

## Primary Corneal Hemangiosarcoma in a Tapir (*Tapirus terrestris*)

Adriana Torrecilhas Jorge<sup>1</sup>, Laura Teodoro de Oliveira<sup>2</sup>, Roberta Teixeira Gomes Soares<sup>2</sup>,  
Geórgia Modé Magalhães<sup>3</sup>, Thaís Gomes Rocha<sup>4</sup> & Cristiane dos Santos Honsho<sup>4</sup>

### ABSTRACT

**Background:** Hemangiosarcoma is a malignant vascular tumor commonly described in veterinary ophthalmology as emerging at the margin of the third eyelid and bulbar conjunctiva. The primary corneal attachment of the tumor is considered rare, as the cornea is an avascular structure, but there are sparse reports of primary occurrences in the cornea of dogs, cats, and horses. No reports were found in wild animals. The *Tapirus terrestris*, commonly known as Tapir, is a perissodactyl mammal that inhabits South America regions, being considered the largest terrestrial mammal of Brazil and one of the most popular animals in zoos in various countries. This paper aims to report the first case of primary corneal hemangiosarcoma in a 25-year-old female Tapir (*Tapirus terrestris*) held in captivity.

**Case:** A 25-year-old *Tapirus terrestris* female presented an irregular mass in the right cornea, mucopurulent secretion, and inconclusive previous cytological evaluation. It also had a history of a milky cornea for many years, and in the last 12 months, a tissue growth was observed, as well as the occurrence of mucopurulent secretion. The menace response in the right eye was negative. In the ophthalmologic examination, a red-colored, lobed, hemorrhagic, and ulcerated mass occupying approximately 90% of the cornea was observed, and in the peripheral cornea, there was an intense discoloration. Due to the extension of the mass and visual loss, the transpalpebral enucleation was performed under general inhalation anesthesia. The histopathological analysis evidenced a vascular tumor restricted to the central peripheral cornea, composed of blood vessels of small and large caliber, showing polygonal endothelial cells with moderate atypia, anisocytosis, and anisocariasis, in addition to dense stroma and inflammatory cells. The mass occupied the anterior corneal stroma, and there was no involvement of bulbar conjunctiva, sclera, or intraocular structures. The immunohistochemical study revealed the positivity of neoplastic cells for CD31, and the proliferative index of the lesion was evaluated by the Ki-67 as inferior to 10%.

**Discussion:** The histopathologic and immunohistochemical examinations evidenced a hypercellular lesion, and the diagnosis of primary corneal hemangiosarcoma (HSA) was possible due to the significant cellular atypia identified in the lesion. To the authors' knowledge, this is the first case of corneal hemangiosarcoma described in *Tapirus terrestris*. The HAS is a malignant neoplasm originating in the vascular endothelial cells. There is a significant correlation between the HSA and prolonged exposure to solar radiation. The tapir of this report lived in a high-altitude region with exposure to ultraviolet rays; therefore, it might be an important predisposing factor for the HSA emergence. The chosen treatment for vascular tumors according to the visual prognostic is the lamellar keratectomy; however, the transpalpebral enucleation was the elected treatment since the eye was not visual, the neoplasm had a great extension, the animal was in advanced age and lived in captivity, and it was difficult to handle the animal without sedation to perform adjuvant therapies. Since the mass corresponded to 90% of the cornea, total removal with free edges would not be possible as described in the literature, and, therefore, there was an increased risk of relapse. In the follow-up after 3 years of surgical excision, the animal remained free of metastasis, reinforcing the diagnosis of primary corneal hemangiosarcoma.

