Bilateral cavernous sinus syndrome in dogs: 6 cases (1999–2004)

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Objective—To determine clinical features, diagnostic imaging abnormalities, underlying disease, disease progression, and outcome in dogs with bilateral cavernous sinus syndrome.

Design—Retrospective study.

Animals—6 dogs.

Procedure—Dogs were included if clinical signs consistent with bilateral cavernous sinus syndrome (ie, deficits of the third, fourth, and sixth cranial nerves and at least 1 of the first 2 branches of the fifth cranial nerve) were present and a lesion of the cavernous sinus was identified by means of diagnostic imaging or postmortem examination.

Results—5 dogs were evaluated because of problems referable to abnormal ocular motility or pupillomotor dysfunction, and 1 dog was evaluated because of partial motor seizures involving the face and bilateral mydriasis. Four dogs had neurologic signs referable to an extrasinusoidal lesion at the time of initial examination, and the remaining 2 dogs eventually developed extrasinusoidal signs. Besides neuroanatomic location, the only consistent neuroimaging feature was variably intense, heterogeneous enhancement of cavernous sinus lesions. Neoplasia was histologically confirmed as the underlying cause in 5 of the dogs and was suspected in the remaining dog. Median survival time for the 4 dogs that were treated was 199 days (range, 16 to 392 days).

Conclusions and Clinical Relevance—Results suggest that bilateral cavernous sinus syndrome is rare in dogs but should be suspected in dogs with compatible clinical signs. Affected dogs have a poor prognosis, and dogs with clinical signs of bilateral cavernous sinus syndrome should be systematically evaluated for neoplastic disease. (*J Am Vet Med Assoc* 2005;226:1105–1111)

Cavernous sinus syndrome (CSS) is a clinical disorder characterized by dysfunction of many of the **cranial nerves (CNs)** that course in intimate association with the cavernous sinuses, including the oculomotor nerve (CN III), trochlear nerve (CN IV), abducens nerve (CN VI), and the maxillary and ophthalmic branches of the trigeminal nerve (CN V).[1,2] Because CN III, CN IV, and CN VI provide innervation to the extraocular musculature and the parasympathetic efferent fibers of CN III are responsible for pupillary constriction, the most common clinical manifestations of CSS are external and internal ophthalmoparesis, ptosis, and mydriasis.[2-5] Sensory deficits that are commonly seen include reduced or absent corneal sensation and periorbital and nasofacial hypalgesia and are attributable to involvement of the ophthalmic and maxillary branches of CN V, respectively.[1-5] Because postganglionic sympathetic nerve fibers also lie in close proximity to the cavernous sinus, CSS can also be associated with signs of oculosympathetic denervation.[1] Diagnostic imaging studies of the brain and orbits are usually needed to differentiate CSS from retrobulbar diseases involving the orbital fissure, which can cause similar clinical signs.

Cavernous sinus syndrome is apparently rare in dogs, and to our knowledge, only 6 reports[2-7] involving a total of 14 dogs with clinical signs compatible with CSS have been published. In dogs, as in humans, CSS commonly results from neoplastic infiltration of the cavernous sinuses.[2-5,8] However, trauma, vascular anomalies, and inflammatory diseases have also been implicated as potential causes of CSS in both species.[5,7-8] Although the clinical signs and diagnostic imaging features of CSS in dogs have been described,[2,5-7] information regarding the antemortem diagnosis and natural history of the disease is limited. Therefore, the purpose of the study reported here was to determine clinical features, diagnostic imaging abnormalities, underlying disease, disease progression, and outcome in dogs with bilateral CSS.

Criteria for Selection of Cases

Medical records of the Virginia-Maryland Regional College of Veterinary Medicine were reviewed to identify all dogs examined between 1999 and 2004 in which a clinical diagnosis of bilateral CSS had been made. Dogs were included in the study if a board-certified veterinary neurologist had localized the lesion to the cavernous sinus on the basis of compatible clinical signs (ie, deficits of CN III, CN IV, CN VI, and at least 1 of the first 2 branches of CN V) and a lesion of the cavernous sinus had been identified by means of diagnostic imaging or postmortem examination. Dogs with diagnostic imaging or necropsy evidence of retrobulbar disease were included in the study only if any retrobulbar mass that was identified was contiguous with a lesion of the cavernous sinus.

Procedures

Information obtained from medical records included signalment; history; results of a complete physical examination, including ophthalmic and neurologic examinations; results of diagnostic imaging and clinicopathologic testing; treatment; outcome; and postmortem findings. For the purposes of the present

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study, the term extrasinusoidal was used in reference to any anatomic location outside of the cavernous sinus for which there existed clinical, diagnostic imaging, or pathologic evidence of a lesion that was ultimately demonstrated to be related to the disease causing CSS.

