal detachment, and glaucoma), retrobulbar disease (eg, abscess, neoplasia, and optic neuritis), and intracranial disease (eg, disease of the optic chiasm, optic tract, and visual cortex).[2] True ocular disease can largely be ruled out with results of ophthalmologic diagnostic procedures (eg, tonometry, anterior segment evaluation, and dilated fundic examination).[2] When no evidence of disease is present on ophthalmologic examination, electroretinography and evaluation of colorimetric PLRs can help rule out diseases of retinal function (eg, SARDS, IMR, and retinal atrophy).[2,3] Affecting the photoreceptor layer of the retina, SARDS and IMR generally cause acute to subacute onset of clinical signs of vision deficits combined with clinically normal–appearing retinas. Dogs affected by SARDS or IMR have a low to absent PLR to red light (wavelength of 630 nm, which stimulates photoreceptors) but a clinically normal PLR to blue light (wavelength of 480 nm, which stimulates retinal ganglion cells),[3,4] similar to the dog in the present report. Dogs with SARDS also have an extinguished electroretinogram tracing (no obvious electrical activity generated by the retina in response to light stimulus), whereas dogs in the early stages of IMR may have electroretinogram tracings that can be clinically normal, high, or low.[4] Further diagnostic imaging, such as ultrasonography, CT, or MRI, is then indicated to rule out retrobulbar and intracranial disease.[2]

Although MRI facilitates identification of masses in the suprasellar region of the calvarium, with contrast enhancement enabling delineation of a mass from surrounding structures, differentiating among tumor types is not possible because of the similar imaging characteristics (eg, contrast enhancement, shape, and compression of adjacent brain parenchyma) of intracranial tumors.[5-7] However, other imaging characteristics of intracranial tumors have been evaluated to help with diagnosis and prognosis. For instance, an invasive pituitary adenoma should be suspected in dogs > 7.7 years old with a mass > 1.9 cm in vertical height[5] in the region of the pituitary. The dog in the present report was 7 years old and had a tumor of 1.5 cm in vertical height; however, the dog's clinical signs of blindness and seizures were atypical for a pituitary tumor, which generally results in vague signs of CNS dysfunction, such as lethargy or mental dullness.[8] The vision deficits in the dog of the present report were likely caused by the mass, owing to its size and proximity to the optic chiasm.

Findings in the dog of the present report helped demonstrate that localizing an underlying cause of blindness requires detailed understanding of the entire visual pathway (from entry of light into the eyes to processing of the stimuli by the CNS) and that cross-sectional diagnostic imaging is essential to confirm an intracranial lesion. Compared with other imaging modalities, MRI is best suited because of its superior contrast resolution of soft tissues.

Footnotes

a. RETIport ERG, An-vision Inc, Salt Lake City, Utah.
b. Melan-100, BioMed Vision Technologies, Ames, Iowa.
c. Magnevist, Bayer HealthCare LLC, Whippany, NJ.

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