PESQUISA VETERINÁRIA BRASILEIRA
Brazilian Journal of Veterinary Research
ISSN 0100-736X (Print)
ISSN 1678-5150 (Online)

Pesq. Vet. Bras. 43:e07114, 2023
DOI: 10.1590/1678-5150-PVB-7114

Original Article
Small Animal Diseases

Increased frequency of pneumonia in dogs with meningioma in ventral rhombencephalon[1]

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ABSTRACT.- Almeida B.A., Henker L.C., Bianchi M.V., Pavarini S.P., Sonne L. & Driemeier D. 2023. **Increased frequency of pneumonia in dogs with meningioma in ventral rhombencephalon.** *Pesquisa Veterinária Brasileira 43:e07114, 2023.* Setor de Patologia Veterinária, Departamento de Patologia Clínica Veterinária, Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul, Av. Bento Gonçalves 9090, Prédio 42505, Porto Alegre, RS 91540-000, Brazil. E-mail: brunoadealmeida@live.com

Intracranial tumors occurring in specific brain regions, such as the cerebellopontine angle, may be associated with cranial nerve dysfunction and dysphagia in humans and animals. Although dysphagia is a known risk factor for pneumonia, only postoperative pneumonia has been investigated in veterinary medicine. This study aimed to describe the clinical and pathological features of dogs with untreated intracranial meningiomas and concomitant pneumonia. Data from *post-mortem* examination registries from 2011 to 2021 were used (n=23). The frequency of pneumonia and other characteristics were compared between dogs with meningiomas in the ventral rhombencephalon region (VR group; n=13) and those with meningiomas in other intracranial sites (OIS group; n=10). The frequency of pneumonia was higher in the VR group than in the OIS group (n=5 vs. n=0; P=0.039). Plaque-like lesions were also more common in the VR group than in the OIS group (P=0.012). Dogs with concomitant pneumonia had cerebellopontine angle (n=3) and basilar meningiomas (n=2), mainly plaque-like lesions extending to or from other brain areas. In dogs with concomitant pneumonia, meningiomas had invasive (n=5) and compressive (n=3) growth behaviors and nerve roots involved in the swallowing process were frequently affected. Microscopically, these meningiomas were classified as atypical (n=4) and meningiomas (n=1). The reported clinical signs included anorexia (n=3), adipsia (n=1), and dysphagia (n=1). Our findings suggest untreated dogs with ventral rhombencephalon meningiomas may develop cranial nerve damage and aspiration pneumonia.

INDEX TERMS: Canine, dogs, pneumonia, meningioma, ventral rhombencephalon, cranial nerves, dysphagia, neuropathology.

RESUMO.- [**Aumento da frequência de pneumonia em cães com meningioma em rombencéfalo ventral.**] Tumores intracranianos que ocorrem em regiões específicas do cérebro, como o ângulo ponto-cerebelar, podem estar associados à disfunção de nervos cranianos e disfagia em humanos e animais. Embora a disfagia seja um conhecido fator de risco para pneumonia, apenas a pneumonia pós-operatória tem sido investigada na medicina veterinária. Este estudo teve como objetivo descrever as características clínicas e patológicas de cães com meningiomas intracranianos não tratados e pneumonia concomitante. Foram utilizados dados de registros de necropsias de 2011 a 2021. A frequência de pneumonia e outras características foram comparadas entre cães com meningiomas na região do rombencéfalo ventral (grupo VR; n=13) e aqueles com meningiomas em outros sítios intracranianos (grupo OIS; n=10). A frequência de pneumonia foi maior no grupo VR do que no grupo OIS (n=5 vs. n=0; P=0,039). Lesões tipo placa também foram mais comuns no grupo VR do que no grupo OIS (P=0,012). Cães com pneumonia concomitante apresentaram meningiomas no ângulo ponto-cerebelar (n=3) e região basilar (n=2), predominantemente lesões em forma de placa que se estendem de ou para outras

[1] Received on January 6, 2023.
Accepted for publication on January 23, 2023.
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áreas do cérebro. Em cães com pneumonia concomitante, os meningiomas apresentaram comportamentos de crescimento invasivo (n=5) e compressivo (n=3) e as raízes nervosas envolvidas no processo de deglutição foram frequentemente afetadas. Microscopicamente, esses meningiomas foram classificados como atípicos (n=4) e papilar (n=1). Os sinais clínicos relatados incluíram anorexia (n=3), adipsia (n=1) e disfagia (n=1). Nossos achados sugerem que cães com meningiomas no rombencéfalo ventral, não tratados, podem desenvolver lesão em nervos cranianos e pneumonia aspirativa.

