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| Objective | To determine CSF characteristics associated with intracranial meningiomas in dogs. |
| Design | Retrospective case series. |
| Animals | 56 dogs with intracranial meningiomas. |
| Procedures | Medical records of dogs with a histopathologic diagnosis of intracranial meningioma, in which CSF analysis had been performed, were reviewed. Information concerning total nucleated cell counts (TNCCs) and differential nucleated cell counts, RBC counts, and total protein concentration in CSF; seizure history and glucocorticoid administration; and location of meningiomas was recorded. |
| Results | TNCCs < 5 cells/µL were detected in 41 of 56 (73%) dogs; 5 of 56 (9%) dogs had TNCCs > 50 cells/µL. Analysis of CSF revealed predominantly neutrophilic pleocytosis in < 20% of dogs. There was a significant association between meningioma location (caudal portion of the cranial fossa or middle and rostral portion of the cranial fossae) and increased TNCCs (≥ 5 cells/µL). |
| Conclusions and Clinical Relevance | Results were significantly different from those routinely reported in the veterinary literature. Neutrophilic pleocytosis, especially with TNCCs > 50 cells/µL, was not typical in CSF samples from dogs with intracranial meningiomas. Neutrophilic pleocytosis may not be detected in CSF samples from dogs with meningiomas located within the middle or rostral portion of the cranial fossae. |

Meningiomas are reported as one of the most common primary intracranial tumors in dogs.1-3 Cerebrospinal fluid analysis rarely is diagnostic for intracranial neoplasia; however, findings that are characteristic of certain tumor types, including meningioma, have been reported. Results of 1 study7 indicate that CSF is always abnormal in dogs with meningiomas; most CSF samples had pleocytosis, and a predominance of neutrophils was common when TNCCs were increased. Similar findings were reported in another study, and it has since been reported that CSF associated with meningioma commonly is characterized by predominantly neutrophilic pleocytosis,4,6 often with TNCCs > 50 cells/µL.8 Results of these reports are contrary to the clinical experience of the authors. The purpose of the study reported here was to determine the CSF characteristics associated with intracranial meningiomas in dogs. A retrospective evaluation of results of CSF analyses was performed to test the hypothesis that predominantly neutrophilic pleocytosis is a typical finding in dogs with intracranial meningiomas. The possible influence of secondary factors, such as glucocorticoid administration and seizure activity, on CSF parameters was evaluated.

Criteria for Selection of Cases

Medical records at the University of California Veterinary Medical Teaching Hospital from January 1, 1985, through December 31, 2004, were reviewed from dogs with a histopathologic diagnosis of intracranial meningioma. Criteria for inclusion in the study included dogs in which tissues had been obtained via surgical resection, CT-guided stereotactic biopsy, or necropsy; collection of CSF from the cerebellomedullary cistern; a total CSF RBC count < 4,000 cells/µL; no other pathologic lesions of the CNS detected via magnetic resonance imaging, CT, or necropsy; CSF obtained prior to performing any invasive procedure such as surgery, CT-guided stereotactic biopsy, radiotherapy, or chemotherapy; and availability of medical records of any seizure history and prior treatment with glucocorticoids.

Procedures

CSF analysis—Total nucleated cell counts, RBC counts, and differential nucleated cell counts were performed within 30 minutes of collection of CSF by use of a standard hemocytometer and methylene blue staining. Cells from 0.2 to 0.3 mL of CSF were concentrated by use of a cytocentrifuge and stained with new methylene blue or Wright stain and examined microscopically. Total and differential cell counts were recorded. Total protein concentration in CSF was determined by use of the Coomassie brilliant blue or pyrogallol red methods. Cerebrospinal fluid collected from the cerebellomedullary cistern with a TNCC < 5 cells/µL, without neutrophils, a total RBC count < 4,000 cells/µL, and a total protein concentration < 25 mg/dL was considered normal.

Statistical analysis—The exact Pearson χ² test was used to determine whether there was a significant association between meningioma location (caudal portion of the cranial fossa or middle and rostral portion of the cranial fossae) and increased TNCC. Caudal portion of the cranial fossa was defined as that area bounded dorsally by the tentorium cerebelli.

| TNCC | Total nucleated cell count |
| CT | Computed tomography |

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Results

Medical records from 56 dogs met the inclusion criteria. Differential nucleated cell counts were not obtained from CSF in 3 dogs, all of which had TNCCs ≤ 1 cell/µL. Determination of total protein concentration in CSF was not performed in 2 dogs, both of which had TNCCs ≥ 5 cells/µL.