Results

The search of the medical records revealed 7 dogs in which a diagnosis of CSS had been made during the study period. However, 1 of these dogs had signs of unilateral, rather than bilateral, CSS (ie, right internal and external ophthalmoplegia), and in this dog, the diagnosis had been made on the basis of clinical examination findings only. Therefore, this dog was excluded from the study. The remaining 6 dogs were included in the study.

Signalment—Dogs included in the study consisted of a 10-year-old sexually intact male Boxer (dog 1), a 2-year-old castrated male mixed-breed dog (dog 2), a 7-year-old spayed female mixed-breed dog (dog 3), a 1-year-old castrated male mixed-breed dog (dog 4), an 11-year-old spayed female mixed-breed dog (dog 5), and a 10-month-old spayed female German Shepherd Dog (dog 6).

History—Five dogs (dogs 1 through 5) were evaluated because of problems referable to abnormal ocular motility or pupillomotor dysfunction. The remaining dog (dog 6) was evaluated because of partial motor seizures involving the face and bilateral mydriasis. Two dogs (dogs 1 and 2) also had a history of dysphagia. Mean duration of clinical signs prior to referral to the veterinary teaching hospital was 31 days (median, 39 days; range, 2 to 87 days). Two dogs did not receive any treatment prior to referral; 2 were treated empirically with broad-spectrum antimicrobials; 1 was treated with a nonsteroidal anti-inflammatory drug, a topical ophthalmic artificial tear preparation, and broad-spectrum antimicrobials; and 1 (dog 6) was treated with phenobarbital and prednisone because of partial facial seizures.

Ophthalmic and neurologic abnormalities—All dogs had clinical evidence of bilateral dysfunction of CN III, CN IV, CN VI, and at least 1 branch of CN V. In particular, all dogs had bilateral external ophthalmoplegia or ophthalmoparesis. Dogs with external ophthalmoplegia were unable to retract the globe (CN VI) or move the globe in a medial, dorsal, ventral (CN III), or lateral direction (CN VI) during testing of the oculocephalic reflex and had oculomotor ptosis characterized by drooping of the lateral two thirds of the upper eyelid. In addition, direct and indirect pupillary light responses were absent or incomplete bilaterally in all dogs (ie, internal ophthalmoplegia or ophthalmoparesis). Palpebral reflexes were absent in 1 dog (dog 2) and diminished in another (dog 5). Initially, none of the dogs had clinical evidence of dysfunction of both the maxillary and ophthalmic branches of CN V.

Aesthesiometry[a] of the central portion of the cornea was performed in 3 dogs, and corneal sensation (ophthalmic branch of CN V) was decreased in 2 of the 3 (dogs 2 and 5), compared with reported values for dogs.[9] Provocative pharmacologic testing of pupillary function was performed with topical administration of 0.1% pilocarpine in dogs 2 and 5. In both dogs, treated pupils constricted within 8 minutes of topical pilocarpine administration, which was interpreted as an indicator of denervation supersensitivity and evidence that a second- or third-order lower motor neuron lesion involving CN III was present.

Left-sided Horner's syndrome was initially diagnosed in 1 dog (dog 3). Topical application of 10% phenylephrine[10] in the left eye of this dog resulted in rapid (< 10 minutes) dilation of the pupil, retraction of the third eyelid, and partial resolution of the ptosis, which supported a diagnosis of a postganglionic sympathetic lesion. The failure of the ptosis to completely resolve following topical application of phenylephrine was attributed to concomitant oculomotor and oculosympathetic ptosis. The right eye of dog 3 was not used as an internal control and similarly tested with topical phenylephrine because the right pupil was mydriatic.

Dogs 1, 2, and 5 had moderate to severe temporalis and masseter muscle atrophy (mandibular branch of CN V). Abnormal, spontaneous electrical activity was detected during concentric needle electromyographic[b] examination of the masticatory muscles in 2 of these dogs. All 3 dogs also had clinical signs of CN IX and CN X dysfunction, manifested as dysphagia and reduced or absent swallowing reflexes.

Dogs 4 and 6 had evidence of nasofacial analgesia. Dog 6 also had a history of partial seizures, and concurrent telencephalic or diencephalic disease was suspected on the basis of history and observation of a partial facial seizure with secondary generalization.

Dogs 5 and 6 were euthanatized shortly after the diagnosis of CSS was made. In the remaining 4 dogs, progressive neurologic deterioration occurred. Dogs 1, 2, and 3, which initially had external or internal ophthalmoparesis, all developed bilateral external and internal ophthalmoplegia. Mean time from diagnosis of CSS to development of bilateral external and internal ophthalmoplegia was 42 days (median, 39 days; range, 13 to 76 days). Late-onset complications, defined as neurologic deficits not present at the time of the original diagnosis, also developed in all 4 dogs. These included generalized seizures (dog 1), bilateral neurotrophic keratitis and tetraparesis (dog 2), bilateral neurotrophic keratitis and blindness (dog 3), and bilateral neurotrophic keratitis and generalized seizures (dog 4). Mean time from initial diagnosis of CSS to identification of late-onset complications was 60 days (median, 62 days; range, 16 to 101 days).

