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PATOLOGIA OCULAR EM ANIMAIS DOMÉSTICOS

TESE DE DOUTORADO

Tessie Beck Martins

Santa Maria, RS, Brasil
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PATOLOGIA OCULAR EM ANIMAIS DOMÉSTICOS

Tessie Beck Martins

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Orientador: Prof. Claudio Severo Lombardo de Barros

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elaborada por
Tessie Beck Martins

como requisito parcial para obtenção do grau de
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Santa Maria, 19 de janeiro de 2015.

RESUMO

Tese de Doutorado
Programa de Pós-Graduação em Medicina Veterinária
Universidade Federal de Santa Maria

PATOLOGIA OCULAR EM ANIMAIS DOMÉSTICOS

AUTORA: TESSIE BECK MARTINS
ORIENTADOR: CLAUDIO SEVERO LOMBARDO DE BARROS
Local e Data da Defesa: Santa Maria, 19 de janeiro de 2015.

Esta tese envolveu o estudo de doenças oculares e perioculares de animais domésticos, e incluiu um artigo sobre lesões de patologia cirúrgica e um artigo sobre hifema em cães e gatos submetidos à necropsia. Para o primeiro trabalho, foram examinados 33.075 laudos de exames histopatológicos realizados num laboratório de diagnóstico de patologia veterinária na Região Central do Rio Grande do Sul durante 50 anos. Destes, 540 (1,6%) eram de lesões oculares e perioculares. Por várias razões, 90 espécimes foram excluídos do estudo, restando 450. Mais da metade dos casos correspondiam a espécimes de cães (53,5%), seguidos por bovinos (28,2%), gatos (11,1%), cavalos (5,1%), ovelhas (1,3%), coelhos (0,4%), e porco (0,2%). As pálpebras foram o local mais prevalente (248/450) de ocorrência das lesões em cada uma das espécies, seguidas da terceira pálpebra (73/450) e conjuntiva (27/450). Em cães, as lesões nas glândulas sebáceas consistiram nos achados mais comuns, seguidos dos tumores melanocíticos e de conjuntivites inespecíficas. Em bovinos, os locais anatômicos afetados por lesões perioculares e oculares, em ordem decrescente de frequência, foram pálpebra, córnea e terceira pálpebra. Somente o carcinoma de células escamosas (CCE) perfez 80,3% de todas as lesões diagnosticadas em bovinos. Em gatos, a maioria (39/50 casos) das lesões diagnosticadas era de neoplasia maligna, e CCE hemangiossarcoma e fibrosarcoma foram os diagnósticos mais frequentes. Em equinos 19 de 23 submissões eram neoplasmas e os mais comuns foram sarcoide (8/23) e CCE (8/23). Em ovinos, todas as amostras correspondiam a casos de CCE de pálpebra (5/6) ou terceira pálpebra (1/6). Para o segundo trabalho, casos de hifema em cães e gatos submetidos à necropsia foram examinados. Vintes casos, 14 cães e seis gatos de várias idades e raças e de ambos os sexos foram incluídos no estudo. O hifema teve uma apresentação unilateral (14 casos dos 20) ou bilateral (6/20), e a extensão da hemorragia variou de mínima a difusa. O hifema era secundário à doença sistêmica (15/20) ou ocorreu como lesão ocular primária em cinco dos 20 casos (quatro cães e um gato). O hifema primário foi sempre unilateral; a causa foi traumatismo em quatro desses casos, e o caso restante foi causado por uveíte facoclástica em um cão com catarata hipermadura bilateral. Várias causas de distúrbios hemorrágicos foram encontradas em relação ao hifema secundário: em ordem decrescente de frequência foram: vasculite (8/15), hipertensão sistêmica (5/15) e coagulopatias adquiridas (2/15).

Palavras-chave: Patologia oftálmica, pálpebra, neoplasma, hemorragia intraocular, vasculite, hipertensão sistêmica

ABSTRACT

Doctoral Thesis
Programa de Pós-Graduação em Medicina Veterinária
Universidade Federal de Santa Maria, RS, Brasil

OCULAR PATHOLOGY IN DOMESTIC ANIMALS

AUTHOR: TESSIE BECK MARTINS
ADVISER: CLAUDIO SEVERO LOMBARDO DE BARROS
Santa Maria, January 19th, 2015.

This doctoral thesis involved the study of ocular and periocular diseases affecting domestic animals, and included one manuscript about lesions of surgical pathology and one manuscript about hyphema in dogs and cats submitted to necropsy. In the first part, 33,075 reports of hystopathological exams performed in a veterinary pathology diagnostic laboratory in the Central Region of the State of Rio Grande do Sul, Brazil, over 50 years. From the total amount, 540 (1.6%) concerned ocular and periocular lesions. For various reasons ninety specimens were excluded from the study, 450 remaining. More than half of all cases consisted of samples from dogs (53.5%), followed by cattle (28.2%), cats (11.1%), horses (5.1%) sheep (1.3%), rabbits (0.4%), and pig (0.2%). The eyelids were the most prevalent (248/450) site of lesions in each of the species studied, followed by third eyelid (73/450), and conjunctiva (27/450). In dogs lesions in sebaceous glands were the most common findings (75/241), followed by melanocytic tumors and nonspecific conjunctivitis. In cattle, anatomical sites affected by ocular and periocular lesions, in decreasing order of frequency, were eyelid, cornea and third eyelid. Squamous cell carcinoma (SCC) alone accounted for 80.3% of all lesions diagnosed in cattle. Neoplasia accounted for most of the lesions diagnosed in cats (39/50 cases); all of these were malignant, and SCC, hemangiosarcoma and fibrosarcoma were the most common types diagnosed. In horses, 19 out of 23 submissions were neoplasms and most were sarcoid (8/23) and SCC (8/23). In sheep, all samples represented SCC of the eyelids (5) and third eyelid (1). For the second manuscript, cases of hyphema in dogs and cats submitted to necropsy were examined. Twenty cases, 14 dogs and six cats of several ages and breeds and of both sexes were included in the study. Hyphema presented as a unilateral (14 cases out of 20) or bilateral (6/20) disorder in dogs and cats and extension of hemorrhage varied from minimal to diffuse. Hyphema was secondary to systemic disease (15/20) or occurred as a primary ocular lesion (5/20) in four dogs and one cat. Primary hyphema was always unilateral. In four of these cases, the cause of hyphema was trauma and remaining case was caused by phacoclastic uveitis in a dog with bilateral hypermature cataract. Various causes of bleeding disorders were found related to secondary hyphema: in decreasing order of frequency, they included vasculitis (8/15), systemic hypertension (5/15), and acquired coagulopathies (2/15).

Key words: Ophthalmic pathology, eyelid, neoplasm, intraocular hemorrhage, vasculitis, systemic hypertension

SUMÁRIO

1 INTRODUÇÃO

O olho, ou órgão da visão, é um importante órgão dos sentidos dos animais vertebrados (FERNALD, 1997), que dele dependem para sobreviver e interagir com o ambiente (VOROBYEV et al., 2001; WILLIAMS, 2010). Além de estruturalmente complexo, o mecanismo da visão exige a participação conjunta de mecanismos físicos, químicos e biológicos para um funcionamento adequado (MILLER, 2008), e danos às estruturas do olho podem comprometer o processo de formação das imagens (WILCOCK, 2008).

Embora doenças que inicialmente afetam os olhos raramente resultem em doenças em outros órgãos, o contrário não é verdadeiro. O olho pode ser afetado por doenças com origem em outros tecidos quando suas barreiras estruturais ou fisiológicas são insuficientes para manter a homeostase ocular, como doenças infecciosas sistêmicas, neoplasmas metastáticos, hipertensão, diabetes, e deficiências nutricionais e toxicoses sistêmicas (WILCOCK, 2008). As lesões oculares podem, ocasionalmente, ser a primeira ou única manifestação de tais condições (PEÑA et al., 2000; REBHUN & DEL PIERO, 1998), o que torna seu diagnóstico muitas vezes relevante para a vida do animal (KOMÁROMY, 1999).

A patologia ocular, ou patologia oftálmica, inclui o estudo das enfermidades que afetam o bulbo ocular (as estruturas que o compõem) e seus anexos (ORELLANA & PIFANO, 2006). Essa é uma área do conhecimento relativamente recente dentro da medicina veterinária, e que para a maior parte dos patologistas veterinários permanece ainda hoje um campo pouco familiar, dados a anatomia peculiar do olho, o vocabulário complexo e singular e os exames clínicos em rápida sofisticação empregados na oftalmologia. Além disso, assim como na dermatologia veterinária, na oftalmologia veterinária o clínico atua também como "macroscopista" (NJAA & WILCOCK, 2012), deixando aos patologistas um papel no diagnóstico da doença ocular que é geralmente restrito ao exame histológico (WILCOCK, 2007).

No Brasil, a patologia ocular é ainda modesta quando comparada à oftalmologia, a especialidade da qual deriva. É importante, no entanto, que essa ciência se desenvolva, visto que, quando da observação de lesões oculares pelos oftalmologistas, o estudo sistemático do tecido obtido cirurgicamente ou durante a necropsia é essencial para o manejo correto do paciente, para a educação continuada e para um melhor entendimento das doenças oculares dos animais (COOK & PEIFFER, 2001).

Embora existam estudos importantes sobre as lesões oculares de cada espécie e sobre entidades etiopatológicas específicas, não foram encontrados na literatura dados sobre a prevalência das lesões oculares de animais domésticos em nossa região. Em verdade, poucos foram encontrados na literatura brasileira. A falta desses dados não impede o diagnóstico das lesões remetidas ao laboratório, mas de certa maneira obriga os estudantes e patologistas a confrontar seus diagnósticos com os dados da literatura estrangeira.

Assim, o objetivo deste trabalho foi reunir dados sobre as lesões oculares e perioculares diagnosticadas nos mamíferos domésticos na área de abrangência do LPV-UFSM. Especificamente, foram estudados casos de patologia cirúrgica provenientes de todas as espécies de mamíferos de 1964 a 2013 e casos de hifema diagnosticados postmortem em cães e gatos entre os anos de 2000 e 2013. Os resultados destes estudos estão apresentados sob a forma de artigos científicos que já foram publicados ou estão em fase de publicação.

