



FULL PAPER

Internal Medicine

Incidence and type of brain herniation associated with intracranial meningioma in dogs and cats

Simone MINATO^{1)*}, Giunio B. CHERUBINI²⁾, Daniele DELLA SANTA³⁾, Stefano SALVADORI⁴⁾ and Massimo BARONI¹⁾

¹⁾Valdinievole Veterinary Clinic, Via C. Nigra 123, 51015, Monsummano Terme, PT, Italy
 ²⁾Dick White Referrals, Station Farm, London Road, Six Mile Bottom, Cambridgeshire CB8 0UH, UK
 ³⁾Vet Hospital Firenze, Via Dei Vanni 25, 50142, Firenze, FI, Italy
 ⁴⁾Institute of Clinical Physiology, National Research Council, Via G. Moruzzi 1, 56124, Pisa, PI, Italy

ABSTRACT. The incidence of brain herniation (BH) in association with intracranial meningioma (ICM) in dogs and cats is poorly described. The aim of this study was to evaluate the rate and type of brain herniations in client-owned dogs and cats with ICMs and to determine the meningioma volume (MV) relative to cranial cavity volume (CCV). A retrospective magnetic resonance imaging (MRI) analysis study of 24 cats and 45 dogs with ICMs was conducted to ascertain the presence and characteristics of BH. MV and CCV were measured and their ratio was calculated for each animal. Correlations of MV/CCV with independent variables were analyzed. BH was encountered in 24/24 cats (100%) and 30/45 dogs (66.7%) with ICMs. In cats, the most frequent presentation was foramenal herniation (FMH; 23/24, 95.8%), followed by caudotentorial (CTH; 21/24, 87.5%) and subfalcine (SH; 18/24, 75.0%) herniation. In dogs, the most frequent presentation was SH (28/45; 62.2%), followed by CTH (9/45; 20%) and FMH (2/45; 4.4%). Relative to dogs, cats with ICM had greater incidences of FMH (P<0.001) and CTH (P<0.001). Mean MV/CCV ratio was altered behavior in cats (43%, P<0.01) and seizures in dogs (74.4%, P<0.001). In conclusion, cats were found to be more likely than dogs to present FMH and CTH, with a proportionally greater neoplasia volume.

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Meningiomas are the most common primary brain tumor in dogs and cats, accounting for about 45% [20] and 85% [23] of primary brain neoplasia and about 22.3% [20] and 59% [23] of all brain tumors in dogs and cats, respectively. Meningiomas are thought to arise from cells forming arachnoid granulations or cells of the leptomeninges [24]. Intracranial meningiomas (ICMs) are slow-growing, extra-axial central nervous system neoplasms that can compress brain parenchyma [1, 13].

The clinical presentation of ICMs depends on their location. Typically, cats with ICM may exhibit circling behavior, an altered state of consciousness (e.g depression, stupor, or coma), and seizures [23]. Meanwhile, dogs with ICMs have been reported to be present with seizures, vestibular dysfunction, and mentation changes [20]. In a study of 93 cats with ICM [23], the median duration of clinical signs at the time of diagnosis was 30 days (range, 1–1,095 days) [22]. Similarly, in a study of 78 dogs diagnosed with meningioma, the median time the animals had been showing clinical signs before being diagnosed was 30 days (range, 0–912 days) [20].

The pathophysiological effects of brain tumors include uncompensated intracranial hypertension and brain herniation (BH) [16], that is dislocation of brain parenchyma [8]. There are five types of BH: subfalcine (SH, characterized by medial displacement of the cingulate gyrus towards the opposite side under the falx cerebri), caudotentorial (CTH, characterized by caudal displacement of the parahippocampal gyrus of the cerebral cortex under the tentorium cerebelli, resulting in compression of the midbrain or cerebellum), foramenal (FMH, characterized by shifting of the cerebellar vermis through the foramen magnum), transcalvarian (characterized by parenchymal protrusion through a cranial defect) [4], and rostrotentorial (characterized by rostroventral displacement of the cerebellar vermis relative to the osseous cerebellar tentorium with compression of the midbrain or temporal cortex) [8], of which FMH and CTH are the most clinically important [8]. CTH has been associated with particularly poor short-term outcomes in dogs and cats [10].