Other physical examination findings—Three dogs had other clinically important abnormalities detected by means of physical examination. Dog 2 had a left-lateralized, 6-cm-diameter mass adherent to the larynx, which was retrospectively identified following computed tomography of the head. Dog 5 had a 5-cm-diameter, multilobular, soft tissue mass that was firmly adherent to the ventral surface of the trachea and hypaxial musculature. Dog 6 had reduced airflow through the right nostril, right mucopurulent nasal discharge, and a submucosal oral mass causing ventral deformation of the hard palate in the region of the right maxillary fourth premolar.

Diagnostic imaging results—Thoracic radiography (left lateral, right lateral, and dorsoventral or ventrodor-

sal projections) was performed in all dogs, and abnormalities were detected in 2 dogs. A soft tissue mass located at the heart base was identified in dog 1, and a generalized linear interstitial infiltrate was identified in dog 4.

Abdominal ultrasonography was performed in dogs 2, 4, 5, and 6, and abnormalities were detected in dogs 4, 5, and 6. Dog 4 had ultrasonographic evidence of multiple enlarged, cavitated intraabdominal lymph nodes; a diffusely hyperechoic splenic parenchyma; and multiple variably sized hypoechoic to anechoic foci throughout the hepatic parenchyma. Dog 5 had echogenic debris in the urinary bladder that was judged to be clinically unimportant. Dog 6 had a single 0.5-cm-diameter hypoechoic cyst in the right renal cortex that was also considered to be clinically unimportant.

Ultrasonography of the neck was performed in dogs 2 and 5. An irregular 5-cm-diameter right thyroid mass with a heterogeneously hypoechoic parenchyma was identified in dog 2. Doppler ultrasound examination of the thyroid mass revealed invasion into the right common carotid artery and jugular vein and multiple tortuous vessels within the mass. A 6-cm-long mass extending from 0.5 cm caudal to the left aspect of the larynx to a level beyond the carotid bifurcation was identified in dog 5. The mass was distinct from the left lobe of the thyroid, had a complex parenchymal echotexture, and was completely encompassing the left common carotid artery. Within the proximal portions of the left common and internal carotid arteries, a 1.5-cm-diameter hypoechoic intraluminal mass was seen.

Echocardiography was performed in dog 1. Abnormalities included a 2-cm-diameter hypoechoic mass in the caudal wall of the proximal portion of the ascending aorta and evidence of mild mitral valvular regurgitation.

Bilateral retrobulbar ultrasonography was performed through a temporal approach[11] in dog 3. A 2-cm-diameter hyperechoic mass lesion extending out of the right orbital fissure into the retrobulbar space was seen (**Figure 1**).

Computed tomography[c] was performed in dogs 1, 2, and 4, and magnetic resonance imaging[d] was performed in dog 3. All 4 dogs had evidence of extramedullary bilateral cavernous sinus masses causing variable degrees of compression of the hypophysis and overlying diencephalon or pyriform lobes of the cerebrum. The mass was confined to the cavernous sinuses and caudal aspects of the orbital fissures in dog 4 (**Figure 2**). The remaining 3 dogs had evidence of extrasinusoidal masses. In dogs 2 and 3, these extrasinusoidal masses were contiguous with the cavernous sinus masses, and in dog 1, the extrasinusoidal mass was not contiguous with the cavernous sinus mass. In dog 3, the extrasinusoidal mass extended rostrally from the cavernous sinus through the right orbital fissure into the retrobulbar space (**Figure 3**). In dog 2, the extrasinusoidal mass appeared to originate in the cranial cervical region at the level of the left carotid arterial bifurcation and extended craniolaterally into the spinal canal and through the foramen magnum and an enlarged left jugular foramen into the cranial vault. The mass then continued rostrally through the cavernous sinuses into the orbital fissures and terminated in the right and left retrobulbar spaces (**Figure 4**). Dog 1 had an extrasinusoidal mass originating in the area of the right carotid arterial bifurcation that extended into the spinal canal and pontomedullary region.

Cavernous sinus masses were isoattenuating, compared with adjacent unaffected brain tissue, in dogs 1 and 2 and hyperattenuating in dog 4. Substantial perilesional edema and a mass effect were evident in dog 2. In dog 3, the cavernous sinus mass was homogenous and isointense, compared with brain parenchyma, on T1-weighted images and heterogeneously hypointense to isointense, compared with unaffected gray matter, on T2-weighted and fluid-attenuated inversion recovery images. Following IV administration of contrast medium, cavernous sinus masses had well-defined margins in dogs 1 and 3 and irregular margins in dogs 2 and 4. Other than the neuroanatomic location, the only consistent feature identified on computed tomographic and magnetic resonance images was moderate

