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CASE REPORT
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Solid Iridociliary Carcinoma in a Dog

Marina Possa dos Reys[1], Mayra Cunha Flecher[1], Laura de Souza Ferraz Matos[1], Fernanda Rezende Souza[2], Geovanni Dantas Cassali[2], Stefania Cecco Sede[3], Beatriz Cristiany de Souza[3] & Clairton Marcolongo Pereira[3]

ABSTRACT

***Background*:** Iridociliary epithelial tumors (ICETs) originate from the iris epithelium or ciliary body. They comprise ciliary body adenoma, carcinoma, pleomorphic adenocarcinomas, medulloepitheliomas, and other primitive neuroectodermal tumors. They are the second most common primary intraocular tumors in dogs and have already been reported in sheep and humans. In dogs, they occur more frequently in middle-aged to elderly animals, and the Labrador and Golden Retriever seem to be more predisposed breeds. This study aimed to describe the clinical and pathological aspects of solid iridociliary carcinoma in a dog.

***Case*:** A 3-year-old Poodle bitch was treated for discomfort in the left eyeball region, increased intraocular pressure and moderate buphthalmia. A direct ophthalmological examination was performed without equipment, and a mass was visualized in the posterior chamber, distorting the pupillary cleft. We opted for unilateral enucleation and forwarded the material for histological analysis. Macroscopically, the eyeball measured 3.4 cm (anteroposterior) x 2.6 cm (vertical), with a brownish mass that occupied the entire anterior chamber and part of the posterior chamber. Histologically, there was a neoformation in the ciliary body and iris pigment epithelium, partially well-delimited and densely cellular. The neoplasm was organized into predominantly solid formations interspersed with a discrete amount of blood vessels, rare bundles of fibrous stroma, and amorphous eosinophilic material forming membranes that were positive for PAS. Sections of the neoplasm were subjected to immunohistochemistry using anti-cytokeratin AE1/AE3, anti-S100 protein, anti-vimentin, and anti-Ki-67. Positive cytoplasmic immunostaining for cytokeratin and S-100 was observed. Only 45.6% of cells were positive for Ki-67 (500 cells). No immunostaining was observed for vimentin.

***Discussion*:** The diagnosis of solid iridociliary carcinoma was based on the histological features and positive immunostaining for cytokeratin AE1/AE3 and protein S100. Iridociliary carcinomas present positive immunostaining for cytokeratin, whereas adenomas and normal iridociliary epithelium do not present this immunostaining. Moreover, the high rate of cell proliferation was indicative of malignant neoplasia, as observed by the high mitotic count and high positivity for Ki-67. The S100 protein helped in the diagnosis of ICETs, as the iridociliary epithelium showed positive staining for this protein. Some histological features are important to consider in the diagnosis of iridociliary tumors in dogs, such as noninvasive growth in the posterior chamber, pigment epithelium, and thick homogeneous membranes on the cell surface. Furthermore, the presence of positive PAS membranes favors the diagnosis of iridociliary epithelial tumors. ICETs must be differentiated from melanocytomas, anterior uveal melanoma, medulloepitheliomas, and metastatic and pleomorphic carcinomas. The histological characteristics, especially the presence of PAS-positive membranes, associated with the immunohistochemical profile of neoplasm cells, help differentiate the ICETs from these tumors. In general, the prognosis is poor for eyeball and vision maintenance in canine iridociliary tumors, and scleral invasion is associated with a higher recurrence rate.

Keywords: neoplasm, eye, immunohistochemistry, cytokeratin, S100 protein.

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[1]Laboratório de Patologia Animal, Universidade Vila Velha (UVV), Vila Velha, ES, Brazil. [2]Laboratório de Patologia Comparada, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil. [3]Faculdade de Medicina Veterinária, Centro Universitário do Espírito Santo (UNESC), Colatina, ES. CORRESPONDENCE: C.M. Pereira [clairton.marcolongo@terra.com.br]. Av. Fioravante Rossi n. 2930. CEP 29703-858 Colatina, ES, Brazil.