2 ARTIGO 1 - Fifty years in the blink of an eye: a retrospective study of ocular and periocular lesions in domestic animals

Tessie Beck Martins e Claudio S. L. Barros

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Fifty years in the blink of an eye: a retrospective study of ocular and periocular lesions in domestic animals[1]

Tessie Beck Martins[2] & Claudio S.L. Barros[2*]

ABSTRACT.- Martins T.B. & Barros C.S.L. 2014. **Fifty years in the blink of an eye: a retrospective study of ocular and periocular lesions in domestic animals**. *Pesquisa Veterinária Brasileira 34(12):1215-1222*. Programa de Pós-Graduação em Medicina Veterinária, Universidade Federal de Santa Maria, Camobi, Santa Maria, RS 97105-900, Brazil. E-mail: claudioslbarros@uol.com.br

A survey was undertaken aiming to obtain an overview of ocular and periocular lesions diagnosed in domestic mammals over a period of 50 years in a veterinary pathology diagnostic laboratory in the Central Region of the State of Rio Grande do Sul, Brazil. In this lab, 33,075 histophatological exams had been performed over the period surveyed, of which 540 (1.6%) concerned ocular and periocular lesions. For various reasons ninety specimens were excluded from the study and the remaining 450 consisted of samples from dogs (53.5%), cattle (28.2%), cats (11.1%), horses (5.1%) sheep (1.3%), rabbits (0.4%), and pig (0.2%). The eyelids were the most prevalent (248/450) site of lesions in each of the species studied, followed by third eyelid (73/450), and conjunctiva (27/450). In dogs (241 samples) lesions in sebaceous glands (including Meibomian glands) were the most common findings (75/241), followed by melanocytic tumors (52/241) and nonspecific conjunctivitis (13/241). Squamous cell neoplasms, both benign and malignant, were relatively common. In cattle, anatomical sites affected by ocular and periocular lesions, in decreasing order of frequency, were eyelid, cornea and third eyelid. Squamous cell carcinoma (SCC) alone accounted for 80.3% of all diagnoses, while all neoplastic lesions made up for 85.0% of the lesions diagnosed in cattle. Neoplasia accounted for most of the lesions diagnosed in cats (39/50 cases); all of these were malignant, and SCC, hemangiosarcoma and fibrosarcoma were the most common types diagnosed. In horses, 19 out of 23 submissions were neoplasms and most were sarcoid (8/23) and SCC (8/23).

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There were six submissions from sheep with unpigmented skin, all of which represented SCC of the eyelids (5) and third eyelid (1).

INDEX TERMS: Ophthalmology, eyelid, neoplasm.

RESUMO.- [**Cinquenta anos num piscar de olhos: um estudo retrospectivo sobre lesões oculares e perioculares em animais domésticos.**] Foi realizada uma investigação para obter-se uma visão geral das lesões oculares e perioculares de mamíferos domésticos diagnosticadas ao longo de um período de 50 anos num laboratório de diagnóstico de patologia veterinária da Região Central do Rio Grande do Sul. Nesse laboratório, durante o período pesquisado foram realizados 33.075 exames histopatológicos, 540 dos quais (1,6%) eram de lesões oculares e perioculares. Por várias razões, 90 espécimes foram excluídos do estudo. As 450 amostras restantes consistiam espécimes de cães (53,5%), bovinos (28,2%), gatos (11,1%), cavalos (5,1%), ovelhas (1,3%), coelhos (0,4%), e porco (0,2%). As pálpebras foram o local mais prevalente (248/450) de ocorrência das lesões, seguidas da terceira pálpebra (73/450) e conjuntiva (27/450). Em cães (241 diagnósticos) as lesões nas glândulas sebáceas (incluindo as glândulas meibomianas) consistiram nos achados mais comuns (75/241), seguidos dos tumores melanocíticos (52/241) e de conjuntivites inespecíficas (13/241). Neoplasmas de células escamosas, tanto benignos como malignos, foram achados relativamente comuns. Em bovinos, os locais anatômicos afetados por lesões perioculares e oculares, em ordem decrescente de frequência, foram pálpebra, córnea e terceira pálpebra. Somente o carcinoma de células escamosas (CCE) perfez 80,3% de todos os diagnósticos, enquanto todas as lesões neoplásicas juntas perfizeram 85,0% das lesões diagnosticadas em bovinos. Em gatos, a maioria (39/50 casos) das lesões diagnosticadas era de neoplasia maligna e CCE, hemangiossarcoma e fibrosarcoma foram os diagnósticos mais frequentes. Em equinos 19 de 23 submissões eram neoplasmas e os mais comuns foram sarcoide (8/23) e CCE (8/23). Em ovinos foram encontradas seis submissões, todas casos de CCE de pálpebra (5/6) ou terceira pálpebra (1/6) de ovinos de pele despigmentada.

TERMOS DE INDEXAÇÃO: Patologia oftálmica, pálpebra, neoplasma

INTRODUCTION

The eye is a major special sense organ in vertebrate animals (Fernald 1997), that depend on it to survive and interact with the environment (Vorobyev et al. 2001, Williams 2010). Ocular pathology, a science that studies pathological processes that affect the eye bulb and its adnexal structures (Orellana & Pifano, 2006), is a relatively new area in veterinary medicine, with its first publications dating from the beginning of twentieth century (Gelatt 2008).

In Brazil, veterinary ocular pathology is still modest when compared to ophthalmology, the specialty from which it derives, but the increasing number of veterinary establishments and teaching institutions that offer ophthalmologic service should soon depend, and luckily, impel, the development of ocular pathology.

It has been shown that the prevalence of diseases varies largely between countries and between regions within a country (Valentine 2006). Although important publications are available considering ocular diseases in specific animal species and ethiopathogenic entities, there is need for data about general prevalence of ocular lesions in our region. Lack of such data does not impair the diagnosis of lesions submitted to pathology labs, but their unavailability somehow forces local pathologists and students to confront their results with those in the foreign literature.

The purpose of this study is to determine the type and prevalence of ocular and periocular lesions in domestic mammals submitted to a veterinary pathology diagnostic laboratory in the Central Area of State of Rio Grande do Sul, Brazil.

MATERIAL AND METHODS

From January 1964 to December 2013, 33,075 histopathologic exams were performed at the Veterinary Pathology Laboratory, at the Federal University of Santa Maria (LPV-UFSM). All protocols were reviewed and cases pertinent to ocular and periocular lesions were filtered. Protocols in which there was no diagnosis or description of the lesions, protocols regarding samples improper for diagnoses (due to autolysis or insufficient material), samples originating from research animals, and samples from normal tissue (those in which no lesions were observed) were excluded.

Lesions were grouped by animal species, site, type of primary process/etiology, and final diagnosis. Only mammals were taken into account for this study. Lesions were grouped firstly according to species – dogs; cattle; cats; horses; sheep; pigs; and other. Subsequently,

lesions were classified considering the main site affected and/or site of origin, as follows: eyelid; third eyelid; lacrimal gland; eyeball; bulbar conjunctiva; cornea; uvea; lens; and "eye". The latter category was created to accommodate diagnosis in which the site of lesion was not specified (eg. "tumor in the eye"). Such cases were not excluded because they accounted for a great portion of the total. The following criteria for classification were based on the primary pathologic process and etiology of the lesions: alterations due to trauma; congenital anomalies; autoimmune processes; infectious and parasitic diseases; degenerative diseases; metabolic and toxic diseases; neoplasia; and disturbances in cellular growth (DCG). The last category included lesions consisting of cellular hyperplasia and metaplasia, and cysts. Inflammatory lesions that could not be classified as infectious, parasitic or autoimmune were grouped under the umbrella term *inflammation*. Data related to animal breed, sex and age were not analyzed in this study.

RESULTS

During the fifty years encompassed by the current study, 33,075 histopathologic exams were performed at the LPV-UFSM. All protocols were reviewed and 540 cases (1.6%) concerning ocular and periocular lesions were filtered. Ninety of these (16.7%) were excluded because were not pertinent to the study, forty-eight of which related to birds and reptiles and forty-three, because their protocols lacked major data. In part of these protocols, information about description and/or diagnosis of the lesions was missing or not clear, and in other part, samples were not adequate for evaluation (due to small size or autolysis) or related to normal tissues (no lesions observed). Four hundred and fifty (83.3%) cases were selected for this study. More than one half (53.5%) of the samples came from dogs, followed by cattle (28.2%), cats (11.1%), horses (5.1%) and other species [sheep (1.3%), rabbits (0.4%), and a pig (0.2%)].

Eyelid was the most prevalent site of lesion in each of the species studied, accounting for 55.1% of all samples submitted (248/450), followed by third eyelid (73/450; 16.2%), and conjunctiva (27/450; 6.0%). Regarding the type of disease, neoplasia was the most numerous process, with 79.1% of all samples (356/450) (Fig.1-4), followed by inflammatory lesions of uncertain cause (50/450; 11.1%) (Fig.5), and congenital anomalies (12/450; 2.7%) (Fig.6). Overall, squamous cell carcinoma (SCC) was the most common entity, with a prevalence of 30.8% (139/450) (Fig.7).

There were 241 samples from 239 individual dogs. One dog had phthisis bulbi and a SCC in the ipsilateral third eyelid, and another one had a carcinoma of unknown origin occupying the orbit and a sebaceous epithelioma in the ipsilateral eyelid. Lesions in the eyelids,

especially in the cutaneous side, accounted for most part of samples in dogs (204/241; 84.6%). When all sites were considered, alterations of the sebaceous glands (including Meibomian glands) corresponded to the most common diagnoses in dogs (75/241; 31.1%), followed by melanocytic tumors (52/241; 21.6%), and nonspecific conjunctivitis (13/241; 5.4%). Squamous cell neoplasms were relatively common, with eight benign occurrences at the skin of eyelid and five malignant counterparts affecting conjunctiva or third eyelid. In one of these dogs, the third eyelid SCC was bilateral, and in another dog, it invaded the eyeball. In one situation, the dog had SCC affecting the conjunctiva and five other cutaneous sites along the body, as well as one cutaneous fibrosarcoma and one cutaneous mast cell tumor.

In cattle, sites affected by ocular and periocular lesions, in decreasing order, were eyelid (cutaneous side), cornea and third eyelid. SCC alone accounted for 80.3% of all diagnoses, while neoplastic lesions in total made 85.0%. Extensive invasion of the eyeball and orbit by SCC, with involvement of periocular tissues, was reported in seven cases. In five other cases, regional lymph nodes that were submitted with the ocular lesion had metastasis of SCC.