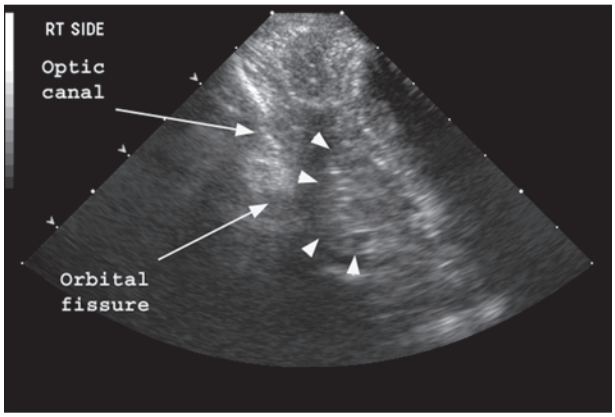

Figure 1—Parasagittal ultrasonographic image of the right retrobulbar region in a dog (dog 3) with bilateral cavernous sinus syndrome (CSS) secondary to a meningioma. The optic canal, orbital fissure, and retrobulbar extension of the mass (arrowheads) can be seen.

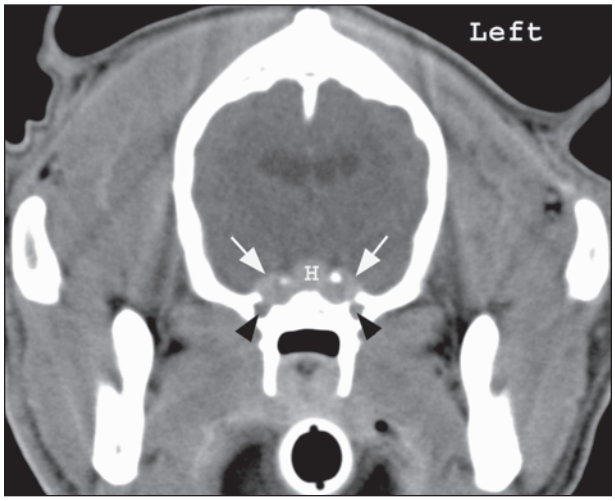

Figure 2—Transverse computed tomographic image obtained at the level of the diencephalon following administration of contrast medium in a dog (dog 4) with CSS secondary to lymphoma. A bilateral, heterogeneously contrast-enhancing mass (white arrows) can be seen in the cavernous sinuses. The mass is compressing the hypophysis (H) and overlying pyriform lobes of the cerebrum and can be seen encroaching on the caudal aspects of the orbital fissures (black arrowheads).

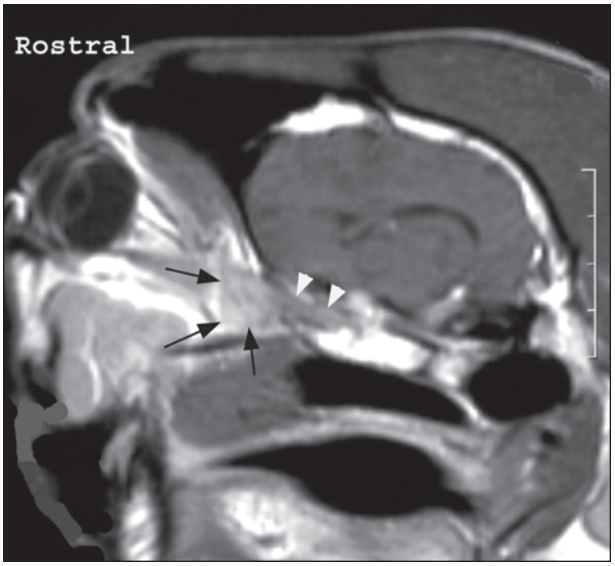

Figure 3—Right parasagittal T1-weighted magnetic resonance image (TR, 650 milliseconds; TE, 14.8 milliseconds) obtained following administration of contrast medium in the dog in Figure 1. A moderately heterogeneously enhancing mass in the right cavernous sinus (white arrowheads) that extends extracranially through the right orbital fissure into the retrobulbar space (black arrows) can be seen.

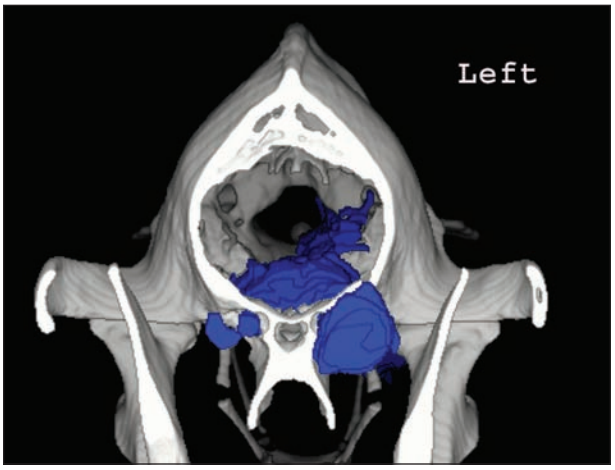

Figure 4—Three-dimensional rostrocaudal reconstruction generated from computed tomographic images obtained from a dog (dog 2) with bilateral CSS secondary to a chemodectoma. Notice the extensive extrasinusoidal lesion (blue) extending rostrally and caudally and contiguous with the cavernous sinuses. From a rostral to caudal direction, the mass involved the retrobulbar spaces and extended through both orbital fissures into the cavernous sinuses and rostral two thirds of the middle cranial fossa. The mass can be seen exiting the foramen magnum and left jugular foramen into the spinal canal in the region of the atlas.

to marked heterogeneous enhancement of the lesions following IV contrast administration.

