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# Complications after cerebrospinal fluid collection in dogs with brain neoplasm<sup>1</sup>

Mathias R. Wrzesinski<sup>2</sup>, Angel Ripplinger<sup>2</sup>, Dênis A. Ferrarin<sup>2</sup>, Marcelo L. Schwab<sup>2</sup>, Júlia S. Rauber<sup>2</sup>, Junior Santos<sup>3</sup>, Diego V. Beckmann<sup>4</sup> and Alexandre Mazzanti<sup>5\*</sup>

**ABSTRACT.-** Wrzesinski M.R., Ripplinger A., Ferrarin D.A., Schwab M.L., Rauber J.S., Santos J., Beckmann D.V & Mazzanti A. 2022. **Cerebrospinal fluid tap complications in dogs with brain neoplasm**. *Pesquisa Veterinária Brasileira 42:e06984, 2022*. Serviço de Neurologia e Neurocirurgia Veterinária, Departamento de Clínica de Pequenos Animais, Universidade Federal de Santa Maria, Prédio 97, Camobi, Santa Maria, RS 97105-900, Brazil. E-mail: alexamazza@yahoo.com.br

Cerebrospinal fluid (CSF) collection in dogs with brain neoplasms (BN) may be associated with complications owing to increased intracranial pressure caused by expansive lesions. Although this procedure has been performed in dogs with BN, no data regarding complications after CSF tap in these animals is available. Thus, this retrospective study aimed to identify the rate and types of complications observed after CSF taps in dogs with BN. Thirty dogs with BN were included in the study. In 83% (25/30) of the cases, clinical recovery after CSF tap was considered normal, and in 17% (5/30) the recovery was abnormal. The main clinical and neurological signs observed in dogs with abnormal clinical recovery were apnea (5/5), absence of pupillary photomotor reflex (3/5), coma (2/5), and stupor (1/5). In 40% (2/5) of the dogs, herniation of the cerebellum through the foramen magnum was observed on necropsy. In conclusion, the rate of complications after CSF taps was 17%, and was characterized by apnea, absent pupillary photomotor reflex, altered level of consciousness, and encephalic herniation.

INDEX TERMS: Intracranial pressure, brain, cerebrospinal fluid, herniation, diseases of dogs, dogs.

**RESUMO.-** Complicações após colheita do líquido cerebroespinhal em cães com neoplasma encefálico. A colheita do líquido cerebroespinhal (LCE) em cães com neoplasmas encefálicos (NE) pode estar associada a complicações devido ao aumento da pressão intracraniana (PIC), causada pela lesão expansiva. Embora o procedimento seja realizado em cães com NE, não foram encontrados dados referentes às complicações após colheita de LCE nesses pacientes. Sendo assim, o objetivo do presente estudo retrospectivo foi identificar a taxa, bem como os tipos de complicações observadas após a colheita de LCE em cães com neoplasma encefálico. Dos 30 cães com NE incluídos no estudo, em 83% (25/30) dos casos a evolução clínica após a colheita do LCE foi considerada normal e, em 17% (5/30) anormal. Os principais sinais clínicos e neurológicos observados nos cães com evolução clínica anormal foram apneia (5/5), reflexo fotomotor pupilar ausente (3/5), coma (2/5) e estupor (1/5). Em 40% (2/5) foi observado herniação do cerebelo na necropsia. Com base nos resultados encontrados, conclui-se que a taxa de complicações após a colheita de LCE foi baixa (17%) e as alterações encontradas foram apneia, seguido de reflexo fotomotor pupilar ausente, alteração no nível de consciência e herniação encefálica.

TERMOS DE INDEXAÇÃO: pressão intracraniana, encéfalo, líquido cerebroespinhal, herniação, doenças de cães, cães.