**Keywords:** immunohistochemistry, vascular tumors, histopathology, veterinary ophthalmology.

DOI: 10.22456/1679-9216.124464

Received: 27 March 2022

Accepted: 28 July 2022

Published: 25 August 2022

<sup>1</sup>Franca University (UNIFRAN), Franca, SP, Brazil. <sup>2</sup>Wild Fauna Conservation Breeding Center, Companhia Brasileira de Metalurgia e Mineração (CBMM), Araxá, MG, Brazil. <sup>3</sup>Federal Institute of Education, Science and Technology of the South of Minas Gerais (IFSULDEMINAS), Muzambinho, MG. <sup>4</sup>University Vila Velha (UVV), Vila Velha, ES, Brazil. CORRESPONDENCE: C.S. Honsho [cristiane.honsho@uvv.br]. Programa de Pós-Graduação em Ciência Animal da Universidade Vila Velha (PPGCA/UVV). Campus Biopráticas. Rua São João n. 48. CEP 29101-420 Vila Velha, ES, Brazil.

## INTRODUCTION

The tumors originating in the vascular endothelium are called hemangioma (HA) and hemangiosarcoma (HSA), which are benign and malignant, respectively [3,7]. The etiology of this tumor is unknown. It is believed that the tumor has a predilection for non-pigmented areas [12] and exposure to ultraviolet rays is probably a predisposing factor [9,10,12,13]. Because of the vascular origin, it has been diagnosed in different organs [2] and has been described in dogs' spleen, lung, liver, peritoneum, kidney, encephalon, pleura, and heart [3].

This type of tumor is described in veterinary ophthalmology literature as affecting primarily the third eyelid margin [12,13], the lateral bulbar conjunctiva [7,12,13], and the ventral conjunctival fornix [13]. In dogs, these tumors represent 27% of the conjunctiva neoplasia, and there is a possibility of corneal invasion [12]. Primary corneal involvement is considered rare, as the cornea is an avascular structure [1,13], with sparse reports in dogs [5,6,10], cats [1,9], and horses [11].

The *Tapirus terrestris*, commonly known as Tapir, is a perissodactyl mammal that inhabits South America regions, being considered the largest terrestrial mammal of Brazil and one of the most popular animals in zoos in various countries.

This paper aims to report the first case of primary corneal hemangiosarcoma in tapirs, diagnosed through clinical signs and histopathological and immunohistochemical evaluation.

## CASE

A 25-year-old *Tapirus terrestris* female was treated in the Veterinary Hospital of the University of Franca, coming from the Wild Fauna Conservation Breeding Center of the Environmental Development Center (CDA), at the Companhia Brasileira de Metalurgia e Mineração (CBMM) of the Moreira Salles Group, located in the city of Araxá-MG/Brazil. The animal presented an irregular right corneal mass, mucopurulent discharge, and inconclusive previous cytological evaluation. Initially, the specimen presented a milky cornea for many years, and in the last 12 months, tissue growth was observed, as well as the occurrence of mucopurulent secretion. The menace response test was negative.

For the ophthalmologic examination, the animal was sedated with detomidine<sup>1</sup> [Dormiun V<sup>®</sup> 1%

- 20 µg/kg, IM], and after 15 min it was induced with ketamine [Ketamine<sup>®</sup> 10% - 2 mg/kg, IV] and midazolam<sup>1</sup> [Dormire<sup>®</sup> 5% - 0.1 mg/kg IV]. Subsequently, an endotracheal tube was placed and the animal was kept in inhalation anesthesia with isoflurane<sup>3</sup> [Forane<sup>®</sup> - 1.5% CAM] associated with the retrobulbar blockade with lidocaine<sup>1</sup> [Xylestesin<sup>®</sup> 2% - 15 mL].

A friable, lobed, hemorrhagic, and red-colored protruding mass with an ulcerated central area occupying approximately 90% of the right cornea was observed (Figure 1). In the peripheral cornea, there was an intense black discoloration without any transparent area, therefore, the intraocular examination, as well as the applanation tonometry, were not possible. A transpalpebral enucleation was performed due to the extension of the mass in the right eye. After the surgical procedure, the tapir received gentamicin<sup>4</sup> [Gentomicin Injetável<sup>®</sup> 4% - 6.6 mg/kg IM, BID], and the association of benzylpenicillin, potassium penicillin, procaine penicillin, streptomycin sulfate and sodium diclofenac<sup>5</sup> [Diclopen<sup>®</sup> - 40,000 UI/kg IM, BID], as well flunixin meglumine<sup>5</sup> [Flumax<sup>®</sup> - 1 mg/kg IM, SID for 5 days].