The aims of this study are: 1) to evaluate the incidence and location of BH in association with histologically confirmed ICMs

*Correspondence to: Minato, S.: Minato.simone@gmail.com ©2021 The Japanese Society of Veterinary Science



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in dogs and cats, 2) to determine the ratio between the meningioma volume (MV) and cranial cavity volume (CCV) in each case using magnetic resonance imaging (MRI) analysis, and 3) identify any variables that correlate with the incidence and kind of BH in animals diagnosed with ICM.

MATERIALS AND METHODS

Case selection

The medical record, the Valdinievole Veterinary Clinic and of Dick White Referrals was searched for dogs and cats with a diagnosis of ICM that underwent surgery or postmortem examination between January 2004 and December 2014. Only cases with a brain MRI study and histopathological confirmation of ICM were included.

Clinical information

Clinical data acquired included signalament, clinical signs, duration of signs, neuroanatomic localization, drugs administered prior to MRI examination for suspected increase of intracranial pressure and the number and location of meningiomas. Age at diagnosis is reported in months, duration of signs is categorized in less than a month (<1 month) and more than a month (>1 month). Neuroanatomical localization was defined as forebrain, brainstem, cerebellum, or intracranial multifocal. Seizures, compulsive pacing, head pressing, altered behavior and circling towards one side were considered to be signs of forebrain tumor localization. Altered gait with ataxia and paresis, cranial nerve deficit, and/or severely altered consciousness (stupor, coma) were considered to be signs of brainstem disease. Ataxia with dysmetric gait, intention tremor and titubation were considered signs of cerebellar disease. If two or more anatomical regions were affected on neurological examination, a multifocal neuroanatomical localization was made. Previous administration of drugs that can influence edema and intracranial pressure, such as diuretics and corticosteroids, was noted. No standardized protocol for drug administration was used.

Image analysis

MRI images were reviewed after histopathological result by a board certified radiologist (D.D.S.), a board certified neurologist (M.B.), and a third-year neurology resident (S.M.) Diagnoses were made by consensus among examiners. All MRI examinations were performed under general anesthesia including intravenous (IV) premedication with butorphanol (0.2–0.3 mg/kg; Dolorex, MSD Animal Health, Madison, NJ, USA; Torbugesic, Zoetis Inc., Parsippany, NJ, USA), anesthetic induction with IV administration of propofol (Proposure, Boehringer Ingelheim, Ingelheim am rhein, Germany; Propoflo, Abbott Laboratories, Maidenhead, UK). Tracheal intubation was performed and general anesthesia was maintained with isoflurane (Isoflo, Zoetis Inc.; IsoFlo, Abbott Laboratories) vaporized in 100 per cent of oxygen to maintain an end tidal concentration of 1.2–1.4%. MRI scans were obtained with a 0.25-T (Vet-Grande, ESAOTE, Genova, Italy) (dogs 1–26, cats 1–21) and 0.4-T scanner (Hitachi Aperto Lucent, Hitachi Medical Corp., Tokyo, Japan) (dogs 27–45, cats 22–24). Sagittal T1-weighted (T1W) images [slice thickness 3–5 mm, repetition time (TR) 434–696

msec, echo time (TE) 14-26 msec] and trasverse T1W images (slice thickness 3.5-5 mm, TR 427-900 msec, TE 13-26 msec) acquired pre- and postcontrast gadoteric acid (Dotarem, Guerbet Laboratories, Villepinte, France) as well as sagittal T2-weighted (T2W) images (slice thickness 3-5 mm, TR 2,680-5,166 msec, TE 90-120 msec). Trasverse T2W images (slice thickness 3.5-5 mm, TR 2,952-5,480 msec, TE 90-120 msec) and transverse FLAIR images [slice thickness 4-5 mm, TR 7,000-12,186 msec, TE 90-120 msec, inversion time (TI) 1,800-2,100 msec] were also examined. ICMs were classified as single or multiple; if there were more than one distinct mass without visible continuity the masses were considered multiple. ICM location was classified as rostrotentorial, caudotentorial, or multifocal. The multifocal designation was given if there were multiple meningiomas or one mass that encompassed more than one compartment. Patients with intracranial abnormalities other than meningioma, such as cranial malformation (i.e. Chiari-like malformation with Foramen Magnum herniation) were excluded from the study.

The type of each observed BH was described. SH was diagnosed in transverse-plane images as a medial displacement of the cingulate gyrus towards the opposite side under the falx cerebri (Fig. 1). CTH was diagnosed in transverse- and sagittal-plane images as a caudal displacement of the parahippocampal gyrus under the tentorium cerebelli (Fig. 2). FMH was diagnosed in sagittal-plane images as a shifting of the cerebellar vermis through the foramen magnum in association with brain



Fig. 1. Transverse T2-Weighted image of a 9 year old Domestic short-haired cat with a right sided parietal meningioma and a sub-falcine herniation with displacement of the cingulate gyrus (star) ventral to the falx cerebri.