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<sup>&</sup>lt;sup>2</sup> Graduate Program in Veterinary Medicine, Serviço de Neurologia e Neurocirurgia Veterinária (SNNV), Hospital Veterinário Universitário (HVU), Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Camobi, Santa Maria, RS 97105-900, Brazil. \*Corresponding author: alexamazza@yahoo.com.br

<sup>&</sup>lt;sup>3</sup> Residency Program in Veterinary Medicine in Anesthesiology, Hospital Veterinário Universitário (HVU), Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Camobi, Santa Maria, RS 97105-900, Brazil.

<sup>&</sup>lt;sup>4</sup> Serviço de Neurologia e Neurocirurgia Veterinária, Hospital Veterinário, Universidade Federal do Pampa (Unipampa), Campus Uruguaiana, Uruguaiana, RS 97508-000, Brazil.

<sup>&</sup>lt;sup>5</sup> Departamento de Clínica de Pequenos Animais, Serviço de Neurologia e Neurocirurgia Veterinária (SNNV), Hospital Veterinário Universitário (HVU), Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Prédio 97, Camobi, Santa Maria, RS 97105-900, Brazil.

### **INTRODUCTION**

Brain neoplasms (BN) are a frequent cause of neurological dysfunction and usually occur in middle-aged to elderly animals (Snyder et al. 2006, McEntee & Dewey 2013); approximately 95% of primary tumors affect dogs over 5-years of age (Higgins et al. 2016). BN results in space-occupying lesions (mass effect), the neurological alterations of which depend on the location, extent, and growth rate of the tumor (Costa 2009, Dewey 2016, Higgins et al. 2016). Signs may be mono or multifocal due to the compression of adjacent structures, direct tissue invasion, circulation interruption, edema, inflammation, and necrosis (Costa 2009, O'Brien & Coates 2010, Rossmeisl & Pancotto 2012, Dewey 2016).

Diagnosis is established based on various parameters including medical history, breed, age, evolution, neurological signs, results of complementary examinations [chest radiography, abdominal ultrasound, cerebrospinal fluid (CSF) analysis, computed tomography (CT), and magnetic resonance imaging (MRI)], and confirmation by histopathological analysis of the sample obtained by biopsy or necropsy (Costa 2009, O'Brien & Coates 2010, Rossmeisl & Pancotto 2012, Dewey 2016).

With the development and advances in imaging techniques, such as CT and MRI, the presumptive *ante mortem* diagnosis of this condition has increased (Kraft et al. 1997). However, due to limited access to CT and MRI in veterinary clinics and hospitals, and the high cost of these examinations, CSF collection in dogs with suspected BN is at times performed in isolation from the advanced imaging methods, thus playing an important role as a diagnostic aid (Dickinson et al. 2006, Snyder et al. 2006, Pastorello et al. 2010, Polidoro et al. 2018, Conceição et al. 2019).

In dogs with BN, the most commonly observed alteration in the CSF is albumin cytological dissociation, in which the concentration of total protein is elevated without a corresponding increase in the number of nucleated cells (O'Brien & Coates 2010, Polidoro et al. 2018). The alterations found in the CSF are nonspecific; however, some types of alterations are seen in 90% of dogs with BN (Costa 2009).

BN can lead to increased intracranial pressure (ICP) owing to its primary (space-occupying) or secondary (edema) effects (Kornegay et al. 1983, Snyder et al. 2006, Terlizzi & Platt 2006, Walmsley et al. 2006, Lewis et al. 2016). The ICP value in normal dogs' ranges from 5 to 12mmHg (Dewey & Fletcher 2016) and is considered high when the value is greater than 13mmHg (Seki et al. 2019). Though ICP measurement can be performed by direct means, such as intracranial optical fibers (Bagley et al. 1995), subdural and intraparenchymal transducers (Sturges et al. 2019 Seki et al. 2019) and indirect transcranial Doppler (Fukushima et al. 2000), due to the difficulty and high cost, they are rarely performed in routine neurological practice (Terlizzi & Platt 2006, Seki et al. 2019).