Neoplasia accounted for the major part of feline diagnosis, with 39/50 (78%) cases. All neoplasms were malignant. SCC, hemangiosarcoma and fibrosarcoma were the most common diagnoses, with 16 (32.0%), 10 (20.0%), and three (6.0%) cases, respectively. Nine of sixteen (56.2%) cats diagnosed with SCC had similar lesions in other parts of the head (ears; lips; nose; and/or contralateral eyelid), and in two occasions the neoplasm had already been removed before. In another two cats, clinicians reported invasion of eyeballs by cutaneous SCC with origin in the eyelids.

In horses, there were 24 submissions from 23 animals. Two out of 24 were samples from the same lesion, taken within a few weeks interval, and both were diagnosed as sarcoid, so they were condensed as a single diagnosis. When considering all samples, 19/23 (82.6%) accounted for neoplasms. Sarcoid and SCC were the most prevalent lesions, with 34.7% (8/23) each. There were six submissions from sheep, all of which represented SCC in the eyelid (5/6) or third eyelid (1/6). In all cases, animals had non-pigmented skin. In three sheep, there were SCC in another site (ear; third eyelid; and inferior eyelid).

Details about the distribution of lesions according to species, site (anatomical location), type of disease and diagnosis are presented in Tables 1-5.

DISCUSSION

Out of 33,075 histopathologic exams, four hundred and fifty cases of ocular and periocular diseases were identified. Dogs corresponded to more than half of the exams, followed by cattle, cats, horses and others. This distribution according to species is, to a certain extent, proportional to the total number exams at LPV-UFSM. The State where LPV is located has strong tradition in meat and wool production, specially from cattle and sheep, with a large population of working horses and dogs, and local veterinarians used to specialize in large rather than small animal practice. Because of that, this lab used to handle primarily samples from cattle along its first decade of actuation. As the decades went by, there was a gradual change in the profile of samples submitted for pathologic examination in the region drained by the LPV-UFSM, when dogs rapidly became the most import species in terms of number of exams. This change probably relates to socio-cultural changes, such as the dramatic increase in the market of pets, but no study has been conducted to confirm that.

When considering anatomical location of lesions, eyelids accounted for the major part of submissions, with 55.1% of all samples, 86.3% of which were neoplasms. Third eyelid and conjunctiva accounted for 16.2% and 6.0% of the total, respectively, also with large proportions of neoplastic processes. One of the possible reasons why these sites are overrepresented is that from a clinical perspective, the diseases of the eyelid and conjunctiva form a major part of what the primary care veterinarian is likely to diagnose and treat (Njaa & Wilcock 2010). When it comes to neoplasms, surgery is the typical therapy, and although each tumor has some characteristic or suggestive clinical features, only histological or cytological examination of the specimen is definitively diagnostic (Maggs 2008). This might explain why 79.1% (356/450) of all samples in this study corresponded to neoplastic disease.

Neoplasms of the eyelids are quite common in dogs, horses, and cattle and less common or rare in cats (Stades et al. 2007), with prevalence varying by species (Maggs 2008). In dogs, sebaceous or Meibomian gland adenomas and epitheliomas, papillomas, and melanocytic tumors constitute more than 80% of canine eyelid neoplasms (Roberts et al. 1986). A substantial majority (75% to 90%) of these tumors are histologically benign, and even histologically malignant eyelid tumors in dogs rarely metastasize, although they are more likely to be locally invasive and recur following surgery (Krehbiel & Langham 1975).

In this study, eyelid neoplasms accounted for 58.9% of all canine samples (142/241), half of which (52.1%; 74/142) were due to alterations of the sebaceous and modified (Meibomian) sebaceous glands. That makes eyelid sebaceous neoplasms the most common

canine lesion in our study, representing a third (30.7%) of all lesions, followed by eyelid melanocytic tumors (49/241; 20.3%), and nonspecific conjunctivitis (13/241; 5.4%). There were originally 31 and 18 diagnoses of eyelid (malignant) melanomas and melacytomas, respectively, something in large disagreement with the literature (Njaa & Wilcock 2010). Cutaneous melanocytic tumors of dogs, including the eyelid, are usually benign melanocytomas, unless they exhibit compelling anaplastic features and evidence of aggressive infiltration (Dubielzig et al. 2010). After reading the macroscopic and histologic descriptions, it was clear that in most cases, presence of junctional activity was used as the primary criterium of malignancy, usually regardless of absence of mitotic figures and stromal invasion. Based on a study about a comparative approach to melanocytic neoplasms (Smith et al. 2002), 25/31 melanomas were reclassified as melanocytomas.

In cattle, cats, and horses, differently than dogs, eyelid neoplasms are usually malignant (Stades et al. 2007). This corroborates the results obtained in this study, where eyelid tumors were malignant in 93.3% of cattle, 100% of cats, sheep and rabbit, and 90% of horses.

SCC was the predominant type of eyelid neoplasm in cattle, cats and sheep, as has been described (Maggs 2008). The cause of ocular SCC is still poorly understood; however, there are several factors including genetic susceptibility, nutrition levels, age, UV light, circumocular apigmentation and viruses that may contribute to its development (Tsujita & Plummer 2010). Besides the eyelids, SCC was observed in the third eyelid in cattle, horses, dogs, cats and a sheep; cornea, in cattle; and bulbar conjunctiva in cattle and one dog. Occasionally, the tumor invaded eyeball and orbit (especially in cattle and cats), was present in the skin in other parts of the head (ears; lips; nose; and/or contralateral eyelid) (cats and dogs) or body (dog), or draining lymph nodes (cattle); and/or had been removed before (especially cats). Indeed, SCC was the most common single entity in this study overall, with a prevalence of 30.8% (139/450).

Sarcoid and SCC were the the major lesions observed in horses, with 34.7% (8/23) of all diagnoses each. When considering eyelids only, sarcoid corresponded to 80% of submissions, whereas SCC was mainly observed in the third eyelid. It has been previously reported that approximately 10% of all equine neoplasms affect the eye or periocular structures, especially the eyelids, and that the most common periocular masses include sarcoid, SCC, papilloma, lymphoma and melanoma (Giuliano 2010), the former two being the most important. There is difference in prevalence of equine sarcoid and cutaneous and mucocutaneous (including ocular mucosa) SCC according to geographic areas (Valentine 2006).

Sarcoid is believed to be a bovine papillomavirus-associated tumor with a genetic predisposition, where Quarter horses and Arabians appear to be at higher risk for development

of this neoplams. The higher prevalence of sarcoid in some areas is apparently related to a higher exposure to bovine papillomavirus, where large number of beef cattle are in close proximity to horses and other equids, and to a higher density of predisposed animals or viral vectors (Giuliano 2010), whereas the increased incidence of equine ocular and cutaneous SCC may reflect increased exposure to solar radiation, especially of horses on pasture and of horses in high desert areas, non-pigmented ocular adnexa (particularly of the nictitating membrane), and pale periocular pigmentation (Valentine 2006).

There were six submissions from ovine, and all corresponded to SCC in the eyelid (5/6) or third eyelid (1/6). Ovine neoplasms are uncommon in general. SCC is the most common ocular and periocular neoplasm in sheep, but it tends to occur in this location only in animals that have non-pigmented skin or white colored head (Ahmed & Hassanein 2012). Other periocular tumors that have been reported in sheep are Meibomian gland adenoma (Rezaie et al. 2012), and basal cell tumor (Gorham et al. 1990).

CONCLUSIONS

From 1964 to 2013, eyelid neoplasms were the most common pathologic diagnosis obtained from ocular and periocular lesions of domestic mammals submitted to LPV-UFSM. Squamous cell carcinoma was the most numerous entity in this study.

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Fig. 1. Canine, product of excisional biopsy. Fragment of eyelid with large Meibomian gland adenoma (V1085-12). Alterations of the sebaceous glands corresponded to the most common diagnoses in dogs, with 31.1% of all lesions.

Fig. 2. Canine, product of exenteration. The orbit was partially filled by a mucinous mass, histologically diagnosed as a myxoma, ventral to the eyeball. The dog was referred to the clinician because of exophtalmia (V0406-11).

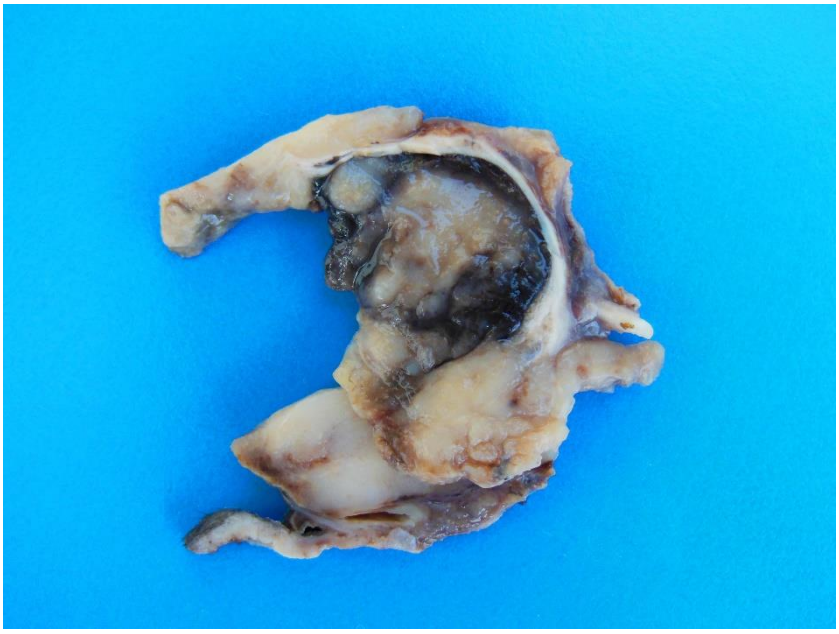

Fig. 3. Canine, product of exenteration. A trasmissible veneral tumor originating at the bulbar conjuntiva invaded eyeball and orbit. Sclera, optic nerve, third eyelid and eyelid (at the bottom) are barely recognizable (V1076-12).

Fig. 4. Feline, product of enucleation. The architecture of eye structures is markedly disrupted by a dense whitish mass that outgrows the eyeball in all directions. Histologically, a diagnosis of fusiform ocular sarcoma was established. Lens (which is not observed here) was ruptured and surrounded by neutrophils (V0003-08).