Fig. 2. Sagittal T2-Weighted image demonstrating cerebral caudotentorial herniation characterized by caudoventral displacement of the cerebral cortex (star) and consequent deformation of the rostral aspect of the cerebellum.



Fig. 3. Foramenal herniation in a 10 year old Domestic shorthaired cat. Sagittal T2-Weighted image with an occipital meningioma and a protrusion of the cerebellar vermis (star) into the foramen magnum.



Fig. 4. Transverse T2-Weighted image showing perilesional hyperintense edema (star).



Fig. 5. Transverse T1-Weighted image obtained after contrast administration and traced with imaging software for volume calculation using a planimetry method.

stem compression/distortion (Fig. 3); transcalvarian herniation that was diagnosed in transverse- and sagittal-plane images as a protrusion of parenchyma through a defect of the calvarium. Finally, rostrotentorial herniation was diagnosed in sagittal-plane images as a rostroventral displacement of the cerebellar vermis relative to the osseous cerebellar tentorium.

Peritumoral edema (PE) as evidenced by peritumoral hyperintensity in T2W/FLAIR images was evaluated (Fig. 4). MV was calculated by one of the authors (S.M.) using a previously described planimetric method [21]. The perimeter of the mass was traced manually in T1W images (all slices) acquired postcontrast in the transverse plane with a dedicated software (Osirix Dicom Viewer, Pixmeo SARL, Bernex, Switzerland) (Fig. 5). Following tracing, the mass area in each slice was calculated automatically, as was the total volume of the mass. CCV was measured in the same software with manual segmentation on a slice-by-slice basis in sagittal T2W images as previously described [18, 19] (Fig. 6). The MV/CCV ratio was calculated for each case.



Fig. 6. Sagittal T2-Weighted image traced with imaging software for volume calculation of the cranial cavity.

Statistical analysis

Results are expressed as means with standard deviations, medians and interquartile range (IQR) or percentages, as appropriate. Differences between species were detected by Fisher exact test or Yates's χ^2 test, Student's *t* test for independent samples, taking into consideration heteroscedasticity, or Mann-Whitney test as appropriate. Associations between herniation type and patient characteristic variables were evaluated by binary logistic regression with backward selection of variables. The regression results are expressed as odds ratios (ORs), and *P* values less than 0.05 were considered significant. Data were analyzed in SPSS software version 20 (IBM Corp., Armonk, NY, USA).

RESULTS

Animals

A group of 45 client-owned dogs (24 males and 21 females), including 13 mixed-breed dogs, 12 German shepherds, 6 boxers, and 10 other breeds [(American cocker spaniel, Border collie, Golden retriever, Labrador retriever, Irish setter, Maremma sheepdog, Pekingese, Rottweiler, Springer spaniel, and West Highland white terrier (WHWT)] were in the study cohort. The dogs' mean age at the time of ICM diagnosis was 115.8 ± 29.3 months (range, 59–174 months). Additionally, 24 cats (17 males and 7 females), including 21 domestic shorthaired, 1 domestic longhaired, 1 Norwegian forest, and 1 Russian blue, were in the study cohort. The cats' mean age at the time of ICM diagnosis was 129.1 ± 40.8 months (range, 40-182 months).

Clinical findings

Clinical signs were reviewed for 43 of the 45 dogs and are summarized in Table 1. Among these 43 canine patients, the most common clinical signs were seizure (32/43, 74.4%) (*P*<0.001), ataxia (5/43, 11.6%), and behavioral changes (4/43, 9.3%). Other clinical signs reported were circling (2/43, 4.7%), head pressing (3/43, 7.0%), and head tilt (4/43, 9.3%). Duration of clinical signs was recorded in 41 dogs, with 28 dogs examinated within a month from the onset of clinical signs (68.3%) and 13 dogs after one month (31.7%) (median duration 0 months, IQR 1.5). Neurological examinations, which were available for 43 of the 45 dogs, revealed that 36/43 dogs had a forebrain localization (83.7%), 6 (13.9%) had a brainstem localization, and 1 had a normal neurological exam (an ICM was discovered as an incidental finding in an MRI examination performed for other reasons). Intracranial hypertension treatment records were available for 40 cases. Of those 40 dogs, 14 were under treatment, including 6 treated with corticosteroids and 8 treated with mannitol.