TERMOS DE INDEXAÇÃO: Canino, pneumonia, meningioma, rombencéfalo ventral, nervos cranianos, disfagia, neuropatologia.

INTRODUCTION

Meningiomas are dogs' most common primary brain tumors (Snyder et al. 2006). This tumor originates from epithelioid cells of the outer surface of the arachnoid villi in the meninges (Mehta et al. 2021). It may present with an altered state of consciousness, seizures, and vestibular dysfunction (Motta et al. 2012). Like many other neurological deficits, the clinical signs commonly reflect neuroanatomical tumor distribution (Areco et al. 2018). A suitable example would be neurogenic swallowing disorders following cranial nerve (CN) deficits due to posterior fossa or skull base tumors (McCulloch & Jaffe 2006, Finsterer & Grisold 2015, Kumar et al. 2017).

Tumour infiltration or compression of the facial, glossopharyngeal, vagus, and hypoglossal nerves are important causes of dysphagia (McCulloch & Jaffe 2006), which is a significant risk factor for pneumonia development in humans (Langmore et al. 1998) and a common cause of pneumonia in dogs (Fransson et al. 2001). Also, resection of posterior fossa meningiomas involving the CNs, brainstem, or basilar artery results in pneumonia in humans (Deng et al. 2020). However, in veterinary medicine, pneumonia has only been investigated and reported as a complication after intracranial surgical procedures (Fransson et al. 2001, Hu et al. 2015, Forward et al. 2018) and radiation intervention (Hu et al. 2015). Brain tumors are not investigated as a cause of pneumonia on their own. Therefore, this retrospective study aimed to investigate the incidence of pneumonia according to the tumor location using necropsy data of dogs with untreated intracranial meningioma.

MATERIALS AND METHODS

In this retrospective study, we reviewed the data from the necropsy database of the Laboratory of Veterinary Pathology of the "Universidade Federal do Rio Grande do Sul" (UFRGS) to identify dogs diagnosed with intracranial meningiomas without a history of surgery or radiation therapy from January 2010 to March 2021. Meningioma cases were classified into two groups according to the tumor location to evaluate the association between tumor location and the CN responsible for swallowing. The first group consisted of meningioma cases in the ventral rhombencephalon regions (VR group), including the cerebellopontine angle, basilar, and foramen magnum. The second group comprised meningioma cases at other intracranial sites (OIS group); these cases exclusively occurred in the olfactory, parasellar, parasagittal, falcine, cerebral convexity, tentorial, or cerebellar convexity regions.

In addition to tumor location, variables such as age, breed, sex, tumor aspect (nodular/lobulated or plaque-like lesions), tumor invasion, and brain compression were assessed and compared between groups. Gross meningioma lesions were diagnosed based on imaging findings and data from the original necropsy reports. Stained slides (hematoxylin and eosin – HE) were examined, and histological tumor subtypes and grades were assigned, as previously described (Louis et al. 2007, Higgins et al. 2017), only when concomitant pulmonary gross or microscopic lesions characteristic of pneumonia were detected. In these cases, the clinical information provided in the clinical history of necropsy reports was further assessed.

Age data were tested for normality and compared between groups using the Mann-Whitney U test. The frequency of breed, sex, tumor aspect, invasion, or compression was compared between groups using Fisher's exact test. Statistical significance was set at $P \leq 0.05$. Age (median plus minimum and maximum) and the frequencies of other variables are summarised.

RESULTS

Intracranial meningiomas were identified in 23 dogs. After tumor evaluation, 13 dogs were categorized into the VR group and 10 into the OIS group. The frequency of pneumonia was higher in the VR group than in the OIS group (n=5 vs. n=0; P=0.039). Plaque-like lesions were more common in the VR group than in the OIS group (n=5 vs. n=0; P=0.012). The frequencies of the other variables are shown in Table 1. Additionally, specific information regarding dogs without pneumonia is summarised in Table 2.