**Figure 1.** Photographic image of *Tapirus terrestris*'s right eye. Extension of the protruding, ulcerated, and red-colored lobed mass. In the peripheral region of the cornea, there is intense dark discoloration (arrow).

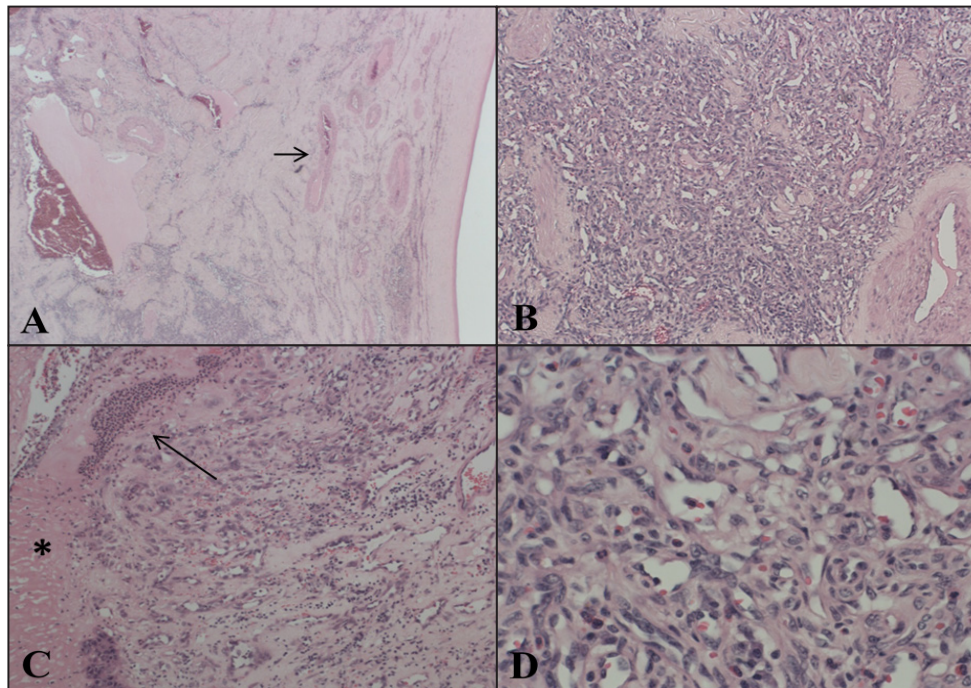
After the enucleation, the material was fixed in 10% formalin and routinely processed by the histopathologic and immunohistochemical examinations, being colored in hematoxylin and eosin (HE) and the antibodies CD31<sup>6</sup> and Ki67<sup>6</sup>, respectively.

The microscopic evaluation of the specimen revealed a vascular tumor involving both peripheric and central portions of the cornea, composed of