Clinical sign records were available and reviewed for 23 of the 24 cats. Among the feline patients, the most common clinical sign was altered behavior (10/23, 43.5%) (*P*<0.01). Other frequently reported clinical signs cats were circling (8/23, 34.8%) and ataxia (8/23, 34.8%), followed by altered consciousness (5/23, 21.7%), head pressing (3/23, 13.0%), and seizures (3/23, 13.0%). Duration of clinical signs was recorded in 22 cats, with 8/22 cats examinated within a month (36.4%) and 14/22 (63.6%) after a month (median duration 1 month, IQR 3). Neurological examination records, which were available for 21 cats, revealed that 13 cats (61.9%) had a brainstem localization, 3 (14.2%) had multifocal intracranial localization. Drug administration data were available in the records of 22 cats. Among those 22 cats, 4 were administered corticosteroids (only), 4 were given mannitol (only), and 1 cat was given both corticosteroids and mannitol.

MRI findings

All 45 dogs were diagnosed with a single ICM. The locations of the masses were recorded as follows: 38 (84.4%) rostrotentorial, 6 (13.3%) caudotentorial, and 1 (2.2%) both rostro- and caudotentorial. Of the 45 dogs in the study, 28 (62.2%) presented with a SH, 9 (20%) had a CTH, and only 2 (4.4%) had a FMH (Table 2). Overall, 30 dogs (66.7%) showed at least one type of herniation, and 8 dogs (17.7%) had more than one type (Table 2). The presence of PE was reported in 37/45 dogs (82.2%) (P<0.001).

Of the 24 cats in the study, 3 (12.5%) had multiple ICMs and 21 (87.5%) had a single ICM. Of the 24 cats, 21 (87.5%) had rostrotentorially located tumors, 2 (8.3%) had multifocal ICMs (both with multiple meningiomas), and just 1 (4.2%) had a caudotentorially located tumor. All 24 cats presented with at least one BH (Table 2) (P<0.001). The most common type of herniation in cats, FMH, was observed in 23 cases (95.8%) (P<0.001), followed by CTH, which was documented in 21 cases (87.5%) (P<0.001), and SH, which was observed in 18 cases (75.0%). PE was reported in 9/24 cats (37.5%).

The mean MV, CCV, and MV/CCV values obtained for dogs and cats are reported in Table 2. The MV in dogs ranged from 0.191 cm³ to 29.368 cm³, with a mean value of 3.6 ± 4.4 cm³.

 Table 1. Clinical signs, neurolocalisation, and meningioma localization in dogs and cats

Variable	Dogs	Cats	P value
Clinical signs (*)	n=43	n=23	
Seizures	32 (74.4%)	3 (13.0%)	< 0.001
Behavioral Change	4 (9.3%)	10 (43.5%)	< 0.01
Ataxia	5 (11.6%)	8 (34.8%)	< 0.05
Circling	2 (4.7%)	8 (34.8%)	< 0.01
Head Pressing	3 (7.0%)	3 (13.0%)	ns
Head tilt	4 (9.3%)	0 (0%)	ns
Altered consciousness	0 (0%)	5 (21.7%)	< 0.01
None	1 (2.3%)	0 (0%)	ns
Neurolocalization	n=43	n=21	
Forebrain	36 (83.7%)	13 (61.9%)	ns (§)
Brainstem	6 (14.0%)	5 (23.8%)	
Cerebellum	0 (0%)	0 (0%)	
Multifocal	0 (0%)	3 (14.3%)	
None	1 (2.3%)	0 (0%)	

(*) multiple percentages, (\S) overall test for comparing the two frequency distributions, ns not significant.