An elevated ICP increases the chance of brain herniation during puncture to collect CSF (Wood et al. 2012, Dewey et al. 2016). Considering these inherent risks in dogs with BN, there remains a controversy about the value of collecting CSF in these animals. CT or MRI is recommended before CSF collection and, in the presence of images suggestive of neoplasms, increased ICP, and/or brain herniations, the procedure should be avoided. However, according to Dewey (2016), the risk of a CSF tap in the presence of elevated ICP in animals with BN is not considered high. To date, the literature related to the rate as well as the types of complications after CSF collection in dogs with BN without prior evaluation of advanced imaging examinations is scare.

Therefore, this retrospective study aimed to identify the rate and types of complications observed after CSF collection in dogs with BN, without previous evaluation using advanced imaging examinations.

### **MATERIALS AND METHODS**

The neurology findings and necropsy reports of dogs treated at the "Serviço de Neurologia e Neurocirurgia Veterinária" (Veterinary Neurology and Neurosurgery Service) of the Universidade Federal de Santa Maria (UFSM) from January 2006 to November 2020, were reviewed. Thirty dogs with suspected intracranial neoplasm that underwent CSF collection and analysis without prior advanced imaging tests evaluation such as CT and MRI, and with a definitive diagnosis of BN, confirmed by necropsy and routine histopathological examination, were included.

CSF collection and analysis were performed to aid in the diagnosis of dogs that presented neurological alterations compatible with intracranial disease, in addition to BN as one of the differential diagnoses. In all cases, the CSF was collected aseptically under general inhalation anesthesia by means of puncture in the cerebelomedullary (CM) and/or lumbar (LC) cisterns (L5-L6 or L6-L7), with a 22G spinal needle, according to the technique described by Terlizzi & Platt (2009). No maneuvers were performed for stabilization/ reduction of ICP in any of the dogs before CSF collection, such as the use of mannitol (Kuo et al. 2017), as this could interfere with the CSF analysis, as well as the elevation of the head at 30° during the procedure (Kuo et al. 2017), making puncture in the CM difficult.

After CSF collection, dogs were monitored until complete anesthetic recovery, euthanasia, or death in which complications occurred. The clinical and neurological evolution after CSF collection was defined as normal when the animal recovered without any clinical and/or neurological signs that were different from those observed before the puncture, or abnormal when there were other clinical/neurological signs, such as the non-recovery of the level of consciousness after the interruption of anesthesia (stupor or coma), failure to recover spontaneous breathing (apnea), requiring assisted ventilation, the presence of miosis or mydriasis, decrease or absence of pupillary and oculocephalic photomotor reflexes, and deficiency of cranial nerves VIII, IX, X, and XII (Walmsley et al. 2006, Lewis et al. 2016).

Necropsy reports were reviewed for details regarding the BN type, neuroanatomical location, and complications related to puncture in the CM and/or LC. Dogs with primary and secondary BN were included in the study. Primary neoplasms are considered to originate from the brain parenchyma (glia and neuron cells), lining cells (internal and external) of the brain (meninges and ependyma), and those of vascular origin, such as the choroid plexus; while the secondary lesions were those that were metastatic or affected the brain by local extension (Dewey et al. 2016). The classification of primary BN included in this study was according to the World Health Organization, referring to the classification of central nervous system tumors (Higgins et al. 2016).

The neuroanatomical location of the lesion, established by necropsy findings, was defined as thalamocortex (TC; telencephalon and diencephalon), brainstem (BT; midbrain, metencephalon and myelencephalon), cerebellum (C; metencephalon) or multifocal (MF), when the neoplasm involved more than one anatomical region (De LaHunta & Glass 2009, Dewey et al. 2016). The presence of brain herniations (subfalcine, rostral transtentorial, caudal transtentorial or cerebellar through the foramen magnum) (Kornegay et al. 1983), iatrogenic trauma to the brainstem or spinal cord, and the presence of hemorrhage were also considered complications, through macroscopic evaluation of the region of puncture.