VR group dogs with pneumonia were primarily female (n=4), mixed breed (n=3), and old (median 11.5 years; 9-13 years). They had plaque-like (n=3), lobulated (n=1), and nodular (n=1) meningiomas, which were located in the basilar (n=2) and cerebellopontine angle regions (n=3, Fig.1); the latter commonly extended to or from adjacent areas. The involvement of the CN responsible for swallowing was observed in four dogs. This information was not available in the necropsy report for the remaining dog. The tumor commonly affected CN XII (n=3) and less commonly affected CNs VII, IX, X, and XI (n=2). Histologically, dogs with pneumonia had atypical (n=4) and papillary meningiomas (n=1) with tumor invasion

Table 1. Comparison of dogs and meningioma variables according to groups

Variables		OIS	VR	*P*-value
Tumour aspect	Nodular/lobulated	10 (43.48%)	4 (17.39%)	0.012
	Plaque	0	9 (39.13%)	
Age (years)	Median (min-max)	12 (6-20)	12 (4-14)	0.702
Breed	Mixed	7 (30.43%)	8 (34.78%)	1.000
	Pure	3 (13.04%)	5 (21.74%)	
Tumour compression	No	1 (4.35%)	5 (21.74%)	0.179
	Yes	9 (39.13%)	8 (34.78%)	
Tumour invasion	No	2 (8.70%)	1 (4.35%)	0.560
	Yes	8 (34.78%)	12 (52.17%)	
Pneumonia	No	10 (43.47%)	7 (30.43%)	0.039
	Yes	0	5 (21.74%)	
Sex	Male	4 (17.39%)	3 (13.04%)	0.650
	Female	6 (26.09%)	10 (43.48%)	

OIS = other intracranial sites meningioma, VR = ventral rhombencephalon meningioma.

(n=5) and compression (n=3) of the adjacent nervous tissue. The brain of these cases also showed inflammatory infiltrate of lymphocytes, plasmocytes and macrophages discrete (n=4) and moderate (n=1), predominantly perivascular; moderate congestion (n=1), edema (n=1), hemorrhages (n=2) and neuropil vacuolation (n=3).

Gross changes consistent with pneumonia were observed in three dogs (Fig.2). The lungs had mild multifocal to coalescent areas of consolidation, commonly involving cranial lobes. Moreover, pneumonia was diagnosed only through microscopic evaluation in two dogs. Lesions were necrotic and characterized by severe, multifocal to coalescent, necrosuppurative bronchopneumonia with intralesional bacteria (n=2, Fig.3) and multifocal to coalescent, suppurative, and fibrinonecrotizing pneumonia (n=1). The remaining dogs had inflammatory changes, with multifocal to coalescent, suppurative pneumonia (n=2), occasionally containing ingesta within respiratory bronchioles and adjacent alveolar lumens, which suggests aspiration bronchopneumonia (n=1, Fig.4).

Clinically, these dogs had circling behavior (n=4), head tilting (n=3), anorexia (n=3), seizures (n=2), blindness (n=2), ataxia (n=2), pulmonary crackles (n=1), dysphagia (n=1), adipsia (n=1), and anisocoria (n=1). Moreover, limb proprioception deficits (n=2) and the following CN loss or impairment of reflexes were observed: corneal (n=1), palpebral (n=1), menace (n=1), and pupillary light reflexes (n=1).

Table 2. Information of the dogs with intracranial meningioma and without pneumonia

Group	Sex	Age (years)	Breed	Meningioma description (aspect, location, histology pattern and behaviour)	Affected CN*
OIS	F	6	German Shepherd	Nodular, olfactory, papillary, compressive and invasive	N
OIS	M	8	Maltese	Nodular, cerebral convexity, atypical, compressive and invasive	N
OIS	F	9	MB	Nodular, tentorial to cerebellar convexity, atypical, compressive and invasive	N
OIS	F	11	MB	Lobulated, parasellar, atypical, invasive	N
OIS	M	12	MB	Lobulated, tentorial, transitional, compressive	N
OIS	M	13	MB	Nodular, cerebellar convexity, atypical, compressive and invasive	N
OIS	F	14	MB	Nodular, olfactory, atypical, compressive and invasive	N
OIS	F	15	Dachshund	Lobulated, olfactory, atypical, compressive and invasive	N
OIS	F	20	MB	Nodular, tentorial, transitional, compressive	N
OIS	M	-	MB	Nodular, olfactory, atypical, compressive and invasive	N
VR	F	4	MB	Nodular, cerebellopontine angle, atypical, compressive and invasive	IX, X, XII
VR	F	7	MB	Plaque, cerebellopontine angle to basilar, atypical, compressive and invasive	XII
VR	M	12	American Bully	Nodular, cerebellopontine angle to basilar, atypical, invasive	VII, XII
VR	M	12	Rottweiler	Lobulated, cerebellopontine angle to cerebral convexity, atypical, compressive and invasive	VII
VR	F	12	Boxer	Lobulated, basilar to tentorial, atypical, compressive and invasive	N
VR	F	12	MB	Plaque, basilar, transitional, compressive	XII
VR	F	14	MB	Plaque, cerebellopontine angle to parasellar, atypical, invasive	VII, IX, X, XII
VR	F	14	MB	Nodular, basilar, atypical, invasive	XII