	e		
Finding D	ogs (n=45)	Cats (n=24)	P value
M number			
Single	45 (100%)	21 (87.5%)	<0.05 (§)
Multiple	0 (0%)	3 (12.5%)	
eningioma localization			
Rostrotentorial	38 (84.4%)	21 (87.5%)	ns (§)
Caudotentorial	6 (13.3%)	1 (4.2%)	
Multifocal	1 (2.2%)	2 (8.3%)	
ritumoral edema	37 (82.2%)	9 (37.5%)	< 0.001
ain herniation (*)	30 (66.7%)	24 (100%)	< 0.001
SH	28 (62.2%)	18 (75%)	ns
CTH	9 (20%)	21 (87.5%)	< 0.001
FMH	2 (4.4%)	23 (95.8%)	< 0.001
SH/CTH ^a	6 (13.3%)	1 (4.2%)	ns
CTH/FMH ^a	1 (2.2%)	3 (12.5%)	ns
SH/CTH/FMH ^a	1 (2.2%)	17 (70.8%)	< 0.001
None	15 (33.3%)	0 (0%)	< 0.001
ean MV	$3.6 \pm 4.4 \text{ cm}^3$	$2.9 \pm 1.2 \text{ cm}^3$	ns
ean CCV 9	$1.6\pm17.5~\mathrm{cm}^3$	$29.7\pm3.4~\mathrm{cm^3}$	< 0.001
ean MV/CCV 0	$.04\pm0.04$	0.10 ± 0.04	< 0.001
ean www.ccv	$.04 \pm 0.04$	0.10 ± 0.04	

 Table 2.
 Summary of Magnetic Resonance Imaging analysis findings in dogs and cats with Intracranial meningiomas



Fig. 7. Measurements of Meningioma volume and Cranial Cavity volume ratio subdivided by species. MV/CCV was significantly different from dogs and cats (*P*<0.001). MV: meningioma volume. CCV: cranial cavity volume. *: *P*<0.001.</p>

CCV, cranial cavity volume; CTH, caudotentorial herniation; FMH, foramenal herniation; ICM, intracranial meningioma; MV, meningioma volume; SH, subfalcine herniation . Numbers are reported with percentages and means are reported with standard deviations and ranges. ^aConcomitant findings of more than one type are shown as SH/CTH, CTH/FMH, and SH/CTH/FMH; these animals are also represented in each single type as appropriate. *, multiple percentages; §, overall test for comparing the two frequency distributions; ns, not significant.

The CCV of the dogs in this study ranged from 47.531 cm³ to 122.558 cm³, with a mean value of 91.6 ± 17.5 cm³. Accordingly, the mean MV/CCV for the dogs in this study was 0.04 ± 0.04 . The MV in cats ranged from 1.189 cm³ to 5.583 cm³, with a mean value 2.9 ± 1.2 cm³. The CCV of the cats in this study ranged from 22.343 cm³ to 36.275 cm³, with a mean value of 29.7 ± 3.4 cm³. Accordingly, the mean MV/CCV for the cats in this study was 0.10 ± 0.04 , which was significantly greater than the MV/CVV obtained for the dogs (*P*<0.001) (Fig. 7).

Among 37 dogs with PE, 21 had only SH (56.7%), 5 had both SH and CTH (13.5%), 2 had only CTH (5.4%) and 1 had SH with CTH and FMH (2.7%). Only 9 cats out of 24 had PE: 7 had SH, CTH and FMH (77.7%), 1 had SH and CTH (11.1%) and 1 had FMH (11.1%). PE was associated with an increased incidence of SH in dogs (P<0.05, OR=35.48), but not in cats (P>0.05, OR=3.56). A MV/CCV greater than 2.86 in dogs was associated with a higher risk (73.1%) of SH (P <0.05, OR=1.86). Due to the low numbers of animals with FMH and CTH, a comparative statistical analysis of the relationship of edema with these two herniation types was not possible.

DISCUSSION

In this study, we evaluated the rate and location of BH associated with histologically confirmed ICMs. The development of at least one type of BH was quite common in dogs (66.7% of cases), with 17.7% showing more than one type of herniation. Among dogs there was a greater prevalence of SH (62.2%) than of CTH (20.0%) and FMH (4.4%). Surprisingly, we observed BH in all examined cats (100% of cases), with the most common type being FMH (95.8%), followed by CTH (87.5%) and SH (75.0%). Despite the fact that ICMs were commonly located rostrotentorially in both dogs (84.4%) and cats (87.5%), FMH and CTH were far more common in cats than in dogs (both P<0.001). The occurrence of SH was similar for both species. Neither transcalvarian nor rostrotentorial herniation was diagnosed in the present study. The greater incidence of BH in cats than dogs with ICMs could be related the tendency of feline species to present a greater MV/CCV ratio than canine species, and therefore to have a proportionally larger mass.