Statistical analyses were performed using Jamovi (version 1.2.27). Clinical and neurological evolution data after LCE collection (normal/abnormal) were used to process the association analysis with respect to age, weight, sex, breed, neuroanatomical location (TC, BT, C, and MF), and neoplasm type. A binomial logistic regression test was used to identify the relationships between recovery, age, and weight. Fisher's exact test was employed to determine any association between recovery and sex. In addition, to identify the relationship between the neuroanatomical location and tumor type, the chi-square test ( $\chi$ 2) was used. In all analyses, *p*<0.05 was considered statistically significant.

## **RESULTS AND DISCUSSION**

Thirty dogs were included in the study on the basis of the preestablished criteria. The details regarding the distribution of breeds, sex, age, location of the neoplasm, clinical signs, type of neoplasm, puncture site, and CSF changes are described in Table 1. As for the clinical evolution of dogs with BN after CSF collection, 83% (25/30) of the cases were considered normal and 17% (5/30) as abnormal. There was no statistical correlation between breed (p=0.507), sex (p=0.355), age (p=0.357), neuroanatomical location of the BN (p=0.877), puncture site (p=0.322), and clinical evolution after CSF collection.

Increased ICP is one of the factors that makes the performance of CSF collection contraindicated because of the possibility of brain herniation (Terlizzi & Platt 2009, Dewey et al. 2016). However, due to the difficulty and high cost of measuring ICP, these techniques are rarely performed routinely based on the suspicion of increased ICP on suggestive clinical signs. In this study, the neurological changes observed before CSF collection in five dogs with complications were epileptic seizures (n=4), circling (n=3), altered level of consciousness (drowsiness) (n=2), and central vestibular syndrome (n=1). However, none of these signs helped in the suspicion of high ICP, as mentioned by Terlizzi & Platt (2009), which made it difficult to use the clinical parameters for not performing the CSF tap. In a study by Lewis et al. (2016), among 119

 Table 1. Distribution regarding to sex, age, breed, neoplasm location, neoplasm type, puncture site and cerebrospinal fluid

 (CSF) alterations of 30 dogs with brain neoplasm submitted to cerebrospinal fluid collection

Dog	Sex, age (years), breed	Neoplasm location	Neoplasm type	Puncture site	CSF alteration
1	F, 8, Boxer	Multifocal	Meningioma	LC	AD
2	F, 6, Airedale terrier	Multifocal	Craniopharyngioma	LC	PP
3	F, 10, Mixed-breed	BT (midbrain)	Astrocytoma	LC	AD
4	M, 8, Boxer	Multifocal	Meningioma	LC	AD
5	F, 9, Miniature Poodle	TC (telencephalon)	Meningioma	СМ	PP
6	M, 10, Boxer	BT (midbrain)	Astrocytoma	LC	AD
7	M, 14, Mixed-breed	TC (telencephalon)	Prostatic adenocarcinoma	LC	AD
8	M, 10, English Bulldog	TC (telencephalon)	Oligodendroglioma	LC	NC
9	M, 8, Boxer	BT (midbrain)	Meningioma	LC	AD
10	F, 11, Boxer	Multifocal	Oligodendroglioma	LC	PP
11	F, 14, German Shepherd	TC (telencephalon)	Meningioma	LC	AD
12	F, 14, Dachshund	TC (diencephalon)	Meningioma	LC	AD
13	M, 12, Mixed-breed	Multifocal	Meningioma	LC	AD
14	F, 13, Mixed-breed	Cerebellum	Cutaneous hemangiosarcoma	LC	AD
15	F, 10, Mixed-breed	Multifocal	Meningioma	LC	AD
16	F, 8, German Shepherd	TC (telencephalon)	Meningioma	LC	NC
17	M, 13, Mixed-breed	TC (telencephalon)	Meningioma	LC	AD
18	F, 13, Mixed-breed	TC (telencephalon)	Mammary carcinoma	LC	AD
19	F, 10, Mixed-breed	Multifocal	Choroid plexus papilloma	LC	AD
20	F, 8, American Pit Bull Terrier	TC (diencephalon)	Cutaneous hemangiosarcoma	LC	AD
21	M, 8, American Pit Bull Terrier	TC (diencephalon)	Oligodendroglioma	LC	NC
22	F, 11, Boxer	Cerebellum	Meningioma	LC	NC
23	F, 9, Labrador Retriever	BT (metencephalon)	MPNST (trigeminal)	LC	AD
24	M, 12, Boxer	BT (myelencephalon)	Ependymoma	LC	AD
25	M, 10, Mixed-breed	BT (midbrain)	Astrocytoma	LC	PP
26	M, 9, Dachshund	TC (telencephalon)	Meningioma	LC	AD
27	F, 4, Boxer	BT (midbrain, metencephalon)	Astrocytoma	LC	AD
28	F, 6, Boxer	TC (telencephalon)	Oligodendroglioma	CM/LC	AD
29	M, 10, Mixed-breed	TC (telencephalon)	Ependymoma	LC	AD
30	M, 8, American Pit Bull Terrier	TC (telencephalon)	Cutaneous hemangiosarcoma	LC	NC