INTRODUCTION

Iridociliary epithelial tumors (ICETs) originate from the iris epithelium or ciliary body and comprise ciliary body adenoma, carcinoma, pleomorphic adenocarcinomas, medulloepitheliomas, and other primitive neuroectodermal tumors [4]. Although rare in domestic animals, they are the second most common primary intraocular tumors in dogs [4,9]. This tumor has also been reported in sheep [3] and humans [13]. In dogs, it occurs more frequently in middle-aged to elderly animals, and the Labrador and Golden Retriever breeds show a higher predisposition [9].

Macroscopically, ICETs appear as expansive and vascularized retroiridal masses that displace the iris or lens [7,9,11]; histologically, they may exhibit a solid, papillary, or cystic arrangement [4]. Furthermore, some ICETs secrete a periodic acid-Schiff (PAS) positive basement membrane from the inner lining of the unpigmented ciliary body epithelium [4,5] with a variable degree of pigmentation; the presence of mitotic figures and metastases are extremely rare [4,9]. ICETs are immunohistochemically positive for vimentin, S100, and neuron-specific enolase (NSE) [4]. Unlike adenomas, carcinomas show anaplasia and infiltration to the sclera, and are positive for cytokeratin [4].

This study aimed to describe the clinical and pathological aspects of solid iridociliary carcinoma in a Poodle bitch.

CASE

A 3-year-old Poodle bitch was treated for discomfort in the left eyeball region, increased intraocular pressure, and moderate buphthalmia. A direct ophthalmological examination was performed without equipment, and a mass was visualized in the posterior chamber, distorting the pupillary cleft. Unilateral enucleation was performed and the material was forwarded for histological analysis.

Macroscopically, the eyeball measured 3.4 cm (anteroposterior) x 2.6 cm (vertical), with a brownish mass that occupied the entire anterior chamber and part of the posterior chamber. A reduced volume and irregular lens, corneal opacification, hemorrhagic vitreous humor, and an enlarged whitish iris was observed (Figure 1). The material was embedded in paraffin and then histologically processed in xylene and alcohol. Sections of 4 μm were prepared and stained with hematoxylin and eosin[1] and periodic acid-Schiff[1] (PAS).

Microscopic analysis revealed an eye fragment showing neoformation in the ciliary body and iris pigment epithelium, partially well-delimited and densely cellular. It extended into the anterior chamber, anterior portion of the choroid, corneal stroma, and a small part of the posterior chamber and vitreous, adhering to the fragmented anterior lens capsule, and obstructing the filtration angle. The neoplasm was organized into predominantly solid formations (Figure 2A) and a few tubular formations; cords and rare papillary projections interspersed with a discrete amount of blood vessels; rare bundles of fibrous stroma, and amorphous eosinophilic material forming membranes that were positive for PAS (Figure 2B). The cells had variable, polygonal, eosinophilic, homogeneous, and moderate cytoplasm. Nucleus-cytoplasm ratio was moderate-to-high with round-to-oval nuclei, vesicular chromatin, and single-to-multiple prominent nucleoli (Figure 2C). Moderate to severe anisocytosis and anisokaryosis, moderate cellular and nuclear pleomorphism, eventual binucleation, and karyomegaly were observed. Seven mitotic figures were found in 12 fields (400 x FN20). Focal extensive discontinuity of the corneal epithelium was also noted, associated with mild multifocal neutrophilic and plasma cell infiltrates in the corneal stroma. Multifocal corneal stromal vascularization and hemorrhage, diffuse anterior chamber, and vitreous hemorrhage were noticed. Other findings included multifocal areas of corneal epithelial hyperplasia, marked multifocal hyperemia of the sclera, absence of Descemet's membrane, absence of the retina and reduced lens, degenerated with pigment cells, and multifocal mononuclear infiltrate.

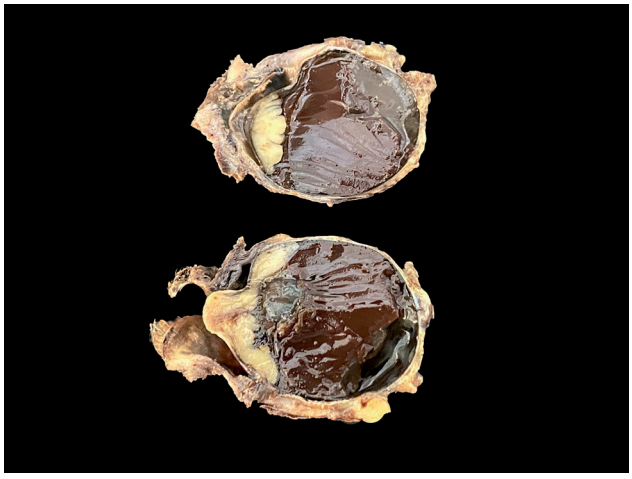

Figure 1. Sagittal section of the eyeball showing a brownish neoplastic mass occupying the entire anterior chamber and part of the posterior chamber. The lens is reduced in volume and is irregular. There is also corneal opacification and the iris is thickened and whitish.