Fig. 5. Feline, right before excisional biopsy of a tumoral lesion in the third eyelid. The lesion was bilateral. Histologically, the mass was diagnosed as eosinophilic conjunctivitis (V0113-08). This inflammatory lesion is an important differential diagnosis for squamous cell carcinoma.

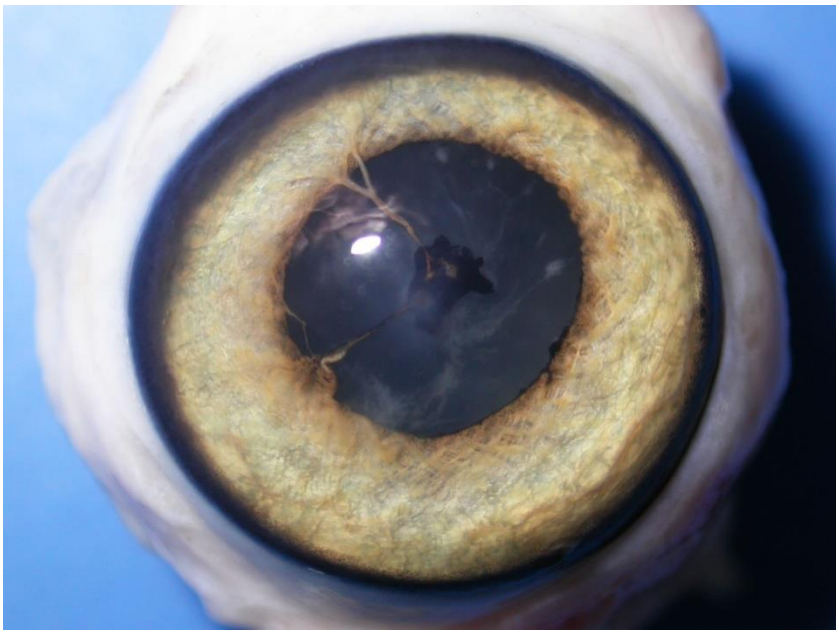

Fig. 6. Feline, product of postmortal enucleation. The cat died due to lower urinary tract disease. There are multiple centripetal projections that extend from the iris and attach to the lens anterior surfarce (posterior synechia). Histologically, the projections consisted of fibrovascular tissue lined by pigmented epithelium. This lesion was present at birth, and final diagnosis was persistent pupillary membranes, a congenital anomaly (V0181-08).

Fig. 7. Presentation of ocular squamous cell carcinoma (SCC) on the eye and periocular tissues in domestic animals. Upper left: Bovine, product of exenteration. A corneal SCC extends and invades the anterior chamber of the eye with resultant phthisis bulbi (V0093-04). Upper right: Bovine, product of exenteration. Periorbital tissues of this bovine have been envolved with and partially replaced by an eyelid SCC (eyelid not shown in the picture). Sclera is disrupted in its caudoventral aspect, but there is no invasion of the posterior chamber by the mass at this stage (V1122-12). Lower left: Ovine before incisional biopsy. Upper and lower eyelids are distorted by a large exophytic and ulcerated mass. The lesion was complicated by a myiasis (V1276-11). Lower right: Canine, product of exenteration. There is exophytic, focal mass in the bulbar conjunctiva, partially effacing the limbus. This dog had SCC in five other anatomical sites (V1565-13).

Table 1. Canine eyelid and third eyelid lesions diagnosed at LPV-UFSM[a] (1964-2013)

Site	N[b]	Type of Disease	N	Diagnosis	N
Eyelid (skin)	126	Neoplasia	107	Melanocytoma	43
				Sebaceous gland adenoma/epithelioma	39
				Squamous papilloma	8
				Melanoma	6
				Cutaneous histiocytoma, Mast cell tumor, Sebaceous carcinoma	2
				Fibrosarcoma, Hemangioma, IKA[c], Sweat gland adenoma, Undifferenciated carcinoma	1
		Autoimmune	9	DLE[d], Uveodermatologic syndrome	3
				Alergic dermatopathy	2
				Pemphigus erythematosus	1
		Inflammation	5	Granulation tissue	2
				Lipogranuloma (chalazion), Cutaneous lymphocytosis, Chronic dermatitis	1
		DCG[e]	4	Collagenous nevus, Follicular cyst, Sweat gland cyst, Cartilagenous metaplasia	1
		Metabolic	1	Zinc-responsive dermatosis	1
Eyelid (margin)	38	Neoplasia	34	Meibomian gland adenoma/epithelioma	32
				Meibomian gland adenocarcinoma	2
		Inflammation	3	Lipogranuloma	2
				Sterile cutaneous granuloma	1
		Congenital anomaly	1	Mesenchymal hamartoma	1
Eyelid (conjunctiva)	3	Infectious	1	Chronic bacterial conjunctivitis	1
		Inflammation	1	Granulation tissue	1
		Neoplasia	1	TVT[f]	1
Third eyelid	37	Neoplasia	21	Third eyelid gland adenocarcinoma	6
				SCC[g]	5
				Hemangioma	4
				Third eyelid gland adenoma	3
				Basal cell carcinoma, Hemangiosarcoma, Lymphoma	1
		Inflammation	15	Conjunctivitis	13
				NGE[h], Plasmacytic conjunctivitis (plasmoma)	1
		DCG	1	Glandular squamous metaplasia	1
Total					204

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]number of cases; [c]infundibular keratinizing epithelioma; [d]discoid lupus erythematous; [e]disturbances in cellular growth; [f]transmissible veneral tumor; [g]squamous cell carcinoma; [h]nodular granulomatous episclerokeratitis

Table 2. Canine ocular and periocular (excluding eyelid and third eyelid) lesions diagnosed at LPV-UFSM[a] (1964-2013)

Site	N[b]	Type of Disease	N	Diagnosis	N
Conjunctiva	15	Congenital anomaly	7	Dermoid	7
		Neoplasia	7	TVT[c]	2
				Conjuntival melanoma	2
				Hemangiosarcoma, Round cell tumor, SCC[d]	1
		Inflammation	1	NGE[e]	1
Eyeball	5	Glaucoma	2	Glaucoma	2
		Congenital anomaly	1	Microphthalmia	1
		Inflammation	1	Phthisis bulbi	1
		Trauma	1	Panophthalmitis secondary to a penetrating wound	1
Uvea	5	Neoplasia	3	Irido-ciliary adenocarcinoma, Melanoma, SCTBED[f]	1
		Inflammation	2	Lymphoplasmacytic uveitis, Suppurative endophthalmitis	1
Cornea	4	Inflammation	3	Superficial chronic keratitis	2
				Keratoconjunctivitis	1
		Congenital anomaly	1	Dermoid	1
Lacrimal gland	4	Neoplasia	3	Lacrimal gland adenoma	2
				Lacrimal gland adenocarcinoma	1
		DCG[g]	1	Lacrimal ductular cyst	1
Orbit	3	Neoplasia	2	Myxoma, Undifferentiated carcinoma	1
		Inflammation	1	Orbital suppurative inflammation	1
Lens	1	Congenital anomaly	1	Aphakia	1
Total					37

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]number of cases; [c]transmissible venereal tumor; [d]squamous cell carcinoma; [e]nodular granulomatous episclerokeratitis; [f]spindle cell tumors of the iris in blue-eyed dogs; [g]disturbances in cellular growth

Table 3. Bovine ocular and periocular lesions lesions diagnosed at LPV-UFSM[a] (1964-2013)

Site	N[b]	Type of Disease	N	Diagnosis	N
Eyelid (skin)	33	Neoplasia	30	SCC[c]	28
				Squamous papilloma	2
		Inflammation	2	Chronic blepharitis	2
		Infectious	1	Dermatophytosis	1
Cornea	24	Neoplasia	16	SCC	14
				Squamous papilloma	2
		Infectious	5	Keratoconjunctivitis	5
		Inflammation	1	Bilateral exposure keratitis secondary to herpesvirus encephalitis	1
		Toxic	1	Acute keratitis secondary to photosensitization	1
		Trauma	1	Corneal perforation secondary to a penetrating injury	1
Third eyelid	20	Neoplasia	17	SCC	17
		Inflammation	2	Conjunctivitis	2
		Congenital anomaly	1	Dermoid	1
Conjunctiva	11	Neoplasia	10	SCC	9
				Sebaceous gland carcinoma	1
		Infectious	1	Lymphoplasmacytic vasculitis (MCF[d])	1
Orbit	2	Neoplasia	2	Lymphoma	2
Eyeball	1	Neoplasia	1	Melanoma	1
Uvea	1	Infectious	1	Bacterial endophthalmitis secondary to encephalitis	1
"Eye"*	36	Neoplasia	36	SCC	35
				Fibroma	1
Total					127

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]number of cases; [c]squamous cell carcinoma; [d]malignant catarrhal fever; * exact location not informed

Table 4. Feline ocular and periocular lesions diagnosed at LPV-UFSM[a] (1964-2013)

Site	N[b]	Type of Disease	N	Diagnosis	**N**
Eyelid (skin)	29	Neoplasia	26	SCC[c]	14
				Hemangiosarcoma	6
				Fibrosarcoma	3
				Basal cell carcinoma, Sebaceous gland epithelioma, Histiocytic sarcoma	1
		Inflammation	2	Granulation tissue, Lipogranuloma	1
		Auto-immune	1	Alergic dermatopathy	1
Third eyelid	10	Neoplasia	7	Hemangiosarcoma	4
				SCC	2
				Third eyelid gland carcinoma	1
		DCG[d]	2	Third eyelid gland hyperplasia	2
		Inflammation	1	Eosinophilic conjunctivitis	1
Cornea	3	Degenerative	1	Corneal sequestrum (bilateral)	1
		Inflammation	1	Granulation tissue	1
		Trauma	1	Perforation secondary to a penetrating wound	
Uvea	3	Neoplasia	2	Iridociliary carcinoma, Feline diffuse iris melanoma	1
		Congenital anomaly	1	Persistent pupillary membranes (bilateral)	1
Lens	1	Neoplasia	1	Fusiform ocular sarcoma	1
Conjunctiva	1	Neoplasia	1	Conjunctival melanoma	1
Orbit	1	Neoplasia	1	Acute lymphoblastic lymphoma	1
"Eye"*	2	Neoplasia	1	Melanoma	1
		Inflammation	1	Granuloma	1
Total					50