OIS = other intracranial sites meningioma, VR = ventral rhombencephalon meningioma, F = female, M = male, MB = mixed breed, N = no; * Cranial nerves VII, IX, X and XII.

Fig.1. Dog with ventral rhombencephalon meningioma and pneumonia. Brain, white to red plaque-like mass (2.6 × 1.5 × 1.7cm), mainly in the cerebellopontine angle region, replacing cranial nerves VII, IX, and X.

Fig.2. Dog with ventral rhombencephalon meningioma and pneumonia. Lung, multifocal to coalescent areas of marked tan-red (atelectasis) and dark red (hemorrhages) discolorations.

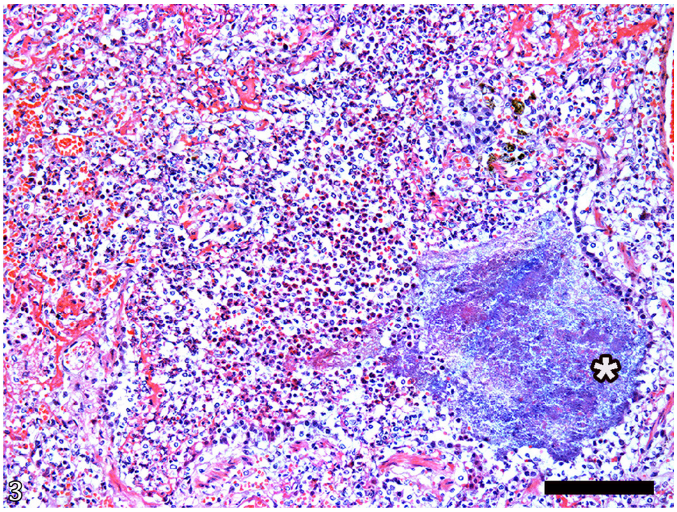

Fig.3. Dog with ventral rhombencephalon meningioma and pneumonia. Lung, severe epithelial necrosis of terminal bronchiole, which is filled with cellular debris and bacteria (asterisk). Neutrophils and macrophages occupy adjacent alveoli. HE, bar = 100µm.

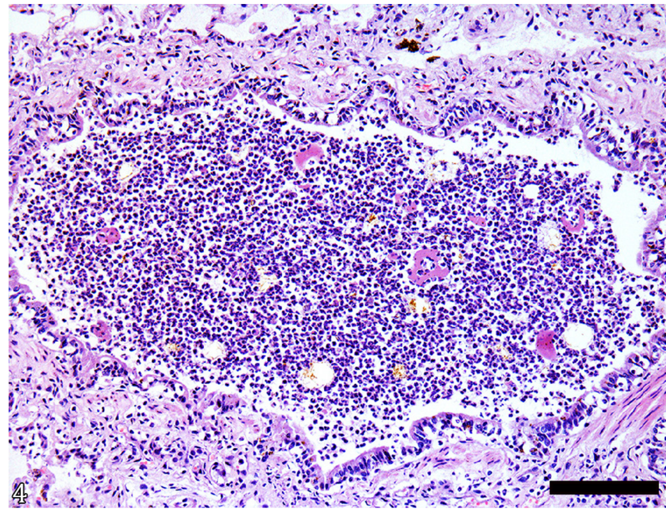

Fig.4. Dog with ventral rhombencephalon meningioma and pneumonia. Lung, mild epithelial necrosis of the bronchiole, which is predominantly filled by neutrophils and eosinophilic hyaline amorphous materials. HE, bar = 100µm.