F = female, M = male, BT = brainstem, TC = thalamocortex, MPNST = malignant peripheral nerve sheath tumor, CM = cerebellomedullary cistern, CL = lumbar cistern, AD = albuminocytological dissociation (protein increase in CSF with normal cell number), NC = no changes, PP = pleocytosis and increased protein.

cases of brain herniation verified on MRI, 64.7% (77/119) showed signs of thalamocortical disease, but no obvious neurological signs of increased ICP or brain herniation. The authors concluded that the clinical signs directly attributed to increased ICP, and brain herniation may be absent in most cases of intracranial neoplasms.

In 25 dogs included in this study, the neurological signs observed after the CSF tap were similar to those observed at the time of consultation (normal clinical evolution after collection), which does not completely exclude some type of complication such as increased ICP, but these were not observed in the neurologic examination after collection or necropsy. Of the five cases in which the evolution was considered abnormal, 40% (2/5) had cerebellar herniation at necropsy. These animals developed coma, apnea, and bilateral light-unresponsive mydriasis (Table 2), consistent with brain herniation (Walmsley et al. 2006, Terlizzi & Platt 2009, Lewis et al. 2016). The other three dogs with neurological complications presented with stupor (n=1), apnea (n=3), and bilateral mydriasis (n=1); however, at necropsy, brain herniation was not observed. Walmsley et al. (2006) reported the limitation of necropsy in the identification of brain herniation and recommended MRI for detection of these alterations (Walmsley et al. 2006, Lewis et al. 2016). Therefore, it is speculated that brain herniation may have been underdiagnosed.

In this study, in addition to CSF tap puncture, other factors may have also contributed to or led to complications in the dogs. One of them is general anesthesia, since even with the emergence of new anesthetic drugs, performing the anesthetic procedure in animals with intracranial diseases is considered high risk (Greene 2010). Anesthetic agents, especially inhalational agents, alter the physiological mechanisms that preserve cerebral perfusion pressure, may increase ICP (Lozano et al. 2009, Greene 2010, Caines et al. 2014) and prolong or prevent anesthetic recovery in patients with BN (Lewis et al. 2016). Iatrogenic trauma to the brainstem or spinal cord due to a needle puncture is a risk factor for CSF collection. Clinical alterations are variable and may present with vestibular signs, tetraparesis, and alterations in the level of consciousness (Terlizzi & Platt 2009, Wood et al. 2012). In our study, however, no macroscopic signs were observed at

Table 2. Distribution regarding clinical and/or neurological signs before and after cerebrospinal fluid (CSF) collection and complications observed at necropsy of dogs with brain neoplasm