Clinicopathologic findings—Results of CBCs and serum biochemical profiles were within reference limits in dogs 2, 3, and 5, and results of urinalyses were unremarkable in all 6 dogs. Dogs 1, 4, and 6 had leukograms consistent with stress (ie, mature neutrophilia and lymphopenia). Biochemical abnormalities were identified in 3 dogs and included hyperglycemia (dogs 1 and 4) and a high alkaline phosphatase activity in dog 6, which was receiving prednisone and phenobarbital.

In dogs 1 and 4, CSF from the cerebellomedullary cistern was analyzed. In both dogs, albuminocytologic dissociation was the only abnormality.

Percutaneous, ultrasound-guided needle biopsies were performed in 4 dogs. Soft tissue masses in the ventral cervical region of dogs 2 and 5, enlarged mesenteric lymph nodes and the liver in dog 4, and a right retrobulbar mass in dog 3 were biopsied. Rhinoscopy was performed in dog 6 because of nasal discharge and a hard palate deformity evident on physical examination. Gross rhinoscopic abnormalities were confined to the right nasal cavity and consisted of copious amounts of mucopurulent exudate and a firm, gray-discolored mass causing substantial turbinate destruction in the caudal aspect of the nasal cavity. Histologic examination of biopsy specimens revealed a chemodectoma in dog 2, meningoepitheliomatous meningioma in dog 3, immunoblastic CD3-reactive (T-cell) lymphoma in dog 4, thyroid carcinoma in dog 5, and a primitive neuroectodermal tumor in dog 6.

Treatment and outcome—Dog 5, which had a thyroid carcinoma, and dog 6, which had a primitive neuroectodermal tumor, were euthanatized shortly after the histologic diagnosis was made. The remaining 4 dogs were all treated.

In dogs 2 and 4, definitive treatment directed at the underlying disease was administered. Dog 2, which had a chemodectoma, was treated with lomustine (68 mg/m^2, PO, q 21 d). Treatment was discontinued after 10 cycles because of persistent thrombocytopenia. Dog 4, which had lymphoma, was treated with a combination of L-asparaginase, vincristine, doxorubicin, cyclophosphamide, methotrexate, and prednisone,[12] modified by substituting cytosine arabinoside for cyclophosphamide during week 2 of treatment. Partial clinical remission was achieved, but bone marrow involvement was documented after 13 days.

Various palliative treatments were administered to the 4 dogs that were treated. Dogs 1 and 2 were fed gruel from an elevated position because of dysphagia. Dogs 1 and 4 were treated with phenobarbital (2.5 mg/kg [1.1 mg/lb], PO, q 12 h) after developing seizures as late complications. Topical artificial tear and triple-antibiotic preparations were administered to all 3 dogs with neurotrophic keratitis, and topical administration of autologous serum was prescribed in 1. Prednisone (0.5 mg/kg [0.23 mg/lb], PO, q 12 h) was prescribed for dogs 2 and 3.

All 4 dogs that were treated were eventually euthanatized because of refractory late-onset complications. Median survival time for all 6 dogs was 79 days (mean, 135 days; range, 3 to 392 days). Median survival time for the 4 dogs that were treated was 199 days (mean, 204 days; range, 16 to 392 days).

Postmortem findings—Postmortem examinations were performed in dogs 3, 4, 5, and 6, and findings confirmed that cavernous sinus masses identified clinically or by means of diagnostic imaging were the same as neoplasms diagnosed antemortem in all 4 dogs.

Necropsy lesions were limited to the head in dogs 3 and 6. Dog 3, which had a meningioma, was found to

have a parasellar mass completely encircling the hypophysis and extending rostrodorsally to compress the optic chiasm. Neoplastic masses were seen in the cavernous and intercavernous sinuses; these masses expanded rostrally through the orbital fissures into the retrobulbar spaces. Dog 6, which had a primitive neuroectodermal tumor, had a semifirm, pale gray-white mass occupying the right caudal nasal passage and frontal sinus that had resulted in destruction of the nasal turbinates and invaded the right caudal maxilla and hard palate. The mass extended through the cribriform plate into the calvarium, where it caused compression of the right olfactory bulb and frontal lobes of the cerebrum. The mass was also infiltrating the cavernous sinuses at the level of the hypophysis. Histologically, the mass consisted of a homogenous population of cells arranged in small acini and rosettes, interspersed within multiple areas of necrosis and hemorrhage. Cells were characterized by eccentrically placed nuclei containing multiple nucleoli and eosinophilic cytoplasm and were surrounded by a delicate fibrovascular stroma. Mitotic figures were numerous. Extension of the neoplastic cells into overlying cerebral cortex was evident in several sections. Moderate to marked neutrophilic leptomeningitis was also seen.