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]number of cases; [c]squamous cell carcinoma; [d]disturbances in cellular growth; *exact location not informed

Table 5. Equine ocular and periocular lesions diagnosed at LPV-UFSM[a] (1964-2013)

Site	N[b]	Type of Disease	N	Diagnosis	N
Eyelid (skin)	13	Neoplasia	10	Sarcoid	8
				Fibroma, SCC[c]	1
		Inflammation	3	Granuloma	2
				Fibrinosuppurative blepharitis	1
Third eyelid	5	Neoplasia	5	SCC	4
				Undifferentiated carcinoma	1
Eyeball	1	Trauma	1	Perforation secondary to a penetrating wound	1
"Eye"*	4	Neoplasia	4	SCC	3
				Fibroma	1
Total					23

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]number of cases; [c]squamous cell carcinoma; *exact location not informed

Table 6. Periocular lesions diagnosed in six sheep, two rabbits and one pig at LPV-UFSM[a] (1964-2013)

Species	Site	Type of Disease	Diagnosis	N[b]
Sheep	Eyelid	Neoplasia	SCC[c]	5
	Third eyelid	Neoplasia	SCC	1
Rabbit	Eyelid	Neoplasia	Melanoma, Undifferentiated sarcoma	2
Pig	Cornea and Eyelid	Inflammation	Keratoconjunctivitis	1
Total				9

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]number of cases; [c]squamous cell carcinoma

3 ARTIGO 2 - Red eyes in the necropsy floor: twenty cases of hyphema in dogs and cats

Tessie Beck Martins e Claudio S. L. Barros

(Artigo enviado para publicação na revista **Pesquisa Veterinária Brasileira**)

Red eyes in the necropsy floor: twenty cases of hyphema in dogs and cats[1]

Tessie Beck Martins[2] & Claudio S.L. Barros[2*]

ABSTRACT.- Martins T.B. & Barros C.S.L. 2015. **Red eyes in the necropsy floor: twenty cases of hyphema in dogs and cats**. *Pesquisa Veterinária Brasileira 00(0):00-00*. Programa de Pós-Graduação em Medicina Veterinária, Universidade Federal de Santa Maria, Camobi, Santa Maria, RS 97105-900, Brazil. E-mail: claudioslbarros@uol.com.br

Hyphema (hemorrhage within the anterior chamber of the eye) can be caused by several mechanisms and can easily be detected in routine ophthalmic or necroscopic examination as discolored red eye(s). The purpose of this study is to report the cause of hyphema diagnosed as a postmortem finding in dogs and cats. Twenty cases, 14 dogs and six cats of several ages and breeds and of both sexes were included in the study. Hyphema presented as a unilateral (14 cases out of 20) or bilateral (6/20) disorder in dogs and cats and extension of hemorrhage varied from minimal to diffuse. Hyphema was secondary to systemic disease (15/20) or occurred as a primary ocular lesion (5/20) in four dogs and one cat. Primary hyphema was always unilateral. In four of these cases, the cause of hyphema was trauma and remaining case was caused by phacoclastic uveitis in a dog with bilateral hypermature cataract. Various causes of bleeding disorders were found related to secondary hyphema: in decreasing order of frequency, they included vasculitis (8/15), systemic hypertension (5/15), and acquired coagulopathies (2/15). The various pathological aspects and pathogenesis of hyphema in dogs and cats are described and discussed.

INDEX TERMS: Ophthalmic pathology, intraocular hemorrhage, vasculitis, systemic hypertension

RESUMO.- [**Olhos vermelhos na sala de necropsia: vinte casos de hifema em cães e gatos.**] Hifema, hemorragia na câmara anterior do olho, pode ser causada por vários mecanismos e pode facilmente ser detectada no exame oftálmico de rotina ou na necropsia como olho(s)

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vermelhos(s). O objetivo deste trabalho é relatar as causas de hifema diagnosticado como um achado postmortem em cães e gatos. Vinte casos, 14 cães e seis gatos de várias idades e raças e de ambos os sexos foram incluídos no estudo. O hifema em cães e gatos teve uma apresentação unilateral (14 casos dos 20) ou bilateral (6/20), e a extensão da hemorragia variou de mínima a difusa. O hifema era secundário à doença sistêmica (15/20) ou ocorreu como lesão ocular primária em cinco dos 20 casos (quatro cães e um gato). O hifema primário foi sempre unilateral; em quatro desses casos, a causa foi traumatismo e o caso restante foi causado por uveíte facoclástica em um cão com catarata hipermadura bilateral. Várias causas de distúrbios hemorrágicos foram encontradas em relação ao hifema secundário: em ordem decrescente de frequência foram: vasculite (8/15), hipertensão sistêmica (5/15) e coagulopatias adquiridas (2/15). Os vários aspectos patológicos e a patogênese do hifema são descritos e discutidos.

TERMOS DE INDEXAÇÃO: Patologia oftálmica, hemorragia intraocular, vasculite, hipertensão sistêmica

INTRODUCTION

Hyphema, or hemophthalmos (Dubielzig et al. 2010), is defined as hemorrhage within the anterior chamber of the eye (Miller 2008). There are numerous potential intraocular causes for hyphema, such as blunt or penetrating trauma, inflammation, retinal detachment (Dubielzig et al. 2010), primary or metastatic neoplasia, iatrogenic procedures (Willis 2003), congenital anomalies, and chronic glaucoma (Powell 2002). Hyphema may also result from systemic diseases, including widespread inflammation (Powell 2002) and vasculitis associated with infectious diseases (Sorrel et al. 2008), severe acute anemia (Komáromy et al. 1999), systemic hypertension, and disorders of hemostasis (Dubielzig et al. 2010), like coagulopathies and hyperviscosity syndromes (Willis 2003). Indeed, many of the mechanisms that cause intraocular hemorrhage may also result in hemorrhage in other parts of the body, and that makes hyphema a "red flag" for life-threatening systemic hemorrhagic disease as well as for sight-threatening ocular illnesses (Komáromy et al. 1999).

In a small animal routine necropsy, seldom there is a detailed dissection of the eyes unless the history, clinical signs, or obvious necropsy changes warrant detailed attention (Moreland 2009), but hyphema is usually easily detectable (Bjerkås et al. 2009), and its observation can be the first clue to the cause of death when clinical history is poor or not

available. The purpose of this study is to report the cause of hyphema diagnosed as a postmortem finding in twenty dogs and cats submitted to necropsy.

MATERIAL AND METHODS

Records from necropsies performed between 2000 and 2013 by the Veterinary Pathology Laboratory, at the Federal University of Santa Maria (LPV-UFSM), were reviewed. Reports from dogs and cats in which hyphema was diagnosed at the time of the necropsy were included in this study. Data collected included signalment, history, cause of death or reason for euthanasia, general and ocular clinicopathologic abnormalities, and final diagnoses. The authors attended the necropsy of part of these animals, especially during the years of 2011 and 2012.

In all cases, eyes were evaluated grossly during necropsy, before removal from their orbits, under natural light and/or fluorescent-lit room. In some cases, the head of the animal was placed facing the sun in order to enhance the red color in the anterior chamber. No ophthalmologic test was performed. After postmortem enucleation, eyebulbs were cleaned from extra-ocular tissues and placed in formalin or Davidson's fixative, cleaved within 48 hours and processed routinely for confection of hematoxylin-and-eosin slides, which were evaluated through optic microscopy.

Hyphema was classified according to distribution, as unilateral [right eye (*oculus dexter*; OD) or left eye (*oculus sinister*; OS)] or bilateral [both eyes (*oculus uterque*; OU)]; according to nature of hemorrhage, as systemic or ocular; and according to mechanism of bleeding. Hemorrhage was considered of systemic nature when the ocular lesions were part of or secondary to a generalized disease [e.g. cardiac failure, feline infectious peritonitis (FIP)], whereas the term ocular nature was used when bleeding could be explained by lesions targeting eye structures specifically (such as corneal trauma or cataract). Classification according to mechanism of hemorrhage was based on a previous study about causes of hyphema in animals (Komáromy et al. 1999), where lesions were divided by categories considering its etiopathogenesis, as follows: trauma; thrombocytopenia; thrombocytopathy; coagulopathy; vasculitis and uveitis; noninflammatory vascular disorders; hyperviscosity syndrome; systemic hypertension; neovascularization of uveal and retinal tissues; congenital anomalies; and anemia.

RESULTS

Twenty cases, fourteen dogs and six cats, were included in this study. Ages varied between seven months and sixteen years. Twelve animals, including all cats, were mixed breed, and seven were purebred; in one protocol, information about breed was not available. Males and females appeared in the same proportion, although there were more male cats and female dogs.

Hyphema presented as collection of blood within, but not always limited to, the anterior chamber of one (14/20) or two (6/20) eyes. Extension of hemorrhage varied from minimal to diffuse, but such feature could not be systematically evaluated because few protocols contained that information. Usually, gross description was limited to "blood in anterior chamber (hyphema)". In most cases (15/20), hyphema was secondary to systemic disease whilst primary ocular lesions were less common (5/20).

Primary ocular disease was cause for hyphema in one cat and four dogs, and these lesions were always unilateral. In the cat and three of the dogs (4/5), hemorrhage was due to head trauma, that was followed by ocular proptosis in one dog. In two dogs, hemorrhage was secondary to perforating corneal injuries (caused by car accident in one dog and presumed animal fight in another dog). Ocular lesions were characterized by multiple small foci of hemorrhage in the anterior and/or posterior uvea, presumably due to vascular rupture. A thin pre-iridal fibrovascular membrane (PIFM) was present in one dog, and traumatic uveitis, in another. Finally, one case of primary ocular lesion causing hyphema was precipitated by phacoclastic uveitis in a dog with bilateral hypermature cataract (Fig.1); a ruptured lens was surrounded by pyogranulomatous inflammation, and blood and fibrin filled the anterior and posterior chamber. Iridal and ciliary blood vessels were markedly ingurgitated, and lymphocytes and plasma cells were present in the iris. This dog died because of mycotic gastritis associated with hyphae invasion of gastric mucosal blood vessels.

Various causes of bleeding disorders were found related to systemic hyphema: in decreasing order of occurrence, they included vasculitis (8/15), systemic hypertension (5/15), and acquired coagulopathies (2/15).