In 8 of 51 (16%) dogs, results of CSF analysis were considered normal. The TNCC was < 5 cells/µL in 41 of 56 (73%) dogs, of which 16 (29%) also had total protein concentrations < 25 mg/dL. Only 5 dogs (9%) had TNCCs > 50 cells/µL. Increased TNCCs ranged from 5 to 580 cells/µL, and 13 of 13 samples had increased TNCCs.

Increased TNCCs were detected in 8 of 10 (80%; 95% confidence interval, 61% to 96%) dogs with meningiomas in the caudal portion of the cranial fossa and 7 of 17 (41%; 95% confidence interval, 23% to 59%) dogs with meningiomas in the rostral portion of the cranial fossa. This difference in the anatomic distribution of meningioma location was significant (P < 0.001) between dogs with or without increased TNCCs.

Neutrophils were detected in 38 of 53 (72%) CSF samples. In samples with TNCCs < 5 cells/µL, neutrophils were detected in 23 of 38 (60%) dogs (range, 1% to 70%; mean, 9.9%; median, 4%). In samples with increased TNCCs, neutrophils were detected in 15 of 15 dogs (range, 1% to 88%; mean, 56%; median, 72%). Greater than 50% neutrophils was detected in only 11 of 56 (20%) samples with TNCCs > 5 cells/µL; median, 4%).

Increased TNCCs were detected in 18 of 23 (78%) dogs with meningiomas in the caudal portion of the cranial fossa. This difference in the anatomic distribution of meningioma location was significant (P < 0.001) between dogs with or without increased TNCCs.

Total protein concentrations were increased (≥ 25 mg/dL) in 25 of 41 (61%) samples with TNCCs < 5 cells/µL and 13 of 13 samples with increased TNCCs. Increased total protein concentrations ranged from 26 to 210 mg/dL (mean, 66 mg/dL; median, 52 mg/dL). Sixteen of 54 (30%) samples had TNCCs < 5 cells/µL and increased total protein concentrations.

Cerebrospinal fluid samples from dogs with a history of glucocorticoid administration at the time of assessment, or within a 1-week period prior to assessment, accounted for 16 of 56 (29%) samples. When all samples from dogs treated with glucocorticoids were removed, 31 of 40 (78%) samples had TNCCs < 5 cells/µL and 25 of 37 (68%) samples contained neutrophils. Only 2 of 40 (5%) samples had a TNCC > 50 cells/µL, and 5 of 37 (14%) samples had > 50% neutrophils.

Eighteen dogs had seizures within 48 hours of CSF collection. Total nucleated cell counts < 5 cells/µL were detected in 14 of 18 dogs with 3 completely normal samples. Three dogs with seizures and TNCCs < 5 cells/µL were being treated with glucocorticoids. Neutrophils were detected in 10 of 17 dogs, of which had increased TNCCs.

Discussion

Results of the study reported here were not in agreement with results of other studies describing CSF collected from dogs with intracranial menin-
has little effect on TNCCs in CSF samples, and although the exclusion criterion for RBCCs was > 4,000 cells/µL, only 5 samples had RBCC counts > 500 cells/µL.

Modest neutrophilic pleocytosis and increased total protein concentration have been reported in as many as 18% of CSF samples from humans with repeated generalized seizures. Pleocytosis usually is greatest 24 hours after seizures and resolves over a few days. Whether a similar alteration in CSF is seen in dogs with seizures with no other causes for altered CSF parameters is not known. Neutrophilic pleocytosis in some dogs with seizures may have been attributable to this phenomenon rather than the presence of a meningioma. Fourteen of 18 dogs reported to have had any seizure activity within 48 hours of CSF collection had CSF TNCCs < 5 cells/µL. Although this suggests that, as in humans, seizures do not necessarily result in pleocytosis, accurate interpretation of samples with increased TNCCs in dogs with seizures is not possible in the presence of concurrent neoplastic disease.

