



Cholesteatoma and hydrocephalus associated to a third ventricle meningioma in a cat

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ABSTRACT: *Meningiomas are neoplasms that commonly involve the central nervous system of cats, while cholesteatomas are nodular granulomatous chronic lesions within the choroid plexus that are rarely reported in cats. This study described a case of cholesteatoma and non-communicating hydrocephalus associated to a third ventricle meningioma in a cat. Clinically, the cat had a 2-year history of behavioral changes, photophobia and motor incoordination. At the necropsy, a tan-brown mass totally occluded the third ventricle, causing a severe dilation of the lateral ventricles (non-communicating hydrocephalus). Microscopically, the mass was composed by a neoplastic proliferation of spindle cells arranged in bundles, containing in the center psammomatous bodies (meningioma), while in the adjacent areas a cholesteatoma was observed, which was characterized by multiple cholesterol cleft formation, hemosiderosis and associated granulomatous inflammation. At immunohistochemistry (IHC), neoplastic cells had a marked immunostaining for vimentin, while were negative for cytokeratin and S100. The diagnosis of transitional meningioma occurring in association to cholesteatoma and non-communicating hydrocephalus in a cat was obtained mainly by the histological and IHC features. These are important methods to distinguish this condition from other neurological disorders in cats.*

Key words: non-communicating hydrocephalus, immunohistochemistry, intraventricular tumors, domestic cats.

Colesteatoma e hidrocefalia associados a meningioma em terceiro ventrículo em um gato

RESUMO: *Meningiomas são neoplasias que comumente envolvem o sistema nervoso central de gatos, enquanto colesteatomas são formações nodulares granulomatosas raramente descritas nessa espécie e que resultam de lesões crônicas em plexo coroide. O objetivo desse trabalho é descrever um caso de meningioma em terceiro ventrículo culminando com a formação de colesteatoma e hidrocefalia não comunicante em um gato. Clinicamente, o gato apresentava alteração de comportamento, fotofobia e incoordenação motora durante dois anos. À necropsia apresentava uma massa acastanhada no terceiro ventrículo que provocava oclusão total do mesmo e acentuada dilatação de ventrículos laterais (hidrocefalia não comunicante). Microscopicamente, havia proliferação neoplásica de células fusiformes arranjadas em feixes com a formação de corpos psamomatosos (meningioma), e em área adjacente havia múltiplas fendas de colesterol e hemossiderose com infiltrado granulomatoso (colesteatoma). À imuno-histoquímica (IHQ), foi observada marcação positiva para vimentina e negativa para citoqueratina e S100 nas células neoplásicas. Os exames histológicos e de IHQ contribuíram para a confirmação do diagnóstico de meningioma transicional associado à formação de colesteatoma e hidrocefalia não comunicante, e são métodos importantes para diferenciar de outras afecções que cursam com quadro clínico neurológico em felinos.*

Palavras-chave: hidrocefalia não comunicante, imuno-histoquímica, tumores intraventriculares, felinos domésticos.

Meningiomas are the most common brain tumors in dogs and cats, originating from the meningotheial cells of the arachnoid and pia mater. These neoplasms may have a wide morphological presentation in dogs, being grouped in subtypes according to its cytomorphologic features. Nevertheless, in the cat these tumors usually have a fairly standard and uniform histological pattern, often as an even mixture of both transitional and fibroblastic subtypes (HIGGINS et al., 2017). Meningiomas usually are observed in the supratentorial region, but, in cats, it also may occur in the tela choroidea of the third ventricle (MOTTA et al., 2012). Conversely, cholesteatomas, or cholesterol granulomas are non-neoplastic nodular lesions resulting from chronic or

intermittent hemorrhage in the choroid plexus. These are mainly observed within the ventricular system of senile horses, while in cats it is a rare condition (CANTILE & YOUSSEF, 2016; CHAWLA et al., 2015; FLUEHMANN et al., 2006). This study aimed to describe the pathological and immunohistochemical features of a case of a cholesteatoma and non-communicating hydrocephalus associated to a third ventricle meningioma in a cat.

A 9-year-old, male, Himalayan cat, that was negative for antibodies of feline immunodeficiency virus (FIV) and for antigens of feline leukemia virus (FeLV) at the SNAP FIV/FeLV Combo (Idexx Laboratories), had a 2-year history of neurologic dysfunction characterized by behavioral changes, mild

motor incoordination, photophobia and dysphagia, in addition to weakness and anorexia. Computed tomography scanning showed that lateral ventricles were dilated by an accumulation of cerebrospinal fluid. Laboratorial and cytological analysis of the cerebrospinal fluid was unremarkable. A therapy to reduce the intracranial pressure was employed with dexamethasone (0,125 mg PO q24h) and omeprazole (20 mg PO q24h), and a good clinical response was obtained for two years. However, in the last 30 days, the cat's clinical condition worsened, resulting in permanent recumbence, persistent photophobia and anorexia. Due to the poor prognosis, euthanasia was elected.

