

Squamous cell carcinoma in the third eyelid of a horse

João Antonio Tadeu Pigatto¹, Luciane de Albuquerque¹, Paula Stieven Hünning¹, Ana Carolina da Veiga Rodarte de Almeida¹, Fernanda Nóbrega¹ & Juliano de Souza Leal²

ABSTRACT

Background: Squamous cell carcinoma (SCC) is a locally invasive malignant tumor of the squamous epithelial cells. This neoplasm affects the eyelid, conjunctiva and third eyelid as well as the cornea. The SCC is the most common neoplasm of equine eye and ocular adnexa. Breeds, Appaloosas, American Paint Horses, Thoroughbreds, and Quarter Horses are reported in literature as being the most predisposed ones to SCC. Although presenting a common occurrence, SCC in the third eyelid of horses is rarely reported in literature. This paper aims to describe clinical and pathological signs, and a surgical intervention of a squamous cell carcinoma case in the third eyelid of a horse.

Case: A 15-year-old, gray, stallion, Criollo horse presented a third eyelid mass in its left eye. The owner of the horse reported the growth of a red mass in the third eyelid of the bulb of its left eye with the presence of intense bloody discharge for two years. During anamnesis, a history of a previous ocular perforation was reported. The owner of the horse also reported that the outdoor housing of the horse is located in a sunny area, resulting in its relatively high exposure to solar radiation. The mass was approximately 3 cm in diameter, ulcerated and located at the free edge of the third left eyelid, but no change was observed in the right eye. We opted for the exenteration of the left eyeball. The CBC and biochemical profile of the patient showed no changes. The radiographic evaluation did not demonstrate any evidence of metastasis. The eye, orbital tissues, eyelids, and nictitating membrane were surgically removed. After establishing a sterile field, the exenteration was performed, and a continuous suture pattern of 2-0 polyglactin was used to close the subcutaneous tissue; the skin was closed with single interrupted sutures with 3-0 nylon. The third eyelid was placed in buffered 10% formalin, processed for light microscopy and sections were stained with hematoxylin eosin. The horse was discharged 10 days after the procedure.

Discussion: The squamous cell carcinoma is a locally invasive malignant neoplasm. It is the most common ocular neoplasm in the horse, affecting eyelids, nictitans, conjunctiva and cornea. It may arise anywhere in the body with a multifactorial etiology, and, the exposure to ultraviolet light and lack of periocular pigmentation are considered the main predisposing factors. The horse observed in this study is Criollo, dapple coat clear, with 15 years of age, set up outdoors and exposed to constant solar radiation. The preconized treatment for squamous cell carcinoma cases is tumor excision through a surgical margin, and, in this case, we opted for the exenteration. The third eyelid was sent for histopathological analysis as revealed islands and nests of pleomorphic epithelial cells and keratin pearls, and the diagnosis of the third eyelid was squamous cell carcinoma. Squamous cell carcinoma is considered malignant, highly invasive with high metastasis. But after 12 months of postoperative follow-up, there was no sign of recurrence or metastasizing. We conclude that the surgical removal of the tumor, with a margin of safety, was effective for the treatment of SCC in the third eyelid of a horse.

Keywords: squamous cell carcinoma, nictitans, horse.

INTRODUCTION

Squamous cell carcinoma (SCC) commonly occurs in animals and may raise anywhere in the body [3,4,7,11,16,19]. The etiology of the SSC is multifactorial. The ultraviolet light exposure and lack of periocular pigment are thought to be the primary predisposing factors [1,7,11,15,16]. SCC is frequently found in areas of the body that are exposed to sunlight, and it can develop in different parts of the eye in differentiated frequencies. The nictitating membrane and the limbus are the most common ocular sites, followed by the eyelids [3,11]. A definitive diagnosis requires histopathological examination [4-6,13,14,19], and the treatment options include surgical excision, cryotherapy, radiofrequency hyperthermia, radiotherapy, topical and intralesional chemotherapy, utilizing cisplatin or 5-fluorouracil, bacille Calmette-Guerin (BCG) cell wall extract, and carbon dioxide laser ablation [2,5,7,9,13,17]. In horses, the most frequent site for ocular involvement of SCC is the nictitating membrane and conjunctiva [4,7,9]. However, the most common ocular tumor of equine eye, SCC, is often described with a limited frequency. The following report outlines clinical and pathological findings, and the surgical intervention of a SCC case in the third eyelid of a horse.