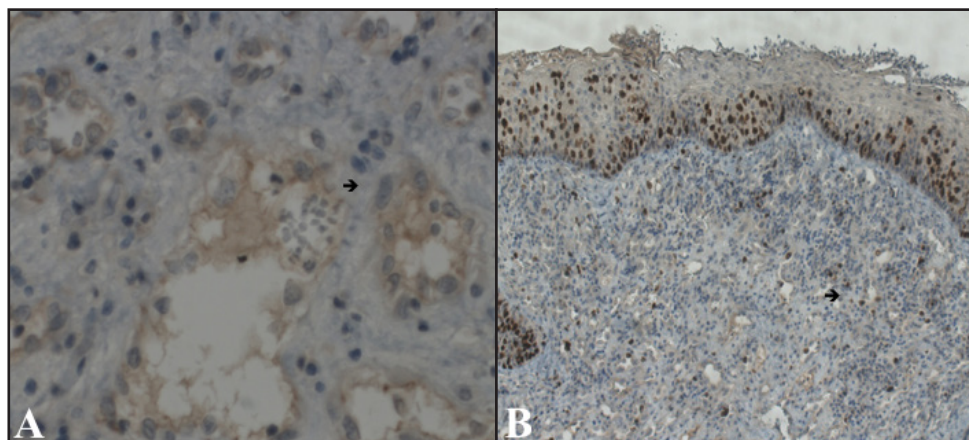


small and large caliber vessels forming a protruding lesion at the central portion of the cornea with ulceration of the surface epithelium. The neoplastic cells were composed of large spindle and polygonal cells with moderate atypia, including anisocytosis and anisocariosis, presenting vesiculous nuclei and small nucleoli (Figure 2). The stroma was very dense, and

foci of inflammatory infiltrate were seen. The lesion was restricted to the anterior corneal stroma. There were no signs of intraocular involvement. The immunohistochemical study showed the positivity of the neoplastic cell for CD31. The proliferative index of the lesion, evaluated with Ki-67, was less than 10% (Figure 3).



**Figure 2.** Photomicrography of primary corneal hemangiosarcoma, *Tapirus terrestris*. A- Observe the central area's neovascularization (arrow) in the corneal stroma [HE; Obj.2.5x]. B- A proliferation of blood vessels [HE; Obj.10x]. C- ulceration area of the cornea (asterisk) with necrosis and accentuated and mixed inflammatory infiltrate (arrow) and bleeding [HE; Obj.20x]. D- Notice endothelial cells with moderate cell pleomorphism, scarce cytoplasm, evident nucleolus, moderate anisocytosis, and anisocariasis [HE; Obj.40x].



**Figure 3.** Photomicrography of a primary corneal hemangiosarcoma, *Tapirus terrestris*, polymer method, DAB. A- Positive immunostaining for CD31 in the cytoplasm and plasmatic membrane of the neoplastic endothelial cells (arrow). B- Observe the nuclear immunostaining for the Ki67 antibody in less than 10% of the neoplasm (arrow).

## DISCUSSION

The HSA is a malignant neoplasm that originated in the vascular endothelial cells [1]. Although its etiology is not established, there is a significant correlation between the HSA and prolonged exposure to solar radiation [9,12,13]. The animal of this report lived in a high-altitude region with high exposure to ultraviolet rays, which might be a predisposing factor for the HAS emergence, corroborating with Richardson & Deykin [13].

Initially, the Tapir revealed chronic ocular alterations, such as corneal whitening and later emergence and tumor growth, according to what was reported in a dog with development of primary HSA after chronic superficial keratitis [6,14] and in a cat [1,9,14].

The clinical aspect of the neoplasm corroborated the description found in literature, as hemorrhagic tissue [1,14] with serohemorrhagic secretion [4], red discoloration [1,12,14], and lobular exophytic nodules [1,4,12,14].

According to the visual prognostic, the treatment of choice for vascular tumors is the lamellar keratectomy [10]; however, since the right eye of this Tapir was not visual, the treatment performed was the transpalpebral enucleation. Other factors that contributed to the selection of such treatment were the extension of the neoplasm, the age of the animal, the fact that it lived in captivity and was difficult to handle, and that sedation was necessary for the accomplishment of adjuvant therapies. Since the mass corresponded to 90% of the cornea, total removal with free edges would not be possible as described in the literature [12,13], which therefore would increase the risk of relapse.