Vasculitis due to FIP was the main cause of hyphema with systemic origin in cats, and accounted for half of feline cases in this study. Two animals presented bilateral hyphema. A third cat, that had a blood clot for hyphema (Fig.2), had also hemorrhagic uveitis in the contralateral eye, but there was no free blood in the anterior chamber. Pyogranulomatous anterior uveitis was present in all animals, and chorioretinits, in one. Vascular necrosis was not

obvious in any of the eyes, but it could be seen in other organs. In one animal, aside from the vascular changes, PIFM was present in both eyes.

Vasculitis was secondary to septicemia/endotoxemia in three cases – two dogs with pyometra (Fig.3-4) and one cat with septic peritonitis secondary to perforated gastric ulcer (Fig.5). Presentation was bilateral in the dogs and unilateral in the cat. Lesions in these cases were composed of discreet neutrophilic vasculitis, thrombi and leucocytostasis in small caliber vessels in the vascular tunic of the eye, as well as in other organs.

In one dog, a unilateral hyphema was secondary to widespread melanoma. In this case, hyphema was attributed to vasculitis due secondary to intravascular, metastatic neoplastic cells. Neoplastic cells could be seen at few uveal vessels and lining the anterior chamber. Metastasis were present in many other organs.

Leucocytoclastic vasculitis as cause of uveitis was the reason for unilateral hyphema in one dog, as part of steroid-responsive meningitis-arteritis syndrome (Fig.6). In this dog, there were multiple foci of hemorrhage throughout the body, including meninges and anterior uvea. Microscopically, hemorrhage was secondary to vascular wall necrosis and infiltration by neutrophils.

Systemic hypertension was the most common underlying cause of hemorrhage in the anterior chamber in dogs, with five occurrences (Fig.7). Cardiac failure was the primary cause of systemic hypertension in three animals, all of which died due to distributive shock. One of these dogs also had bilateral mature cataract due to diabetes (Fig.8). A fourth dog, that use to be treated for epilepsy, died after an episode of seizure and pulmonary edema. Microscopic lesions in these four cases were subtle, and restricted to dilated vessels with mildly thickened walls in the uvea, choroid and retina. In all of them, hemorrhage was restricted to the anterior chamber. Lastly, one dog had bilateral hyphema due to systemic hypertension, but in this case, hemorrhage was due to retinal detachment. This dog was euthanized due to end-stage-kidney disease that culminated with nephrotic syndrome. There was bilateral retinal detachment and severe intraocular hemorrhage, both in the anterior and posterior chamber and vitreous body, as well as in the subretinal space (Fig.9). Retinal arterial vessels had markedly thickened walls. This was the most severe case of hyphema in this study.

Two animals, a dog and a cat, presented hyphema due to acquired coagulopathy presumably caused by rodenticide poisoning (Fig.10). Toxicological analysis was not performed in any of these cases. The presumptive diagnosis was based in the clinical history, gross findings of large amounts of dark granules (which resembled a commercial presentation of rodenticide) amidst the gastric contents, multifocal hemorrhages, and non-clotted blood,

including the blood within the eye. In both cases, there were foci of hemorrhage in multiple internal organs, and blood did not clot during necropsy. Microscopically, multifocal areas of acute, moderate hemorrhage were observed in the anterior and posterior uvea and retina, without other signs of vascular damage.

Data on signalment, characteristics of hyphema, and cause of death or reason for euthanasia of each case are present at Table 1.

DISCUSSION

Hyphema was considered secondary to systemic disease in a large proportion of cases in this study (75%) when compared to primary ocular disease (25%). Vasculitis from various causes and systemic hypertension were the most common underlying causes for the development of hyphema, 45% and 25%, respectively, followed by trauma, either blunt or penetrating (20%), and acquired coagulopathy (10%). Concurrent involvement of more than one mechanism is common in hyphema formation (Komáromy et al. 1999), and we believe that this happened at least in three situations in this study. Discussion starts with hyphema caused by primary ocular lesions.

According to internal medicine literature, blunt or sharp trauma to the globe is the most frequent cause for hyphema in small animals (Powell 2002), while here it was the third in decreasing order. This difference might relate to the way hyphema was approached in this study, where ocular hemorrhage was evaluated during necropsy. Perhaps traumatic hyphema is less complicated than other types of hyphema in everyday practice and simply does not reach the necropsy floor as frequently as other systemic, life-threating diseases that manifest intraocular hemorrhage, as most hyphemas are small and resorbed spontaneously in a few days (Miller 2008).

Whereas blunt trauma to the head seldom results in hyphema because the eyeball is protected by anterior portions of the bony orbit and orbital soft tissues, severe blunt trauma to the anterior orbital rim or periorbital soft tissues and eyeball may cause hemorrhage in the anterior chamber (Komáromy et al. 1999) due to retinal detachment or tear of the ciliary body (Book et al. 2008). The dog that suffered blunt trauma presented hyphema after being hit by a car and suffering ocular proptosis. Penetrating trauma with corneal laceration and traumatic uveitis were due to car accident (two cases) and a presumed animal fight (one case).

Cataract was considered the primary underlying cause of hyphema in one dog. It is believed, however, that there was concurrent involvement of, at least, one mechanism in this

case. This dog presented bilateral cataract with unilateral phacoclastic uveitis and profuse intraocular hemorrhage, especially in anterior chamber. Because hyphema is a frequent manifestation of traumatic uveitis, but is rarely seen with phacolytic uveitis (Grahn 2002), we believe that the hemorrhage was influenced by an ongoing septicemic condition due to zygomycotic gastritis. There were no evidence of hyphae within the hyphemic eye, but a marked vascular invasion was observed in the gastric wall. Mild protein exudation was observed in the contralateral eye.

Vascular endothelial cell abnormalities may result in transmural extravasation of blood from vascular channels in the iris and ciliary body, resulting in breakdown of the blood-aqueous barrier and hyphema. Vasculitis may result from primary or secondary immune-mediated destruction of endothelial cells (e.g., immune-mediated vasculitis, toxoplasmosis), infectious diseases (e.g., leptospirosis, Rocky Mountain spotted fever, feline infectious peritonitis), neoplasia, or systemic inflammatory response syndrome (e.g., sepsis) (Komáromy et al. 1999).

Half of feline cases of hyphema happened as part of FIP. Hemorrhage was bilateral in two cats and unilateral in one. Ocular involvement is very common in "dry" form of FIP (Aroch et al. 2008) and less common in the purely effusive form of the disease (Dubielzig 2010). Because the nature of the disease is vasculitis, hemorrhage into the anterior chamber, retinal hemorrhages and detachment may develop (Stiles 2006, Aroch et al. 2008), although the classic necrotizing vasculitis is seen only rarely (Njaa & Wilcock 2012). Additional to the damaged vascular walls as source of bleeding, bilateral PIFM were present in at least one cat.

Three animals presented hyphema due to septicemic vasculitis, two dogs and one cat. Both dogs died due to pyometra, while the cat died after a perforated gastric ulcer lead to a severe peritonitis. In all cases, small caliber vessels with thrombi and neutrophilic leukocytostasis could be seen diffusely, including in the ocular vessels. In the eyes, there was anterior and posterior mild neutrophilic uveitis and choroiditis and intravascular microthrombi. Ocular reflexes of septicemia are more commonly reported in large animals, especially horses and cattle (Aroch et al. 2008), but may happen in small animals due to, for instance, pyometra (Komáromy et al. 1999). A second mechanism might have played a role in these cases. In overwhelming septicemia, thrombocytopenia can occur from the excessive consumption of platelets, which can lead to disseminated intravascular coagulation (Aroch et al. 2008), and hyphema (Komáromy et al. 1999).

Hyphema was secondary to metastatic neoplasia in one dog. In this case, bleeding was attributed to intravascular neoplastic thrombi, and its nature was classified as vasculitis (Komáromy et al. 1999). Spontaneous unilateral hyphema has long been cited as a clue to the

presence of intraocular neoplasia, even though the explanation was obscure. It now seems that the bleeding originates from the fragile vessels of a PIFM, which is no more than a proliferation of granulation tissue from the stroma of the iris (or retina) formed as an “accidental” response to the diffusion of growth factors produced by the tumor itself (Wilcock 2008). However, no PIFM was observed in this dog. Besides the widespread neoplasm, this dog had bilateral cortical cataract.

Vasculitis due to steroid-responsive meningitis-arteritis (SRMA) was implicated as cause of hyphema in one dog. The authors could not find a report of hyphema due SRMA, but the histologic ocular lesions seem to justify such diagnosis. The dog presented leucocytoclastic, neutrophilic vasculitis with thrombi and hemorrhage in the brain and ocular vessels. The characteristic lesion of SRMA is fibrinoid arteritis and leptomeningeal inflammation consisting of predominantly neutrophils and scattered lymphocytes, plasma cells and macrophages and associated necrotizing fibrinoid arteritis. Acute thrombosis of the vasculature may create ischemic changes in the nervous parenchyma, and in chronic lesions re-canalization of thrombi may occur (Summers et al. 1995).

Hyphema attributable to systemic hypertension is most common in old cats and dogs, and is usually caused by cardiac (Miller 2008) or renal insufficiency (Komáromy et al. 1999). Chronic high arterial pressure results in arteriosclerosis and autoregulatory arteriolar vasospasm. Arteriolar disease causes ischemia and capillary permeability changes and eventually hemorrhage. Intraocular hemorrhage may therefore occur as a direct result of vascular damage (Dubielzig 2010). However, most cases of hyphema from vascular hypertension are attributable to retinal detachment and hemorrhage, most likely in response to choroidal vascular hypertension (Komáromy et al. 1999). Retinal detachment can also lead to pre-iridal fibrovascular proliferation, another possible source of bleeding in the anterior chamber (Dubielzig 2010). Hyphema may be less commonly caused by tearing of retinal vasculature that occurs during retinal detachment (Komáromy et al. 1999). In this study, systemic hypertension was observed in five dogs, with seven to eleven years of age. Cardiac failure was the most common cause, with three occurrences, while renal failure was observed in a dog that was euthanized because of a severe nephrotic syndrome. This dog was the only to present retinal detachment. In the other dogs, hemorrhage was presumed to occur secondarily to vascular damage. A dog that died due to a dilated cardiomyopathy also had diabetes mellitus and bilateral cataract. As cardiac failure, diabetes can cause systemic arterial hypertension, and the primary cause for vascular damage was not clear in this case because both diseases were in advanced stage of development.