CASE REPORT

A 15-year old, gray, stallion, Criollo horse was referred for the evaluation of an enlarging mass on its left eye, which was perceived by its owner two years before the presentation. During anamnesis, a history of previous ocular perforation was reported. The owner of the horse reported that the outdoor housing of it is located in a sunny area, resulting in its relatively high exposure to solar radiation. Ophthalmic examination revealed a 3cm diameter, red, ulcerated protruding from the free edge of the third eyelid of the left eye (Figure 1). The left eye was blind, atrophy and had severe hemorrhagic ocular secretion. Moreover, severe hyperemia of the palpebral and bulbar surface of the nictitating membrane was noted. The right eye was normal and the complete blood count and serum chemistry profile were within normal ranges. Procaine penicillin, 22.000 U/kg, BID, was initially utilized prior to surgery and continued 7 days after it. The horses received 1 dose of flunixin meglumine 1.1 mg/kg, IV, preoperatively and continued receiving it 5 days after surgery. The horse



Figure 1. Appearance of the squamous cell carcinoma of the third eyelid in an initial examination.

was routinely prepared for surgery; it was pre-medicated with intravenous 0.25 mg/kg acepromazine and anesthesia induced with midazolam (0.01 mg/kg) and quetamin (2 mg/kg), through intramuscularly route and maintained with halothane⁶ vaporized in oxygen, delivered through a circle re-breathing system. Intravenous fluids were administered throughout the surgical procedure.

After establishing a sterile field, eyelids, eye, third eyelid, and orbital tissues were surgically removed. A continuous suture pattern of 2-0 polyglactin was used to close the subcutaneous tissue, and the skin was closed with single interrupted sutures with 3-0 nylon. The third eyelid was placed in buffered 10% formalin, processed for light microscopy, and sections were stained with hematoxylin eosin. The histopathological evaluation was performed by the Sector of Veterinary Pathology (SVP), Department of Veterinary Clinical Pathology, Faculdade de Veterinária (FaVet), Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. The horse was discharged 10 days after the procedure.

RESULTS

Following surgery, the horse was comfortable, and skin suture was removed in 10 days. The patient was re-evaluated after 15, 30, 45, and 180 days post-operatively, revealing an uncomplicated healing of the lesion. Although the orbit had a sunken appearance post-operatively, owners were pleased with the procedure. SSC was diagnosed based on the results of histological examination of formalin-fixed tissue specimen, which revealed islands and nests of pleomorphic epithelial cells and keratin pearls (Figure 2). The mass was composed of irregular vascular channels

containing blood and lined by fusiform to plump oval cells with scant to moderate pale eosinophilic cytoplasm, indistinct cell margins and moderate anisocytosis. Re-examination was performed one year after surgery and neoplasm recurrence or other related abnormalities were not found.

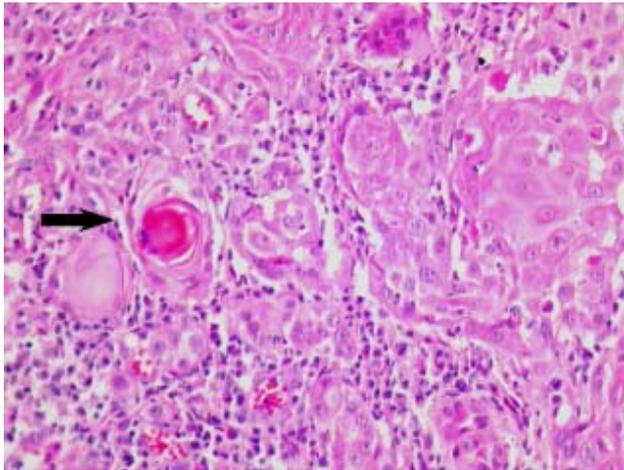


Figure 2. Histological section showing malignant epithelial cells forming keratin pearls (arrow) representing a squamous cell carcinoma (H&E stain x40).