Tumor relapse was reported 15 days after the lamellar keratectomy in a dog with corneal HSA [5]. In 2 dogs, there was relapse after the HSA resection, and in 8 patients after the removal and cryotherapy [12]. In an equine with HSA and squamous cell carcinoma in the third eyelid, there was HSA metastasis in the upper and lower eyelid, sclera, cornea, and retropharyngeal region after 16 months of the third eyelid removal and adjuvant therapy, and the horse was euthanized later [4]. To this date, the Tapir did not present tumor relapse.

The differential diagnosis must be performed between HSA, HA, squamous cell carcinoma, and sarcoma. The differentiation between HSA and HA is not always simple [7,14]: the HSA growth is faster and aggressive when compared to the HA [12,14]. Therefore, there was an initial concern about the tumor type of this report, since it was described as a slow-growing tumor.

Nonetheless, the microscopic techniques confirmed the malignant mesenchymal neoplasm.

The tumor growth speed reflects the mitotic index, and this is one of the differences between HA and HAS. In HA, the mitosis is absent or rare [7,10,11,14] and it is present in the HSA [5,7,13,14] also varying according to the cellular density [7]. However, as reported in the dog with primary corneal HSA [6] in this report there was no mitosis.

The pleomorphism is the variation in size (anisocariasis) and form (anisocytosis) of the nuclei or cells, and their moderate presence suggests tumor aggressiveness, which is an HSA diagnosis [11,14]. Corroborating with the literature on this subject, there was a moderate presence of anisocariasis and anisocytosis [5,6,8,11,14]. Another difference in the corneal HA in the dog was the low pleomorphism [10,14].

Extensive vascular proliferation was observed [4] with several vascular spaces [1,6], some filled by red blood cells [4,11], with spindle endothelial cells [3,6], scarce cytoplasm and evident nucleolus, being these signs present both in the HA [10,14] and in the HSA in any animal species and regardless of tumor location.

The central cornea was ulcerated [6] with an area of necrosis, and accentuated and mixed inflammatory infiltrates [11].

The histologic examination showed that the neoplasm was located in the cornea, which corroborates with the diagnosis of a primary tumor, as also described in dogs [6,14], cats [1], and a horse [11]. According to what was described in the literature [7] the HSA endothelial cells are immunopositive to the CD31 antibody, thus confirming the diagnosis.

The histopathological and immunohistochemical exams showed hypercellularity of the lesion and important cellular atypia. These findings, associated with the absence of metastases in the follow-up after 3 years of enucleation, demonstrated that it was a primary corneal HSA, in the knowledge of the authors, the first case described in a Tapir.

## MANUFACTURERS

<sup>1</sup>Cristália Produtos Químicos Farmacêuticos Ltda. São Paulo, SP, Brazil.

<sup>2</sup>Agener União Saúde Animal. Embu-Guaçu, SP, Brazil.

<sup>3</sup>Abbott Laboratórios do Brasil Ltda. Rio de Janeiro, RJ, Brazil.

<sup>4</sup>Syntec do Brasil Ltda. São Paulo, SP, Brazil.

<sup>5</sup>J.A. Saúde Animal Ltda. São Paulo, SP, Brazil.

<sup>6</sup>Laborclin Produtos para Laboratório Ltda. Pinhais, PR, Brazil.

<sup>7</sup>Dako North America Inc. Carpinteria, CA, USA.

**Acknowledgments.** Wild Fauna Conservation Breeding Center of the Environmental Development Center (CDA), at the Companhia Brasileira de Metalurgia e Mineração (CBMM) of the Moreira Salles Group and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES, Finance Code 001).