At the necropsy, the brain was enlarged and softened, with flattening of gyri and convolutions, in addition to cerebellar coning into the foramen magnum (Figure 1A). Transverse cuts of the brain revealed a multinodular firm to hard tan-brown mass

within the interthalamic adhesion, occupying the third ventricle and extending to the lateral ventricles, measuring 0.9 x 0.8 x 0.8 cm. The lateral ventricles were severely dilated and filled with a clear serous fluid (non-communicating hydrocephalus) (Figure 1B). Multiple samples of the organs were collected and fixed in 10% neutral buffered formalin, routinely processed for histology and stained with hematoxylin and eosin (HE). Cut sections of the third ventricular mass were submitted to immunohistochemistry exams (IHC) with the following antibodies according to previously described protocols (PEREIRA et al., 2017): cytokeratin (clone AE1/AE3; 1:80; DakoCytomation), vimentin (clone V9; 1:200; Zymed) and S100 (1:200; DakoCytomation).

Histologically the mass was well demarcated in the third ventricle and in the adjacencies to the choroid plexus, and exhibited two cellular components: neoplastic and inflammatory.

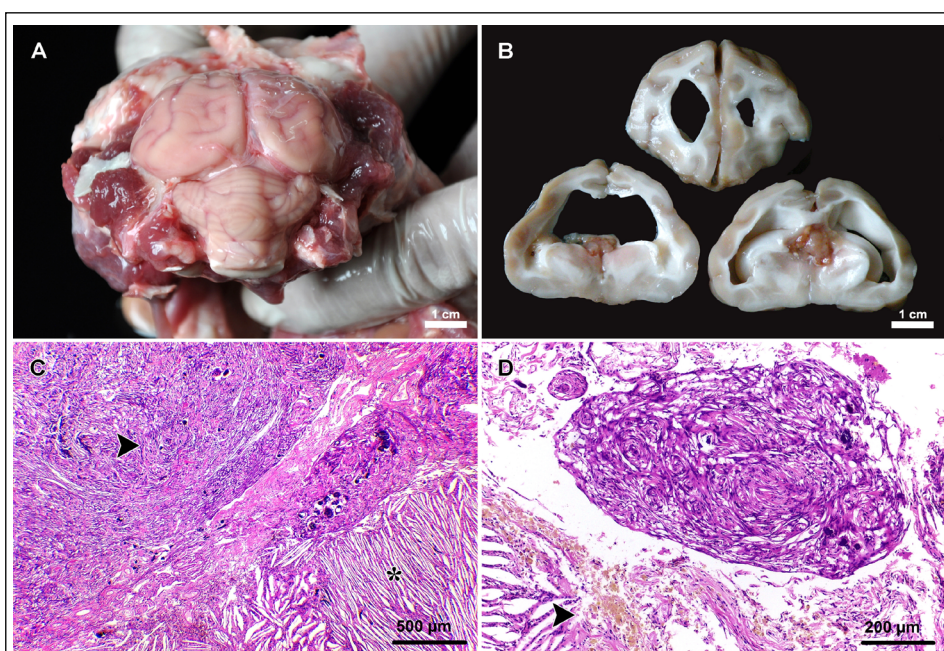


Figure 1 - Cholesteatoma and hydrocephalus associated to a third ventricle meningioma in a cat. (A) The brain was enlarged, with flattening of gyri and cerebellar coning into the foramen magnum. (B) Transverse cross section of the brain revealed a tan-brown multinodular mass measuring 0.9 x 0.8 x 0.8 cm causing a total occlusion of the third ventricle and, consequently, a severe dilation of the lateral ventricles (non-communicating hydrocephalus). (C) The mass was composed of neoplastic component with spindle cells arranged in bundles in multiple directions (meningioma; arrowhead), and an inflammatory component composed by numerous cholesterol clefts (cholesteatoma; asterisk). HE, obj. 10x. (D) Neoplastic cells were also arranged in whorls which occasionally had in the center psammoma bodies. Cholesteatoma occurred in the adjacent areas of the neoplasm (arrowhead), and was composed of multiple hemosiderin-laden macrophages interspersed by cholesterol clefts. HE, obj. 20x.

The neoplastic component was composed of meningothelial cells arranged in bundles in multiple directions and whorls, which occasionally had in the center psammoma bodies. These cells were spindle, with poorly-defined eosinophilic cytoplasm, elongated nuclei, dense chromatin and inconspicuous nucleoli (transitional meningioma). Moderate anisocytosis and anisokaryosis were noted, and mitotic figures were rare (Figure 1C). The inflammatory component was occasionally more prominent than the neoplasm and composed of numerous cholesterol clefts and hemosiderin-laden macrophages (cholesteatoma) (Figure 1D). At the IHC, the neoplastic cells had a moderate intracytoplasmic immunostaining for vimentin, while were negative for cytokeratin and S100. No other microscopic lesions were observed.