Presumed rodenticide poisoning was the cause of widespread hemorrhages, including unilateral hyphema, in two animals, a dog and a cat. Lesions included multifocal hemorrhages throughout the body and non-clotting blood, including the blood within the eye. Interestingly, it is considered valuable to establish whether the blood is clotted or not. Clotted blood in the anterior chamber is often seen when the cause is anterior uveitis or trauma, whereas hemorrhage caused by coagulation disorders is unclotted (Townsend et al. 2009). Hyphema has been documented with anticoagulant rodenticide exposure (Trbolova 2009), but it is rarely mentioned in texts that discuss clinical signs of this toxicity. This may be because ocular lesions are uncommon relative to other signs, or because they are usually mild in comparison to the more life-threatening hemorrhage that typically occurs (Kuhn & Hendrix 2013).

CONCLUSIONS

In twenty cases of hyphema diagnosed postmortem in dogs and cats, hyphema secondary to or occurring as part of systemic diseases was three times more common than hyphema due to primary ocular diseases. All cases of hyphema primary to the eye were unilateral, and bilateral hyphema was always part of systemic diseases. FIP was the main cause of hyphema in cats, while septicemia and systemic hypertension were the most common entities associated to hemorrhage in the anterior chamber in dogs.

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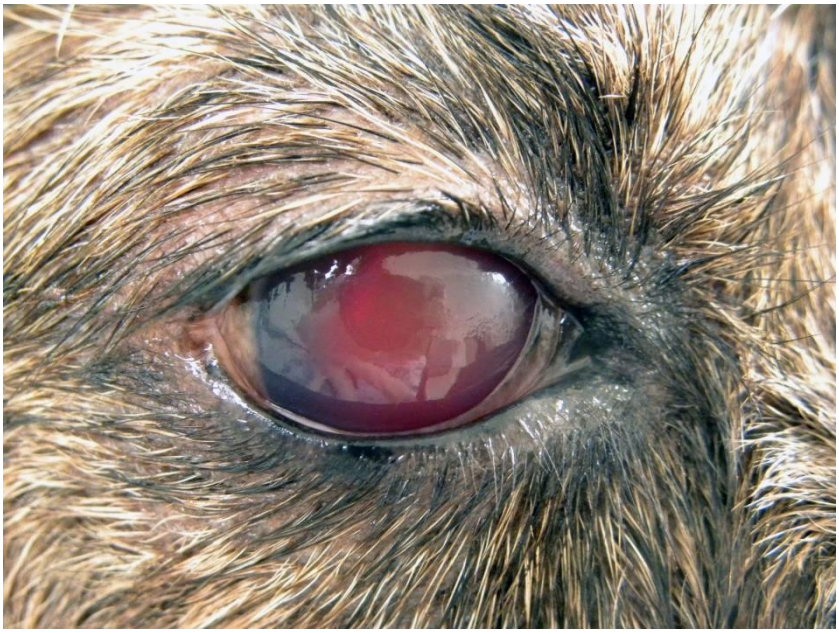

Fig.1. Dog #10, unilateral hyphema, right eye (OD), ocular nature. The anterior chamber contains a large amount of blood due to a phacoclastic uveitis. Cataract also affected the left eye. This dog died due to septicemia.

Fig.2. Cat #3, unilateral hyphema, left eye (OS), systemic nature. There is a blood clot occupying half of the anterior chamber. Iris and pupil are easily seen here. Icterus can also be noted, and that explains why the color of the eyes changed from blue to green, as noticed by the owner. This cat was euthanized at an advanced stage of feline infectious peritonitis.

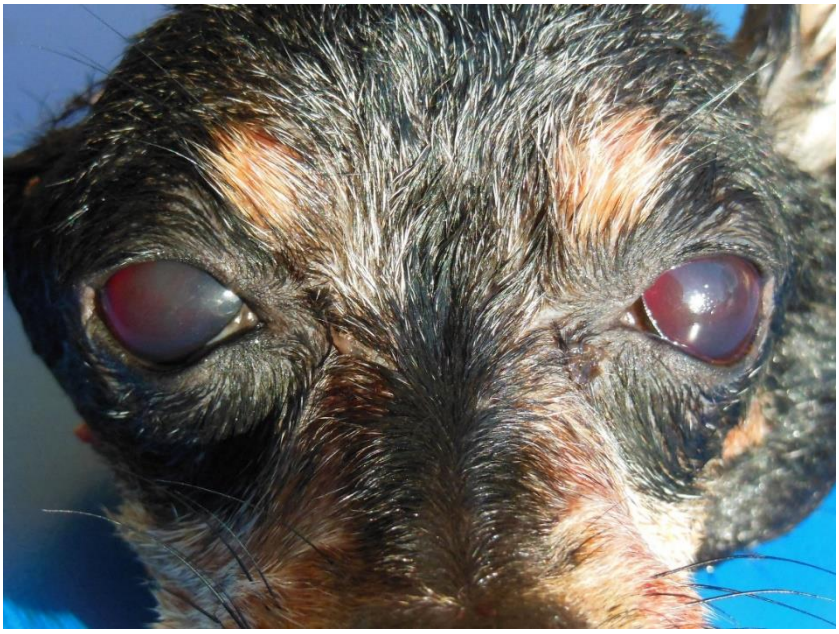

Fig.3. Dog #17, bilateral hyphema (OU), systemic nature. Both anterior chambers are completely filled with blood. Death occurred as a consequence of pyometra.

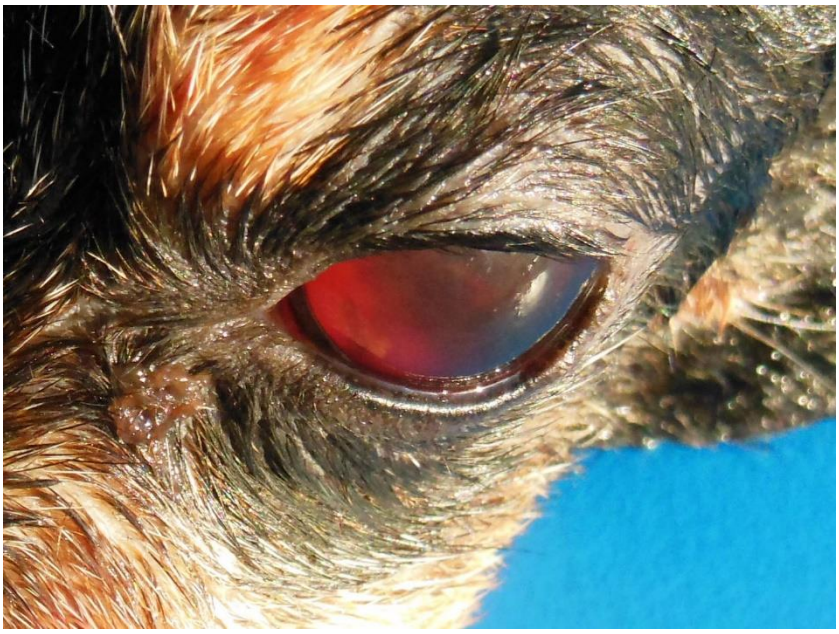

Fig.4. Dog #17, bilateral hyphema (OU), systemic nature, same as Fig.3. Head was positioned towards the sun to highlight the red color. Blood is lightly translucent in this case.

Fig.5. Cat #2, unilateral hyphema, right eye (OD), systemic nature. In contrast with the hemorrhagic eye, one can notice the clearness of the contralateral eye. This cat suffered a septic peritonitis secondary to a perforated gastric ulcer.

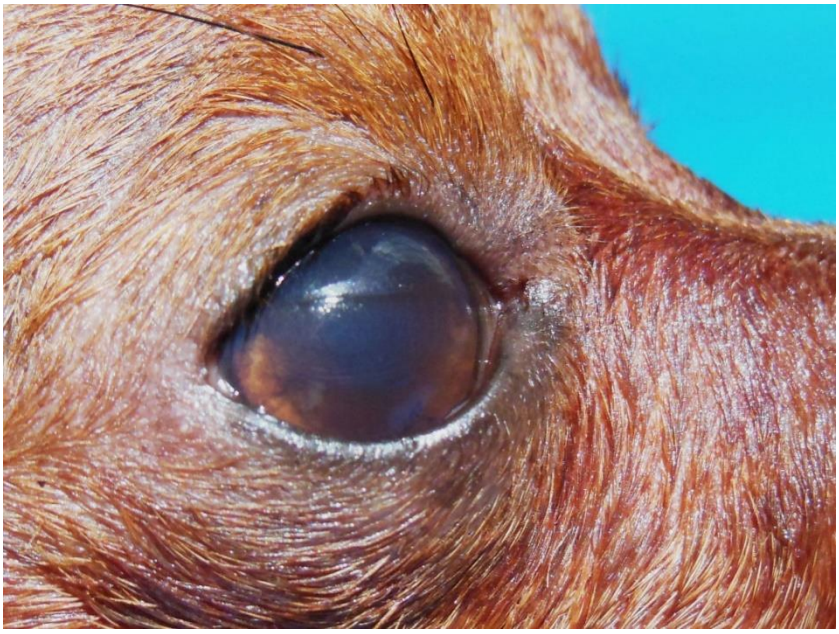

Fig.6. Dog #19, bilateral hyphema (OU), systemic nature. Instead of the traditional red color, in this dog a light brown blood is present in both eyes. Cause of death was steroid-responsive meningitis-arteritis syndrome.

Fig.7. Dog #14, unilateral hyphema, right eye (OD), systemic nature. The anterior chamber is diffusely red, effacing internal structures such as iris. Scleral vessels are lightly ingurgitated and third eyelid is hyperemic. This dog died due to cardiac failure.

Fig.8. Dog #13, unilateral hyphema, left eye (OS), systemic nature. There is a minimal collection of blood in the anterior chamber as a result of systemic hypertension. Bilateral cataract is also present. This dog died due to cardiac failure.