Dog 5, which had a thyroid carcinoma, had a firm red 6-cm-diameter, multilobular right thyroid cervical mass encompassing the trachea and right carotid sheath and adherent to the underlying musculature. Neoplastic invasion of the right jugular vein and carotid artery was demonstrated histologically, along with metastatic infiltration of the cavernous and intercavernous sinuses. A single neoplastic nodule was detected in the parenchyma of the left caudal lung lobe.

Dog 4, which had lymphoma, had diffuse infiltration of the liver; spleen; renal cortices; bone marrow; interstitium of the lung; and mesenteric, hilar, and sternal lymph nodes with neoplastic lymphocytes. The right cavernous sinus and rostral and caudal intercavernous sinus were infiltrated with an identical population of lymphocytes, and the lumen of the left cavernous sinus was occluded by a thrombus extending from the left orbital fissure to the left ventral petrosal sinus. Small nests of neoplastic emboli were seen in the thrombus. Multiple neoplastic foci were scattered throughout the white and gray matter of both cerebral hemispheres and the cerebral leptomeninges.

Discussion

Results of the present study suggest that bilateral CSS is rare in dogs but that a mass lesion involving the cavernous sinuses should be suspected in dogs with clinical evidence of concurrent dysfunction of CN III, CN IV, CN VI, and the first 2 branches of CN V, with or without evidence of oculosympathetic denervation, once retrobulbar disease has been adequately ruled out. In 5 of the 6 dogs in the present study, bilateral CSS was a result of neoplasia (the underlying cause was not determined in the remaining dog), suggesting that neoplasia should be the primary diagnostic consideration in dogs with bilateral CSS, particularly in dogs with concurrent physical abnormalities and neurologic deficits referable to an extrasinusoidal region. Ultrasonography, computed tomography, and magnetic resonance imaging were useful in characterizing the lesions causing CSS in these dogs. All dogs had advanced clinical signs at the time of initial examination and were eventually euthanatized because of progressive disease.

Ten of 14 dogs with CSS described in previously published reports[2-7] had unilateral clinical signs, whereas all 6 dogs in the present study had bilateral clinical signs. In humans, bilateral CSS occurs more frequently secondary to vascular, infectious, and sterile inflammatory diseases but bilateral CSS may also be a manifestation of aggressive solid neoplasms.[8,13,14] A report[2] of a dog with CSS secondary to a neuroendocrine carcinoma indicated that the dog initially had unilateral signs but eventually developed bilateral CSS, and attempts were made in the present study to identify evidence that clinical signs were initially unilateral. However, this information could not be retrieved from the medical records, and all dogs had been referred for evaluation of bilateral ocular signs. Mean time from the onset of clinical signs to referral was 31 days. Therefore, even if dogs in the present study had initially had unilateral signs, the disease quickly progressed to bilateral involvement.

Ophthalmic abnormalities associated with CSS that have been reported previously[2-7] were similar to abnormalities detected in dogs in the present report. External and internal ophthalmoparesis or ophthalmoplegia were the primary complaints for dogs in the present study and are common reasons humans with CSS seek medical care.[8,13] However, in contrast to previous reports[2,3,5] of dogs with CSS in which extrasinusoidal neurologic deficits were rarely identified, signs referable to multifocal intracranial disease were identified in 4 of the 6 dogs in the present study at the time of initial examination and eventually developed in all dogs. In addition, these 4 dogs had physical abnormalities that prompted clinical investigations that ultimately lead to the histopathologic diagnosis. Thus, our findings suggested that dogs with CSS should be thoroughly and systematically evaluated for extrasinusoidal physical abnormalities, as identification of such abnormalities may allow for a definitive antemortem diagnosis.

Results of routine clinicopathologic testing (ie, CBCs, serum biochemical profiles, urinalyses, and CSF analyses) of dogs in the present report were nonspecific and generally not beneficial in identifying the underlying cause of the CSS. Albuminocytologic dissociation was the only CSF abnormality documented and is a sensitive, but nonspecific, indicator of a variety of degenerative, anomalous, inflammatory, metabolic, and neoplastic CNS diseases. Although CSF analysis was not diagnostic in the dog with lymphoma in this study, neoplastic lymphocytes were observed in CSF from a dog with lymphoma in a previous report,[15] and CSF analysis should be considered in dogs with systemic lymphoma that have clinical signs of CNS disease.