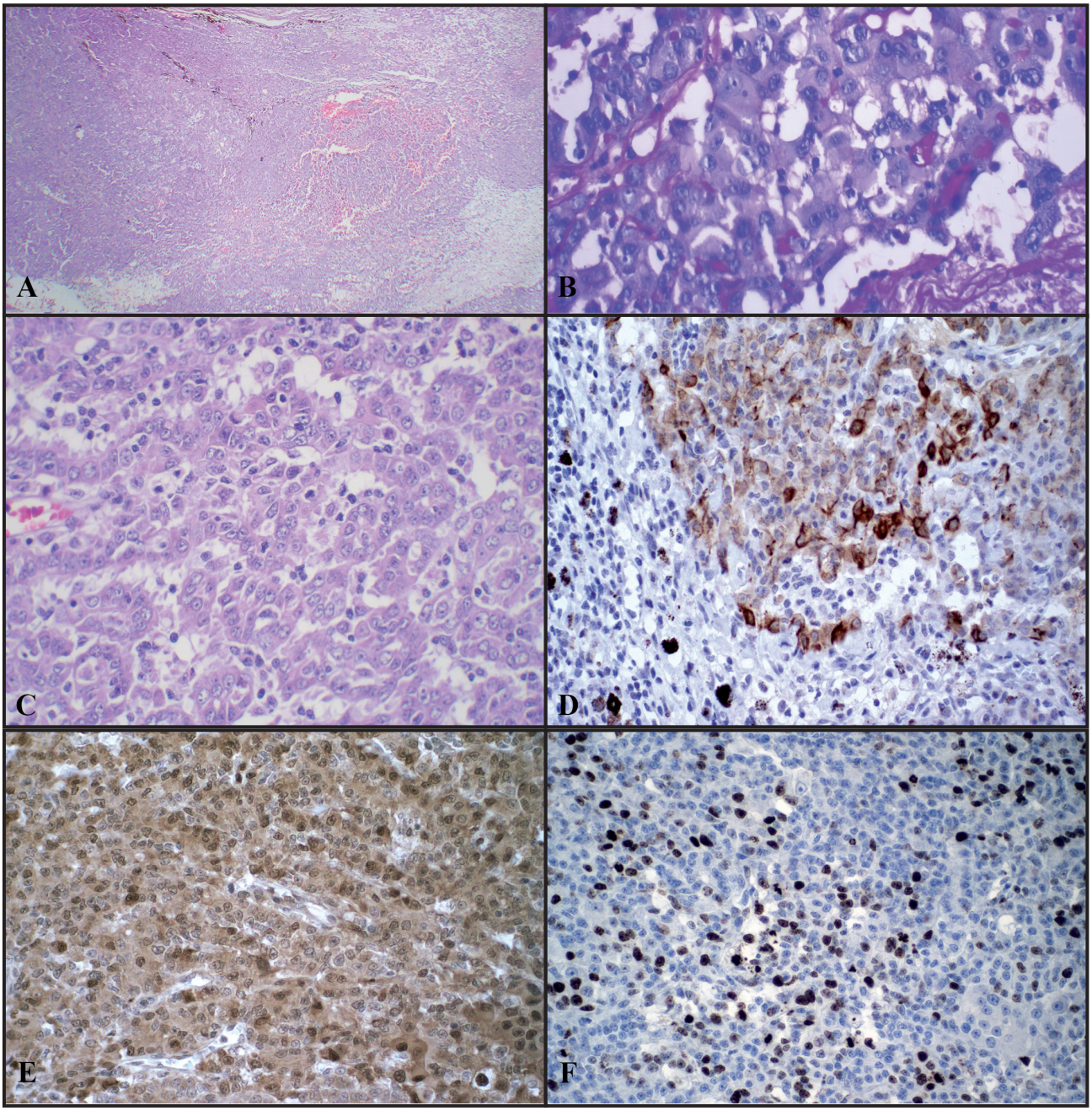

Figure 2. A- A neoformation originating in the ciliary body and iris is observed, extending to the anterior portion of the choroid and corneal stroma organized into solid formations [HE; 40x]. B- Interspersed with the neoformation cells is amorphous eosinophilic material forming PAS-positive membranes [PAS; 40x]. C- Note that the cells have polygonal, eosinophilic, and homogeneous cytoplasm; moderate to high nucleus-cytoplasm ratio; round to oval nuclei; vesicular chromatin, and single to prominent multiple nucleoli [HE; 40x]. D- Cytoplasmic immunostaining is positive for cytokeratin AE1/AE3 [IHC-DAB; 40x]. E- Positive cytoplasmic immunostaining for S100 in neoformation cells [IHC-DAB; 40x]. F- Positive immunostaining for Ki-67 (45.6% at 500 cell count) [IHC-DAB; 40x].

Neoplastic tissue sections were processed for immunohistochemical evaluation using anti-cytokeratin AE1/AE3[2], anti-S100 protein[2], anti-vimentin[2], and anti-Ki-67[2]. Neoplastic cells exhibited immunostaining for cytokeratin (Figure 2D) and S-100 protein (Figure 2E). Only 45.6% of these cells were positive for Ki-67 (500 cells) [Figure 2F]. Immunostaining was negative for vimentin. After enucleation, the patient exhibited no signs of recurrence or metastasis.

DISCUSSION

The diagnosis of solid iridociliary carcinoma was based on the histological features and positive immunostaining for cytokeratin AE1/AE3 and S100. Iridociliary carcinomas show positive immunostaining for cytokeratin, whereas adenomas and normal iridociliary epithelium do not exhibit this immunostaining [4]. Besides, the high rate of cell proliferation is indicative of

malignant neoplasia, which is confirmed by the high mitotic count and high positivity for Ki-67 [8]. Furthermore, the iridociliary epithelium showed positive staining for S100 protein, thereby helping diagnose ICETs [4].

Some histological features are important for the diagnosis of iridociliary tumors in dogs, such as noninvasive growth into the posterior chamber, pigment epithelium, and thick homogeneous membranes on the cell surface [5]. Furthermore, the positive PAS membranes favor the diagnosis of iridociliary epithelial tumors [4].