Dee	Clinical and/or neurological sig			
Dog —	Before	After	Necropsy findings	
1	Cerebellar ataxia	WC	NC	
2	BC	WC	NC	
3	Circling	WC	NC	
4	ES, BC	WC	NC	
5	ES, circling	Apnea, absent PPR, stupor	NC	
6	BC, circling	WC	NC	
7	CVS	WC	NC	
8	BC	WC	NC	
9	ES	WC	NC	
10	ES	WC	NC	
11	ES, amaurosis	WC	NC	
12	ES, BC, drowsiness	WC	NC	
13	Circling, tetraparesis	WC	NC	
14	CVS, drowsiness	WC	NC	
15	CVS	WC	NC	
16	Tetraparesis	WC	NC	
17	ES, BC, tetraparesis	WC	NC	
18	ES, BC, amaurosis	WC	NC	
19	CVS, drowsiness	Apnea, absent PPR, coma	Cerebellar herniation	
20	ES, CVS, drowsiness	WC	NC	
21	ES, circling	WC	NC	
22	CVS, cerebellar ataxia	WC	NC	
23	CVS	WC	NC	
24	CVS	WC	NC	
25	ES	WC	NC	
26	BC	WC	NC	
27	ES, circling	Apnea, absent PPR, coma	Cerebellar herniation	
28	ES, circling, drowsiness	Apnea	NC	
29	ES	Apnea	NC	
30	ES	WC	NC	

BC = behavior change, ES = epileptic seizures, CVS = central vestibular syndrome, PPR = pupillary photomotor reflex, WC = without changes (same neurological signs as before the CSF collection), NC = no changes.

necropsy, which could indicate injury and hemorrhage caused by the needle during puncture to collect the CSF.

According to Dewey et al. (2016), there is lack of studies that could clarify the advantages of harvesting CSF in the LC instead of the CM regarding the risk of brain herniation in expansive lesions, such as BN. In our study, in dogs that had complications after CSF collection, in 20% (n=1), the puncture was performed in the CM, 20% (n=1) in the CM and LC, and 60% (n=3) in the LC, including two dogs that presented with herniation of the cerebellum through the foramen magnum. Even with no statistical difference regarding the puncture site (p=0.322), it was noted that most dogs with BN presented complications after collection, and the puncture occurred in the LC.

The main limitations of this study were the small number of dogs, non-standard anesthetic protocols, and its retrospective nature. In contrast, all BN cases were confirmed using histopathological analysis. Furthermore, studies on the rate and types of complications after CSF collection in dogs with BN are scarce, reinforcing the relevance of the results obtained.

CSF analysis rarely provides a definitive diagnosis but plays an important role in aiding the diagnosis of central nervous system disorders, particularly where access to MRI and CT is limited (Terlizzi & Platt 2006). However, CSF collection is associated with the risk of complications (Terlizzi & Platt 2006). Knowledge of the complication rate after CSF collection can help at the time of decision making with the owner, helping clarify the risks and benefits of CSF collection in dogs with BN. Therefore, we recommend the performance of advanced imaging tests before puncture for CSF collection in dogs with suspected BN, and if this resource is not available, indicate the procedure, as CSF analysis can aid in the diagnosis and offer a relatively low risk of complications (Lewis et al. 2016). In addition, CSF analysis can reinforce the suspicion of BN or reduce the suspicion of other diseases, such as inflammatory diseases, since the clinical signs can be similar between the two (Dewey 2016). It needs to be emphasized that ICP measurement is rarely performed in routine neurological practice, and it is difficult to use clinical and neurological parameters in suspicious high ICP for not performing CSF collection.

#### CONCLUSION

The complication rate after cerebrospinal fluid (CSF) collection in dogs with brain neoplasm was low (17%), and the most observed alterations were apnea, followed by absence of pupillary photomotor reflex, alteration in the level of consciousness (stupor and coma), and brain herniation.

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**Conflict of interest statement.-** The authors have no conflict of interest to declare.

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