The effect of glucocorticoid administration on CSF nucleated cell counts is not known; however, it is likely that anti-inflammatory actions may result in decreased cell counts. If glucocorticoids substantially affect CSF parameters, the number of dogs with normal CSF may have been overestimated. Approximately 30% of dogs with TNCCs < 5 cells/µL or increased TNCCs had received glucocorticoid medications of various dosages within 1 week of CSF analysis. Removing these dogs did not significantly alter the general pattern of findings. However, either removing these potentially more abnormal cases or including them while they were receiving glucocorticoids may have biased the data by increasing the number of CSF samples that were considered normal.

A significant association was detected between meningiomas involving structures within the caudal portion of the cranial fossa and increased TNCCs (80%), compared with meningiomas located in the middle and rostral portion of the cranial fossae (15%). This association may have been attributable to anatomic constraints within the caudal portion of the cranial fossa resulting in a greater degree of compression of CNS tissue and inflammation or may have been associated with the sampling site being in close proximity to a pathologic lesion. Sufficient data are not available from other studies to determine whether selection bias for caudal portion of the cranial fossa tumors may explain the historical association of increased TNCC with intracranial meningioma. Bailey and Higgins’ speculated that there was an association between CSF neutrophilic pleocytosis and degree of necrosis or polymorphonuclear cell infiltration seen histologically; although other types of tumors in which necrosis was detected were not associated with pleocytosis. In the study reported here, an apparent association between meningioma necrosis and CSF pleocytosis was not detected. Necrosis was detected in meningiomas with both increased TNCCs and TNCCs < 5 cells/µL. Necrosis was not detected in approximately half of the samples with increased TNCCs.

Differences in results between the study reported here and results of other studies may be attributable to the increased sample size in our study and the lack of data associated with tumor location, presence of seizures, and use of glucocorticoid medication in other studies.

Results of CSF analysis from dogs with intracranial meningioma may be considered normal in as many as 30% of cases, depending on the precise definition of normal CSF and tumor location. In the study reported here, the most common finding for all meningioma locations was a TNCC < 5 cells/µL (73%) with a total protein concentration that was < 25 mg/dL (39%) or moderately increased (61%). In contrast to results of other reports, pleocytosis with a predominance of neutrophils (19%) was not the most common finding in our study when CSF samples from all dogs with intracranial meningiomas were analyzed together. However, there was a significant association between increased TNCCs and whether the location of meningiomas was within the caudal portion of the cranial fossa or middle and rostral portion of the cranial fossae.

References

b. Coomassie brilliant blue, Environmental Chemical Specialties, Anaheim, Calif.
c. Pyrogallol red, Sigma Diagnostics, St Louis, Mo.
Objective — To develop an assay to measure canine von Willebrand factor (vWF):collagen-binding activity (CBA) to screen for type II von Willebrand disease (vWD) in dogs.

Sample Population — 293 plasma samples submitted for analysis of canine vWF antigen (vWF:Ag) and 12 control plasma samples from dogs with inherited type II or III vWD.

Procedure — Bovine collagens were evaluated for suitability as binding substrate for vWF. Assay sensitivity to depletion, proteolytic degradation, or a genetic deficiency of high–molecular-weight vWF were determined. Amounts of vWF:Ag and vWF:CBA were measured. The ratio of vWF:Ag to vWF:CBA was used to discriminate between type I and type II vWD.

Results — An assay for canine vWF activity was developed by use of mixed collagen (types I and III). When vWF:Ag was used to subtype vWD, 48% of the dogs were classified as clinically normal, 9% as indeterminate, and 43% as type I vWD. Inclusion of vWF activity resulted in reclassification of 5% of those identified as type I to type II vWD. However, vWF:CBA of the reclassified dogs was not consistently abnormal, a finding compatible with acquired type II vWD. Some Doberman Pinschers had lower antigen-to-activity ratios than other breeds with type I vWD, suggesting that Doberman Pinschers have more functional circulating vWF.

Conclusions and Clinical Relevance — Analysis of canine vWF activity should be included among the vWF-specific assays used to confirm type II vWD. The prevalence of inherited forms of type II vWD in screened dogs is lower than acquired forms that can result secondary to underlying disease. (Am J Vet Res 2006;67:242–249)