The diagnosis of cholesteatoma and non-communicating hydrocephalus associated to a third ventricle meningioma in a cat was confirmed through the pathological and IHC features. Although meningiomas are the most frequent primary tumors in the central nervous system of domestic animals (HIGGINS et al., 2017), often involving the third ventricle in cats (TROXEL et al., 2003), the simultaneous occurrence of meningioma and cholesteatoma within the choroid plexus is uncommon (ONDREKA et al., 2013). Cholesteatomas are rare in cats, both as primary condition (FLUEHMANN et al., 2006) or in association to other neoplasms (CHAWLA et al., 2015; ODRENKA et al., 2013). Etiology and pathogenesis of these tumor-like nodules are still unknown, with two mechanisms postulated: i) general dysfunction of lipid metabolism (FLUEHMANN et al., 2006); ii) chronic or intermittent congestion and edema along with congestive hemorrhage in the choroid plexus (CANTILE & YOUSSEF, 2016). The later seems to be most likely in the present case, since the location of the neoplasm combined to the long survival of the cat contributed to the slow compressive expansion of the mass on the adjacent nervous tissue and choroid plexus, leading to repeated hemorrhages. Moreover, cholesterol crystals observed within the lesion were probably derived from erythrocytes and other cellular membrane breakdown released during these hemorrhage episodes (JACKSON et al., 1994), which was followed by hemosiderin laden-macrophages in a similar pathogenesis observed in senile horses (CANTILE & YOUSSEF, 2016).

The cat in the present study had neurological clinical signs mainly involving the motor function, which is consistent with the compressive behavior of both the neoplasm and the cholesteatoma. The most common neurological clinical signs related

to intracranial meningiomas in cats include impaired consciousness (circling or coma), ataxia, vestibular dysfunction and behavioral changes, in addition to unspecific signs (lethargy and anorexia) (TROXEL et al., 2003; MOTTA et al., 2012). Photophobia, even if it is rarely reported in association with meningiomas, was a consistent clinical sign in the present case.

Meningiomas in cats are usually presented as single or multiple firm, encapsulated and sometimes cystic masses (CHAWLA et al., 2015; TROXEL et al., 2003), often with a compressive and non-infiltrative behavior (HIGGINS et al., 2017). Still, third ventricle meningiomas may cause neurological clinical signs due to the obstruction of the ventricular system, which culminates with non-communicating hydrocephalus and an increase in intracranial pressure (ONDREKA et al., 2013), as observed in this report. This was initially caused by the neoplasm, and, possibly, was aggravated by the concomitant cholesteatoma occurrence. Furthermore, cerebellar coning occurred as a result of hydrocephalus, similarly to a previous description in a forebrain meningioma in a cat (CHAWLA et al. 2015).

Choroid plexus tumors and ependymomas should be considered as differential diagnosis in cases of intraventricular tumors such as meningiomas (MOTTA et al., 2012; TROXEL et al., 2003). Choroid plexus tumors usually are arranged in a branching arboriform pattern, with cuboidal or columnar cells, while ependymomas often have neoplastic cells arranged in pseudorosettes (HIGGINS et al., 2017). In the present study, morphological features of the neoplastic cells, arrangement in bundles and whorls with psammoma bodies formation, in addition to the positive immunostaining for vimentin were essential to obtain a final diagnosis. Independently of the histological subtype, meningiomas are uniformly positive for vimentin expression, while some tumors may have a variable expression of low/high molecular weight cytokeratins (HIGGINS et al., 2017) and S100 (MARCASSO et al., 2015), similarly to the present study, in which neoplastic cells were consistently positive for vimentin, while were negative for cytokeratin and S100.

Cholesteatoma and hydrocephalus associated to intraventricular meningioma may occur in cats, causing neurological clinical dysfunctions. Thus, it should be included in the differential diagnosis of other conditions that may cause persistent clinical signs. In this study, the slow growth of the intraventricular meningioma probably caused damage to the adjacent tissue, resulting in the cholesteatoma formation in an unusual location, and aggravating the non-communicating hydrocephalus.

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DECLARATION OF CONFLICT OF INTERESTS

The authors declare no conflict of interest. The funding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

AUTHORS' CONTRIBUTIONS

All authors contributed equally for the conception and writing of the manuscript. All authors critically revised the manuscript and approved the final version.

BIOETHICS AND BIOSECURITY COMMITTEE APPROVAL

We authors of the article entitled "Cholesteatoma and hydrocephalus associated to a third ventricle meningioma in a cat" declared, for all due purposes, the project that gave rise to the present data of the same has not been submitted for evaluation of the Ethics Committee of the Universidade Federal do Rio Grande do Sul (UFRGS), but we are aware of the content of the Brazilian resolutions of the Conselho Nacional de Controle de Experimentação Animal (CONCEA) <<http://www.mct.gov.br/index.php/content/view/310553.html>> if it involves animals. Thus, the authors assume full responsibility for the presented data and are available for possible questions, should they be required by the competent authorities.

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