Iridociliary epithelial tumors can present in 3 ways based on their histological organization: solid, papillary, or cystic [1,5]. In this case, despite also presenting tubular and papillary structures, the predominant organization of the neoplasm was solid. In dogs, solid iridociliary tumors tend to be more invasive in the posterior chamber than the papillary ones, as observed in this case [5].

In this study, the tumor occurred in a 3-year-old bitch contrastingly to the reported literature. ICETs usually occur in elderly dogs aged 8-10 years [1,5,7,11,12].

Regarding clinical signs, the animal presented with ocular alterations compatible with glaucoma. This change is a complication often seen in dogs with ICETs as these tumors can predispose dogs to the formation of a periridal fibrovascular membrane which can further lead to peripheral anterior synechiae or neovascular membranes that obstruct the iridocorneal angle [6].

ICETs must be differentiated from melanocytomas, anterior uveal melanoma, medulloepitheliomas, metastatic and pleomorphic carcinomas. Histological characteristics, including the presence of positive PAS membranes [10], that are associated with the immunohistochemical profile of neoplasm cells, help differentiate the ICETs from these tumors.

In the present case, enucleation was the treatment of choice. The literature advocates this treatment for such cases of carcinoma, although some authors have reported surgical techniques for excisional biopsy of the neoplasm [9]. The postoperative success of excision of canine iridociliary epithelial tumors is highly variable; moreover, complete tumor excision is not always performed, and recurrence may occur [1]. Overall, the prognosis is poor for eyeball and vision maintenance in canine iridociliary tumors, and scleral invasion is associated with a higher recurrence rate [1,2]. In this case, the patient had no recurrence of the neoplasm or metastasis.

MANUFACTURERS

[1]EasyPath-Diagnósticos. Indaiatuba, SP, Brazil.
[2]Dako North America Inc. Carpinteria, CA, USA.

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