DISCUSSION

Squamous cell carcinoma (SCC) is the most common ocular tumor occurring in horses probably related to their exposure to sunlight [1,3,8,11,15,16]. SCC is more often unilateral in horses, but it can be bilateral in approximately 16% of the cases [4,7,9]. This neoplasm can arise in any ocular tissue, but lower eyelid, lateral cantus and the third eyelid are the most common sites of the development of the tumor in horses [3,4,9,11,17]. In the present case, the tumor was unilateral and involved only the nictitating membrane of the left eye. The owner of the horse was advised to frequently nictitate the membrane of the right eye once the horses affected by SCC can develop the same lesion in the contralateral eye in the coming years.

Previous reports suggested a greater frequency of ocular squamous cell carcinoma in horses lacking pigmentation around the eye [1,4,7,10,11,16]. The ultraviolet (UV) radiation is believed to be the primary carcinogen associated with SCC [1,7,11,13]. The over-expression of the tumor-suppressor gene p53, which is targeted by UV radiation, has been found in SC equine [7,18]. The farm management for this horse may

have contributed to the development of these tumors because it was maintained outside on pasture for 24 h a day all year long in most of its life. In order to protect horses against this type of cancer, the ones with non-pigmented eyelids should be kept out of the bright sunlight, by keeping them in the stable or by providing them with shade during bright days.

Nearly all horse breeds are susceptible, however breeds such as the Appaloosa, Paints, and Pinto, or colors such as Palomino or Caramel have an increased prevalence for ocular SCC [1,5,7,8,16]. The occurrence of ocular SCC in horses increases with their advanced age [12]. Schwink, in a previous study, reported higher SCC occurrence in horses between 5 and 8 years of age [17]. Another study reported that the mean age with the diagnosis of SCC in horses occurred between 8 and 11.8 years of age [10]. The horse reported in our study fit in several mentioned predisposing factors. Beyond pelage clear and constant exposure to sunlight, the animal had a previous history of ocular trauma and advanced age.

The appearance of the SCC may vary depending on the location of the tumor. When they affect the cornea or limbus, SCC usually presents a high mass level and papillary and clear pink appearance [5,13,16], and the third eyelid may develop a wavy or thickened look as well [2]. In the eyelid, the SCC has usually been shown as a smooth mass and may become ulcerated [1,3]. In our case, ophthalmologic examination revealed a red mass, ulcerated and protruding at the free edge of the third eyelid of the left eye. Definitive ocular SCC diagnosis requires histopathological examination [2,6,13-15]. In the present case, SSC was diagnosed based on the results of histological examination of the formalin-fixed third eyelid, which revealed keratin pearls. This case was similar to previously reported SCC cases in horses in terms of their histopathological characteristics.

The biological behavior of SCC is variable and depends on its location, however, most of it, if locally invasive and present, can result in blindness involving some intraocular component. The treatment modalities for ocular squamous cell carcinoma depend on the location and extent of the tumor [2,3,13]. Generally, treatments include surgical removal or debulking, combined with a variety of ancillary procedures, such as cryotherapy, β -irradiation, γ -irradiation, radio frequency hyperthermia, immunotherapy, and intralesional chemotherapy

[2,5,7,8,13,16,17]. The involvement of the nictitating membrane often requires their removal, however, this procedure should be avoided because of the predisposition for the development of keratoconjunctivitis sicca [3]. The surgical excision is the most common treatment. The enucleation and exenteration should be shown when SCC spread involves the eyeball and complete resection of the tumor can not just remove the third eyelid [3,4,6,10].

There is little literature reporting the success of the treatment of SCC only by surgical removal as compared to a treatment together with adjacent therapies such as cryotherapy, radiotherapy, among others. The prognosis is favorable when the tumor is discovered and treated early [5,7]. SCC is an aggressive tumor that is associated with a high rate of local recurrence, but with a low rate of metastasis [5,7,17]. The recurrence is significant in cases where surgical excision is performed adjacent untreated or when

you can not remove the tumor with margins of safety conditions, and complementary therapies are not going to eliminate residual tumor cells [4,5,7,17]. In the case described, the horse was blind in its left eye due to a previous trauma; therefore, we opted to eye removal in conjunction with the third eyelid and orbital tissues adjacent not using any adjuvant treatment. The horse has passed through periodic evaluations and there is no evidence of metastasis and recurrence after observing it for 1 year.

In the case presented, the treatment of the neoplasm was apparently successful because the horse is still alive with no evidence of metastasis and recurrence in the next first year. This investigation may contribute to early diagnosis and improved treatment of SCC, as well as the patient's increased mean survival time and an improved quality of life for patients with ocular SCC.

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