**Declaration of interest.** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

#### REFERENCES

- 1 Cazalot G., Regnier A., Deviers A., Serra F., Lucas M.N., Etienne C.L. & Letron I.R. 2011.** Corneal hemangiosarcoma in a cat. *Veterinary Ophthalmology*. 14(Suppl 1): 117-121. DOI: 10.1111/j.1463-5224.2011.00928.x.
- 2 Chandler H.L., Newkirk K.M., Kusewitt D.F., Dubielzig R.R. & Colitz C.M. 2009.** Immunohistochemical analysis of ocular hemangiomas and hemangiosarcomas in dogs. *Veterinary Ophthalmology*. 12(2): 83-90. DOI: 10.1111/j.1463-5224.2008.00684.x.
- 3 Flores M.M., Panziera W., Kommers G.D., Irigoyen L.F., Barros C.S.L. & Figuera R.A. 2012.** Aspectos epidemiológicos e anatomopatológicos do hemangiossarcoma em cães: 40 casos (1965-2012). *Pesquisa Veterinária Brasileira*. 32(12): 1319-1328. DOI: 10.1590/S0100-736X2012001200017.
- 4 Gearhart P.M., Steficsek B.A. & Petersen-Jones S.M. 2007.** Hemangiosarcoma and squamous cell carcinoma in the third eyelid of a horse. *Veterinary Ophthalmology*. 10(2): 121-126. DOI: 10.1111/j.1463-5224.2007.00510.x.
- 5 Guberman Ú.C., Merlini N.B., Perches C.S., Fonzar J.F., Mamprim M.J., Ranzani J.J.T. & Brandão C.V.S. 2015.** Corneal hemangiosarcoma in a dog. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*. 67(2): 343-346. DOI: 10.1590/1678-7685.
- 6 Haeussler Jr. D.J., Rodríguez L.M., Wilkie D.A. & Premanandan C. 2011.** Primary central corneal hemangiosarcoma in a dog. *Veterinary Ophthalmology*. 14(2): 133-136. DOI: 10.1111/j.1463-5224.2010.00849.x.
- 7 Labelle A.L. & Labelle P. 2013.** Canine ocular neoplasia: a review. *Veterinary Ophthalmology*. 16 (Suppl 1): 3-14. DOI: 10.1111/vop.12062.
- 8 Pascoli A.L., Mendonça A.P.R., Lira R.N., De Nardi A.B. & Reis Filho N.P. 2014.** Primary conjunctive-sclero-corneal hemangiossarcoma in a feline: case report. *Medvop - Revista Científica de Medicina Veterinária - Pequenos Animais e Animais de Estimação*. 12(40): 214-216.
- 9 Perlmann E., Silva E.G., Guedes P.M. & Barros P.S. 2010.** Co-existing squamous cell carcinoma and hemangioma on the ocular surface of a cat. *Veterinary Ophthalmology*. 13(1): 63-66. DOI: 10.1111/j.1463-5224.2009.00760.x.
- 10 Perlmann E., Abranches L.S., Rodrigues E.A.K. & Goés A.C.A. 2014.** Primary corneal hemangioma: case report. *Medvop - Revista Científica de Medicina Veterinária - Pequenos Animais e Animais de Estimação*. 12(40): 206-211.
- 11 Pinn T.L., Cushing T., Valentino L.M. & Koch S.A. 2011.** Corneal invasion by hemangiosarcoma in a horse. *Veterinary Ophthalmology*. 14(3): 200-204. DOI: 10.1111/j.1463-5224.2010.00856.x.
- 12 Pirie C.G., Knollinger A.M., Thomas C.B. & Dubielzig R.R. 2006.** Canine conjunctival hemangioma and hemangiosarcoma: a retrospective evaluation of 108 cases (1989-2004). *Veterinary Ophthalmology*. 9(4): 215-226. DOI: 10.1111/j.1463-5224.2006.00471.x.
- 13 Richardson S. & Deykin A.R. 2021.** Surgical treatment of conjunctival hemangioma and hemangiosarcoma: A retrospective study of 52 dogs. *Veterinary Ophthalmology*. 24(5): 432-441. DOI: 10.1111/vop.12921.
- 14 Shank A.M.M., Teixeira L.B.C. & Dubielzig R.R. 2019.** Canine, feline, and equine corneal vascular neoplasia: A retrospective study (2007-2015). *Veterinary Ophthalmology*. 22(1): 76-87. DOI: 10.1111/vop.12571.