In both humans and dogs, intracranial diagnostic imaging studies are the most useful tools for characterizing lesions causing CSS.[2,6-8,13] Computed tomography and magnetic resonance imaging are also often used in

human patients to guide selection of invasive intracranial diagnostic procedures.[8,13] Although intracranial biopsies were not performed in dogs in the present study, computed tomography and magnetic resonance imaging were beneficial in confirming involvement of the cavernous sinus and identifying extracranial lesions that were amenable to biopsy. Because of the small number of cases, it was not possible to determine whether specific imaging features could be used as predictors of the underlying cause. All dogs in the present study had variably intense, heterogeneously contrast-enhancing lesions involving the cavernous sinuses and extrasinusoidal structures.

A definitive antemortem diagnosis of neoplasia was made in 5 of the 6 dogs in the present study by use of ultrasound-guided or endoscopic-assisted biopsy procedures. The 1 dog in this study for which a histopathologic diagnosis was not obtained (dog 1) was suspected of having a chemodectoma following identification of soft tissue masses at the base of the aorta and the level of the carotid bifurcation by means of ultrasonography and computed tomography. Although lesions identified in this dog were accessible to percutaneous aspiration or biopsy techniques, the owner did not grant permission for these procedures, and necropsy was declined at the time of euthanasia.

Neoplasia is the most commonly reported cause of spontaneous CSS in humans and dogs.[2-8,13] Neoplasms were diagnosed in 10 of 14 dogs with CSS described in previous reports[2-7] and were identified as the definitive cause of CSS in 5 of the 6 dogs in the present study. To the authors' knowledge, primitive neuroectodermal tumor has not previously been implicated as a cause of CSS in people or animals. However, the cellular origin, microscopic features, and nomenclature of primitive neuroectodermal tumors are a continual source of debate among pathologists, and additional immunohistochemical or ultrastructural examinations were not performed to better characterize the lesion defined as a primitive neuroectodermal tumor in the present study. Soft tissue malignancies that originate in the head and neck, such as thyroid carcinoma and carotid body tumors, may result in CSS because of their propensity to invade vascular structures supplying the skull.[14] Once vascular invasion has occurred, the cavernous sinuses can become involved as a result of direct intravascular tumor proliferation or embolization of neoplastic cells.[14] Both phenomena were observed in the dogs described in the present report. It is not uncommon for humans with CSS secondary to malignant head and neck tumors to have extrasinusoidal deficits,[13,14] and the 4 dogs in the present study with phenotypically and histologically malignant tumors had extrasinusoidal deficits and other physical abnormalities at the time of initial diagnosis.

Follow-up information was available for the 4 dogs in the present study in which treatment was attempted. Median survival time was 199 days, and all 4 dogs eventually developed external and internal ophthalmoplegia and were euthanatized because of medical complications. Neurotrophic keratitis, defined as ulcerative keratitis secondary to corneal denervation, was the most common complication and occurred in 3 dogs. Neurotrophic keratitis has not previously been associated with CSS in dogs and may be a late manifestation of a lesion involving the nasociliary branch of CN V.[1,9] Progressive involvement of the corneal surface was the factor that directly led to the euthanasia of 2 dogs with neurotrophic keratitis. Generalized seizures were observed as a late-onset complication in 2 dogs and were attributed to invasion of the telencephalon by malignant lymphocytes in dog 4 and to intracranial hypertension associated with a mass effect in dog 1. Asymmetric tetraparesis occurred as a late-onset complication in dog 2 and was likely a result of compression of the cervical portion of the spinal cord. Dog 3 developed blindness that was attributed to compression of the optic chiasm by a meningioma.

Considering the frequency with which neoplasms are identified as a cause of CSS in dogs, it should not be unexpected that the prognosis associated with this syndrome was guarded to poor in this and previous studies.[2-7] In addition, outcome for several dogs in the present study was likely negatively influenced by multiple variables independent of cavernous sinus involvement. For example, dog 2 had a phenotypically malignant, nonresectable chemodectoma that had invaded local vascular structures, all of which are negative prognostic indicators in humans with carotid body neoplasia.[16] Although carotid body tumors are reportedly radiosensitive, the role of radiotherapy in the treatment of dogs with carotid body tumors is currently unknown and poor results were previously reported[16] for 2 dogs treated with external-beam radiotherapy for carotid body chemodectomas. Dog 4 had multiple negative prognostic indicators previously associated with lymphoma, including high histologic grade, T-cell immunotype, advanced clinical stage (stage Vb), and bone marrow and sternal lymph node involvement.[17] Poor prognostic indicators for thyroid carcinoma in dogs include adherence of the tumor to regional anatomic structures and distant metastatic disease, both of which were identified in dog 5. Extracerebellar and supratentorial primitive neuroectodermal tumors are considered highly malignant neoplasms and are associated with a poor prognosis in children, despite treatment with radiotherapy and chemotherapeutics.[18] In dog 6 in the present study, the primitive neuroectodermal tumor had both clinical and histologic features of a biologically aggressive neoplasm.