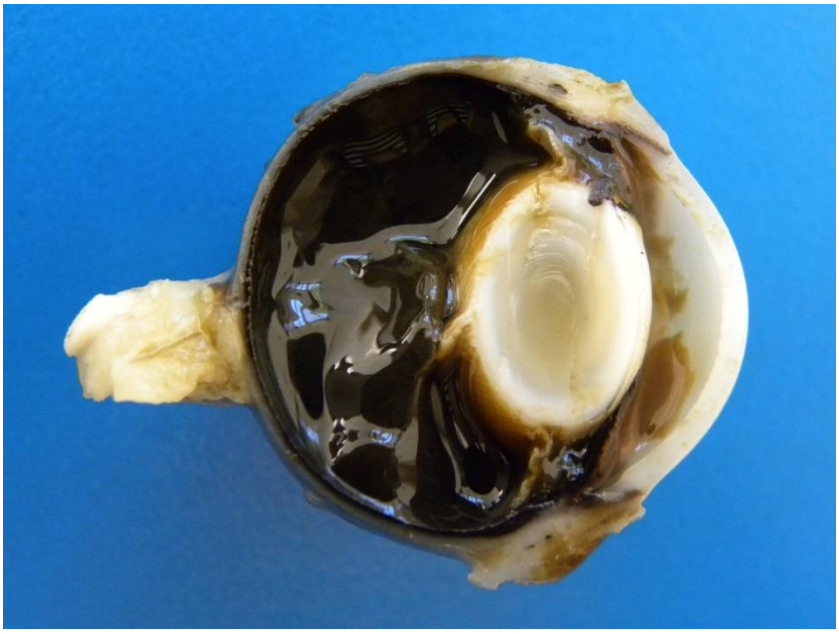

Fig.9. Dog #16, bilateral hyphema (OU), systemic nature. Vertical section of this globe shows diffuse retinal detachment and hemorrhage that occupies sub-retinal space, anterior and posterior chamber, and vitreous body. Contralateral eye was identical. This animal was euthanized due to nephrotic syndrome. Hyphema was caused by systemic hypertension secondary to renal failure.

Fig.10. Dog #20, unilateral hyphema, left eye (OS), systemic nature. In this case, hyphema is characterized by dark blood filling part of the anterior chamber. Blood did not clot during or after the necropsy. One can also notice the marked diffuse hyperemia in the third eyelid. Acquired coagulopathy presumably due to rodenticide poisoning lead this dog to death.

Table 1. Canine and feline hyphema diagnosed during necropsy at LPV-UFSM[a] (2000-2013)

	Signalment				Features of hyphema		Type/Cause of death
#	Sp.[b]	Sex	Breed	Age[c]	Nature/ Distribution	Mechanism	
1	Cat	F[d]	Mixed	3	Ocular/OS[e]	Trauma, penetrating (retinal detachment)	E[f]/Multiple trauma
2	Cat	F	Mixed	11	Systemic/OD[g]	Vasculitis, septicemic	N[h]/Septicemia (peritonitis)
3	Cat	M[i]	Mixed	1	Systemic/OS	Vasculitis and uveitis, pyogranulomatous	E/FIP[j] (dry form)
4	Cat	M	Mixed	<1	Systemic/OU[k]	Vasculitis and uveitis, pyogranulomatous	E/FIP (dry form)
5	Cat	M	Mixed	<1	Systemic/OU	Vasculitis, uveitis and chorioretinits, pyogranulomatous	E/FIP (dry form)
6	Cat	M	Mixed	NA[l]	Systemic/OU	Coagulopathy, acquired	N/ Presumed rodenticide poisoning
7	Dog	F	Pinscher	3	Ocular/OD	Trauma, blunt (eye proptosis)	N/Multiple trauma
8	Dog	M	NA	4	Ocular/OD	Trauma, penetrating	N/Multiple trauma
9	Dog	F	Mixed	16	Ocular/OD	Trauma, penetrating	N/Septicemia (intestinal necrosis)
10	Dog	F	Mixed	8	Ocular/OD	Vasculitis, lens-induced (phacoclastic uveitis)	N/Septicemia (mycotic gastritis)*
11	Dog	M	Mixed	15	Systemic/OD	Vasculitis, neoplastic	N/Widespread melanoma*
12	Dog	CF[m]	Pinscher	10	Systemic/OD	Systemic hypertension	N/Cardiac failure (endocardiosis)
13	Dog	F	Mixed	11	Systemic /OS	Systemic hypertension	N/Cardiac failure (HCM[n])*
14	Dog	M	Mixed	10	Systemic/OD	Systemic hypertension	N/Cardiac failure (DCM[o])
15	Dog	M	Dachshund	8	Systemic/OS	Systemic hypertension	N/Idiopathic epilepsy
16	Dog	M	Dobermann	7	Systemic/OU	Systemic hypertension (retinal detachment)	E/Renal failure (NS[p])
17	Dog	F	Pinscher	9	Systemic/OU	Vasculitis, septicemic	N/Septicemia (pyometra)
18	Dog	F	Pinscher	1	Systemic/OU	Vasculitis, septicemic	N/Septicemia (pyometra)
19	Dog	F	Pinscher	11	Systemic/OS	Vasculitis (leucocytoclastic)	N/SRMA[q]
20	Dog	CM[r]	Mixed	6	Systemic/OD	Coagulopathy, acquired	N/ Presumed rodenticide poisoning

[a]Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria; [b]species; [c]in years; [d]female; [e]left eye (*oculus sinister*); [f]euthanasia; [g]right eye (*oculus dexter*); [h]natural; [i]male; [j]feline infectious peritonitis; [k]both eyes (*oculus uterque*); [l]not available; [m]castrated female; [n]hypertrophic cardiomyopathy; [o]dilated cardiomyopathy; [p]nephrotic syndrome; [q]steroid-responsive meningitis-arteritis; [r]castrated male; *bilateral cataract

4 DISCUSSÃO

A oftalmologia veterinária é uma ciência muito promissora e que tem demonstrado crescimento acelerado em todo o mundo nos últimos anos. Atrelada à oftalmologia está a patologia ocular, ou patologia oftálmica, que é de essencial importância para o seu avanço e desenvolvimento (GELATT, 2008). Embora os patologistas veterinários em geral exibam certa resistência em avaliar e diagnosticar doenças oculares, a correta interpretação de tais lesões é essencial para o manejo correto do paciente, para a educação continuada e para um melhor entendimento das doenças oculares dos animais (COOK & PEIFFER, 2001).

A carência de dados sobre lesões oculares e perioculares em animais domésticos na nossa região motivou a realização dos Artigos 1 e 2. No primeiro trabalho, foram computados dados acerca dos diagnósticos de lesões oftálmicas realizados no LPV-UFSM num período de cinquenta anos, com base especialmente em amostras de patologia cirúrgica. No segundo trabalho, foram estudados vinte casos de hifema em cães e gatos diagnosticados entre os anos 2000 e 2013.

Os resultados do Artigo 1 demonstraram que mais da metade das amostras correspondeu a cães, seguido por bovinos, gatos, cavalos, ovelhas, coelhos e um porco. Estes números se assemelham aos dados da literatura, onde amostras das espécies canina e felina geralmente predominam (DUBIELZIG et al., 2010). Isso provavelmente decorre do valor afetivo que estes animais representam para seus donos, e ao fato de que animais de estimação geralmente vivem mais que os animais de produção e, por isso, têm mais chance de atingir a velhice e desenvolver doenças oculares degenerativas e neoplásicas. Já no caso dos animais de produção, a importância das lesões oculares está classicamente atrelada às consideráveis perdas econômicas que causam ao rebanho (BLOWEY & WEAVER, 2011; COLITZ & MCMULLEN, 2005; POSTMA et al., 2008) e ao fato de que, dependendo do grau de comprometimento da visão, o animal pode se tornar inadequado para o trabalho a que se destina (COLITZ & MCMULLEN, 2011).

No caso de massas oculares, biópsias incisionais ou excisionais representam a ferramenta de auxílio de maior valor diagnóstico para o clínico (HAMOR, 2011), o que justifica por que neoplasmas corresponderam ao principal tipo de lesão no primeiro estudo. A maior prevalência de lesões nas pálpebras e conjuntivas, por sua vez, provavelmente se deu ao fato de

que as doenças nestes locais representam a maior parte das lesões que o clínico veterinário identifica (NJAA & WILCOCK, 2012).

Além das lesões primárias e dos insultos específicos a cada estrutura do olho, que podem, em casos graves, comprometer permanentemente a visão do animal, as lesões oculares muitas vezes representam doenças sistêmicas que podem ameaçar a vida do animal (KOMÁROMY, 1999), como ficou demonstrado no Artigo 2. Neste trabalho foram estudados casos de hifema em vinte cães e gatos necropsiados, e em 75% dos casos o hifema foi reflexo de doenças sistêmicas, que incluíam hipertensão sistêmica, coagulopatias e várias causas de vasculite. No restante dos casos, o hifema foi secundário a lesões oculares primárias, como traumas e catarata. Ao mesmo tempo em que este estudo fornece dados novos sobre os aspectos patológicos sobre a patogenia do hifema, serve também como um incentivo para a avaliação ocular metódica na rotina de necropsia de cães e gatos.

5 CONCLUSÕES

- De 1964 a 2013, neoplasmas palpebrais foram os principais diagnósticos obtidos a partir de lesões oculares e perioculares submetidas ao LPV-UFSM;
- As espécies mais prevalentes no estudo foram, em ordem decrescente, cães, bovinos, gatos, equinos, ovelhas, coelhos e porco;
- A grande maioria das lesões caninas consistia de neoplasmas palpebrais benignos;
- Todos os neoplasmas oculares e perioculares diagnosticados em gatos eram malignos;
- Carcinomas de células escamosas foi o diagnóstico mais importante, em número de ocorrências, em bovinos, felinos e ovinos;
- Carcinoma de células escamosas e sarcoide equino foram os diagnósticos mais frequentes na espécie equina;
- Carcinoma de células escamosas foi a entidade mais diagnosticada neste estudo.
- Nos vinte casos em que hifema foi diagnosticado como achado postmortem em cães e gatos, o hifema secundário a doenças sistêmicas foi três vezes mais comum que o hifema por doenças oculares primárias;
- Todos os casos de hifema de causa primária ocular eram unilaterais;
- Hifema bilateral ocorreu sempre como parte de doenças sistêmicas;
- Peritonite infecciosa felina foi a principal causa de hifema em gatos; e
- Septicemia e hipertensão sistêmica foram as entidades mais comumente associadas à hemorragia na câmara anterior em cães.

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