DISCUSSION

Aspiration pneumonia has not been previously associated with specific intracranial meningioma tumor locations or CN dysfunction in untreated dogs. This study showed that pneumonia might occur as a significant comorbidity of ventral rhombencephalon meningiomas, suggesting a possible pathogenesis for its occurrence. In addition, CN injury was observed in all VR group dogs and was commonly associated with dysphagia or its related signs and subsequent pneumonia.

Although the tumor invasion and compression frequencies did not differ between the groups, all VR group dogs with pneumonia had invasive meningiomas (grade II). Invasive meningiomas are associated with CN and brain dysfunction in humans and small animals (Rossmeisl & Pancotto 2012, Kumar et al. 2017). Other peritumoral factors, such as edema, neuroinflammation, obstructive hydrocephalus, and intracranial hemorrhage, may also contribute to brain dysfunction in these cases (Rossmeisl & Pancotto 2012). Tumor size is another factor that could be related to brain dysfunction due to compression. In humans, increased tumor size increases the risk of postoperative pneumonia (Wang et al. 2017). However, we could not retrieve precise tumor and cranial cavity volumes in our retrospective study to investigate this aspect. In the opinion of these authors, magnetic resonance imaging or computed tomography would provide more accurate data regarding this aspect. Plaque-like meningiomas are more common in the VR group than the OIS group and could reduce cranial cavity volume due to bone invasion, hyperostosis, and thickening of the dura mater (Simas & Farias 2013).

Aspiration pneumonia shares gross features similar to those of other suppurative bronchopneumonia causes, such as bacteria or mycoplasma infections, inadequate intubation, and gastric content aspiration (López & Martinson 2017). In our study, pulmonary lesions were characterized mainly by necrotic or suppurative pneumonia rather than vegetable or food material; the latter is commonly found in humans (Mukhopadhyay & Katzenstein 2007) and animals with aspiration pneumonia (Caswell & Williams 2016). A possible explanation for the absence of vegetable material or food remnants is that the aspiration of saliva, nasopharyngeal secretions, bacteria, or liquids also could cause aspiration pneumonia (Son et al. 2017).

CN invasion and, occasionally, compression were identified in VR group dogs with pneumonia, commonly presenting with related clinical signs. A retrospective study showed that CNs V, VII, IX, X, and XII dysfunction was observed in 16.7% of dogs with intracranial meningioma (Areco et al. 2018). CN dysfunction was the most common clinical sign after convulsive crisis, absent thalamocortical reactions, altered consciousness or behavior, and circling behavior. Nonetheless, no dogs had dysphagia in the study, distinguishing our study, where two dogs with pneumonia had dysphagia. However, dysphagia could be underreported because some subclinical or transient forms of laryngeal dysfunction could allow content aspiration (Ramsey et al. 2005, Kogan et al. 2008). Dysphagia may also be suspected due to related clinical signs such as anorexia and adipsia. Additionally, dogs in our study lacked some post-surgical risk factors involved in pneumonia development, such as regurgitation, vomiting, and megaesophagus (Fransson et al. 2001). As dysphagia was the only predisposing factor for pneumonia development, swallowing disorders after CN damage and dysfunction were considered the primary mechanisms leading to pneumonia in these dogs.

Pneumonia was observed in 21.7% of dogs in our study, while some dogs had foreign material in the lungs. A previous etiology investigation of aspiration pneumonia identified neurological disorders as the underlying cause in 27.3% of dogs, but no intracranial tumors or CN dysfunctions were reported (Kogan et al. 2008). The frequency of brain tumors in a population could be minor (BRAIN TUMORS..., 1986), limiting its detection in investigations of aspiration pneumonia. Furthermore, due to low brain tumor frequency, grouping brain regions was also necessary for statistical analysis.

CONCLUSION

This study suggests an association between plaque-like meningiomas in the ventral rhombencephalon and pneumonia in dogs. Furthermore, dogs with ventral rhombencephalon meningiomas and pneumonia frequently showed invasion and compression of the cranial nerve (CN) responsible for swallowing. This injury could result in neurological dysfunction, seen as dysphagia and related clinical signs, leading to fluid or alimentary bolus aspiration and pneumonia.

Acknowledgments.- We would like to thank "Conselho Nacional de Desenvolvimento Científico e Tecnológico" (CNPq) and "Coordenação de Aperfeiçoamento de Pessoal de Nível Superior" (CAPES) for supporting this study. This work did not involve living animals; therefore, Ethical Approval was not required.

Conflict of interest statement.- The authors declare no potential conflict of interest concerning the research, authorship or publication of this article.

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