The greater MV/CCV observed in cats could be due to several factors. One possibility could be related to the differing clinical signs between dogs and cats. In our study, the most common sign of ICM was abnormal behavior in cats and seizures in dogs, in accordance with previous reports [20, 23]. The emergence of seizures as a predominant clinical sign in dogs could alert owners of an abnormality at an earlier disease stage. Second, meningioma has a different biological behavior in the canine and feline species: in the cat meningiomas typically appear well capsulated, compressing the parenchyma without infiltrating it. In dogs, on the other hand, a clear distinction between neoplastic margins is less evident, and up to 30% of cases show infiltration of the cerebral parenchyma [1]. Histologically, ICM in the cat appears less aggressive than the canine counterpart [12], and less aggressive growth in cats could give their brain parenchyma an opportunity to adapt to the space-occupying lesion slowly, perhaps contributing to

later diagnosis.

An association between PE and SH was observed in dogs, but not in cats: edema was taken into account because it can contribute to increased intracranial pressure [16] and thereby favor the development of BH. Surprisingly, a lower percentage of cats (37.5%) showed PE than dogs (82.2%). Cerebral edema is known to be a consequence of brain tumors. Various mechanisms are at the basis of the formation of peritumoral vasogenic edema, including the altered vascular architecture of the neoplasia, with the presence of fenestrations and anomalous tight junctions that allow the leakage of plasma fluid and proteins in the surrounding parenchyma. Furthermore, the tumor tissue produces various cytokines, among which VEGF, which increases the permeability of the vessels, increases blood flow and vasodilation contributing to the formation of brain edema [17]. In recent times, studies have shown that upregulation of molecules such as aquaporins is linked to the formation of PE [9]. Edema can also be a consequence of repeated seizures [5], or even the cause of seizures [14]. Investigating the cause of cerebral edema is not among the aims of this work, but it is conceivable that the clinical presentation of dogs with seizures may be linked to the presence of PE. Future studies are needed to resolve the clinical differences between ICMS in dogs versus cats.

Inter-species and inter-breed anatomical differences might influence susceptibility to BH. In a recent imaging study examining the morphology of the cerebellum and caudal fossa [6], apparent overcrowding of the caudal cranial fossa or cerebellar herniation was found to be present in 40% of clinically healthy cats. Based on that study, it could be argued that the high incidence of FMH in cats in this study could be influenced or even misdiagnosed due to anatomical variation. Notwithstanding, in humans, it is possible to distinguish between a cerebellar herniation due to a space occupying lesion versus that consequent to anatomical variation because in the former case there is medullary displacement associated with loss of cerebrospinal fluid space [7]. All FMHs in this study involved herniation of the cerebellar vermis through the foramen magnum in association with compression/distortion of the medulla, which makes it unlikely that they were artefacts of anatomical variation. However, cerebellar shifting, even in healthy cats, could be a factor that predisposes cats to FMH, even with a rostrotentorial meningioma.

Clinical signs associated with BH in dogs and cats include altered consciousness, changes in pupillary size, an abnormal pupillary light reflex, and altered cardiorespiratory patterns [2, 8]. Similar to the literature with humans, BH studies with dogs do not always relate clinical signs with herniation rate and type [15, 25]. However, meningoencephalitis of unknown etiology has been reported to be associated with an increased risk of death in dogs with FMH [11], and among dogs with traumatic brain injury [3]. A positive correlation between CTH and decreased short-term survival in dogs and cats was reported recently [10]. Elevated intracranial pressure can cause various sequelae of considerable clinical importance, such as decreased cerebral perfusion pressure, catecholamine release, and consequent myocardial ischemia [2]. Presumed intracranial pressure elevation has been associated with CTH and SH in dogs [4]. Our herniation incidence data in cats differs from a previous report of 33 feline ICM cases in which FMHs and CTHs were observed in 21% and 42% of cases, respectively [22]; comparing our results with these prior results is difficult because MV was not reported in the prior paper.

This study has the notable limitations of having low numbers of cats without an FMH or CTH, having low numbers of dogs with FMH, and being of a retrospective nature. The relatively limited representation of cats without FMH and CTH or dogs with FMH could be due to the inherent pathophysiological characteristics of the disease and/or to the number of cases recruited.

In conclusion, we found an extremely high incidence of BH associated with ICM in cats, with FMH being observed in the vast majority of cases, very frequently together with CTH. A proportionally greater MV/CCV ratio was found in cats than in dogs at the time of diagnosis. Earlier diagnostic imaging in cats, perhaps in the presence of even mild clinical signs, may permit earlier diagnosis and therapeutic intervention, thereby perhaps reducing the risk of increased intracranial pressure, which could yield better short-term outcomes.

CONFLICT OF INTEREST. The authors declare that they have no conflicts of interest related to the subject materials discussed in this study.

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