Although minimally invasive microsurgical, endoscopic, and radiosurgical techniques have greatly improved the quality of life and survival times for human patients with primary intracranial neoplasms that are anatomically confined to the cavernous sinus or parasellar region,[8,13] clinical manifestations of CSS secondary to metastatic head and neck cancers are infrequent, occur late in the clinical course of disease, and are associated with a mean survival time of only 4 months.[14] Similarly, overall mean survival time in the present study was only 135 days. This short survival time likely was reflective of the fact that all dogs had extensive tumor burdens with extrasinusoidal involvement at the time of diagnosis. Clinical management of CSS in dogs is further complicated by the currently limited availability of intracranial microsurgical and

endoscopic techniques. In addition, the blood-brain barrier presents an obstacle to effective delivery of many chemotherapeutic agents.[2] Radiotherapeutic procedures have been demonstrated to be beneficial in human patients with CSS caused by neoplasia,[8] but the role of radiotherapy in the management of dogs with CSS is currently unknown.

a. Luneau aesthesiometer 12/100 mm, Lunaeu Ophtalmologie, Chartres, France.
b. Nicolet Viking IV electrodiagnostic system, Nicolet Biomedical Inc, Madison, Wis.
c. Picker IQXtra, Philips Medical Systems, Cleveland, Ohio.
d. GE Horizon 1.5T, GE Medical Systems, Milwaukee, Wis.

References

1. Evans HE, Kitchell RL. Cranial nerves and the cutaneous innervation of the head. In: Evans HE, ed. *Miller's anatomy of the dog*. 3rd ed. Philadelphia: WB Saunders Co, 1988;953–987.

2. 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.

3. Valentine BA, Summers BA, de Lahunta A, et al. Suprasellar germ cell tumors in the dog: a report of five cases and review of the literature. *Acta Neuropathol (Berl)* 1988;76:94–100.

4. Lewis GT, Blanchard GL, Trapp AL, et al. Ophthalmoplegia caused by thyroid adenocarcinoma invasion of the cavernous sinuses in the dog. *J Am Anim Hosp Assoc* 1984;20:805–812.

5. Lee R, Griffiths IR. A comparison of cerebral angiography and cavernous sinus venography in the dog. *J Small Anim Pract* 1972; 13:225–238.

6. Fransson B, Kippenes H, Silver GE, et al. Magnetic resonance diagnosis: cavernous sinus syndrome in a dog. *Vet Radiol Ultrasound* 2000;41:536–538.

7. Tidwell AS, Ross LA, Kleine LJ. Computed tomography and magnetic resonance imaging of cavernous sinus enlargement in a dog with unilateral exophthalmos. *Vet Radiol Ultrasound* 1997;38: 363–370.

8. Johnston JL. Parasellar syndromes. *Curr Neurol Neurosci Rep* 2002;2:423–431.

9. Weigt AK, Herring IP, Marfurt CF, et al. Effects of cyclophotocoagulation with a neodymium:yttrium-aluminum-garnet laser on corneal sensitivity, intraocular pressure, aqueous tear production, and corneal nerve morphology in eyes of dogs. *Am J Vet Res* 2002;63: 906–915.

10. Scagliotti RH. Comparative neuro-ophthalmology. In: Gelatt KN, ed. *Veterinary ophthalmology*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999;1307–1400.

11. Stuhr CM, Scagliotti RH. Retrobulbar ultrasound in the mesaticephalic and dolichocephalic dog using a temporal approach. *Vet Comp Ophthalmol* 1996;6:91–99.

12. Keller ET, MacEwen EG, Rosenthal RC. Evaluation of prognostic factors and sequential combination chemotherapy with doxorubicin for canine lymphoma. *J Vet Intern Med* 1993;7:289–295.

13. Keane JR. Cavernous sinus syndrome. Analysis of 151 cases. *Arch Neurol* 1996;53:967–971.

14. Bumpous JM, Mabes MD, Gomez SM, et al. Cavernous sinus involvement in head and neck cancer. *Head Neck* 1993;15: 62–66.

15. Couto CG, Cullen J, Pedroia V, et al. Central nervous system lymphosarcoma in the dog. *J Am Vet Med Assoc* 1984;184:809–813.

16. Owen TJ, Bruyette DS, Laytaon CE. Chemodectoma in dogs. *Compend Contin Educ Pract Vet* 1996;18:253–264.

17. Vail DM, MacEwen EG, Young KM. Canine lymphoma and lymphoid leukemias. In: Withrow SJ, MacEwen EG, eds. *Small animal clinical oncology*. 3rd ed. Philadelphia: WB Saunders Co, 2001; 558–590.

18. Lantos PL, Louis DN, Rosenblum MK, et al. Tumours of the nervous system. In: Graham DI, Lantos PL, eds. *Greenfield's neuropathology*. Vol 2. 7th ed. New York: Oxford University Press, 2002;873–896.