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Case Report

A case of metastatic non-teratoid ocular medulloepithelioma in an adult horse

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Abstract

This case reports an eight-years-old horse that presented a unilateral tumor in the left ocular orbital region diagnosed on the basis of clinical signs, gross anatomopathological and histopathological investigations. The affected area was exenteration and submitted to histopathological evaluation and was diagnosed as a non-teratoid medulloepithelioma. This is a rare ocular neoplasm that usually affects young individuals – and was composed by neuroepithelium arranged in tubules and Flexner-Wintersteiner rosettes without presence of heteroplastic components. The animals died and was submitted to post-mortem evaluation, revealing presence of medulloepithelioma metastases at the internal region of the head, lymph nodes, lungs, and liver. This neoplasm usually presents a benign frame; however, the case herein described shows that it can be highly malignant and aggressive since it can cause extensive lesions and spread metastases to visceral organs.

Key words: equine, metastatic neoplasms, ocular neoplasms.

Intro

Neoplasms present in the ocular globe and adjacent structures can seriously affect the quality of life of the affected animal, which can cause discomfort, blindness, loss of the ocular globe and sometimes death of the individual (19). Medulloepithelioma is an intraocular neoplasia arising from embryonic neural tissue (16) that occurs unilaterally (18).

Intraocular medulloepithelioma tumor is a rare neuroepithelial intraocular neoplasms had already been described in several animal species as equines (2, 3, 8, 15, 18, 19, 25, 27, 29), dogs (1, 6, 7, 12, 14, 17), cats (5, 6, 11, 17), llamas (9, 22), goldfish (13) and cockatiel (5). This neoplasm can be classified as benign or malignant and, as teratoid or non-teratoid nature depending on the presence of heterogenous or homogenous characteristics (10, 20). Non-teratoid ocular medulloepitheliomas are composed of undifferentiated neuroepithelium, while teratoid ocular medulloepitheliomas contain additional heteroplastic components such as cartilage or neuronal tissue (20).

This report describes the clinical and post-surgical evolution of an medulloepithelioma case in an adult horse, originating from the ciliary body, showing local aggressive behavior with recurrence after local excision and the presence of metastasis diagnosed by necropsy and histopathological findings.

Case report

A mixed breed gray-haired mare, approximately eight-years-old, was conducted for veterinary medical examination and it was observed that the animal had an increased volume in the region of the left eye. No precise information was obtained about the previous history of the case evolution however, the owner of the animal suspected of mechanical trauma. The animal was followed up and,

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Figure 1. Equine presenting neoplastic mass that protrudes externally the left eye before the surgical procedure. **A.** Left side view. **B.** Front view of the animal.

after two months, it was noted that an increase in ocular volume developed rapidly and projected outwards the left eye (Fig. 1), what raised suspicion about the possibility of being a squamous cell carcinoma. Surgical removal was recommended and performed by exenteration of the left ocular globe with together the increased local mass. The surgical procedure was performed on the farm where the animal lives. It was done trichotomy of the left eye region, sedation with 2% xylazine (1.1 mg/kg IV) and local anesthesia with 2% lidocaine with vasoconstrictor. The animal had a good recovery from the procedure, feeding easily and had no difficulties in adapting, and 15 days after surgery it maintained a good body score condition.

The removed surgical specimen was sent for pathological analysis. The presence of the left eye, the eyelids and the adjacent mass on the globe was found in the piece. It was observed that the ocular globe was increased in size, while the mass adhered to the ocular globe measured 5 x 6 centimeters and had a firm consistency and was resistant to cutting (Fig. 2). The neoplastic mass was within and adjacent to the ocular globe, infiltrated by all the sclera area and replacing the all the choroid plexus and retina. After gross analysis, fragments were collected for routine histopathological processing - fixation with 10% formalin solution, inclusion in paraffin and hematoxylin and eosin (HE) staining.

On histopathological examination, the neoplasm was identified as a non-teratoid medulloepithelioma. It was composed of neoplastic neuroepithelial cells arranged in tubules and real rosettes (numerous Flexner-Wintersteiner rosettes) separated by thin septa or fibrovascular stroma (Fig. 3). The Flexner-Wintersteiner rosettes were lined with columnar pseudo-stratified neoplastic cells around a central lumen. The neoplastic cells that formed the tubules and rosettes were cuboidal to columnar and contained vesicular to hyperchromatic nuclei with a moderate amount of slightly acidophilic cytoplasm, with no evidence of cartilaginous tissue in the neoplasm mass, that reinforces the non-teratoid origin.

Neoplastic cells showed discrete anisocytosis, anisocariosis and pleomorphism, in addition to two to ten mitotic figures per field (400x). In the exenteration ocular globe, tumor cells invaded the cornea, conjunctiva, and all sclera area, in addition to replacing the all the choroid

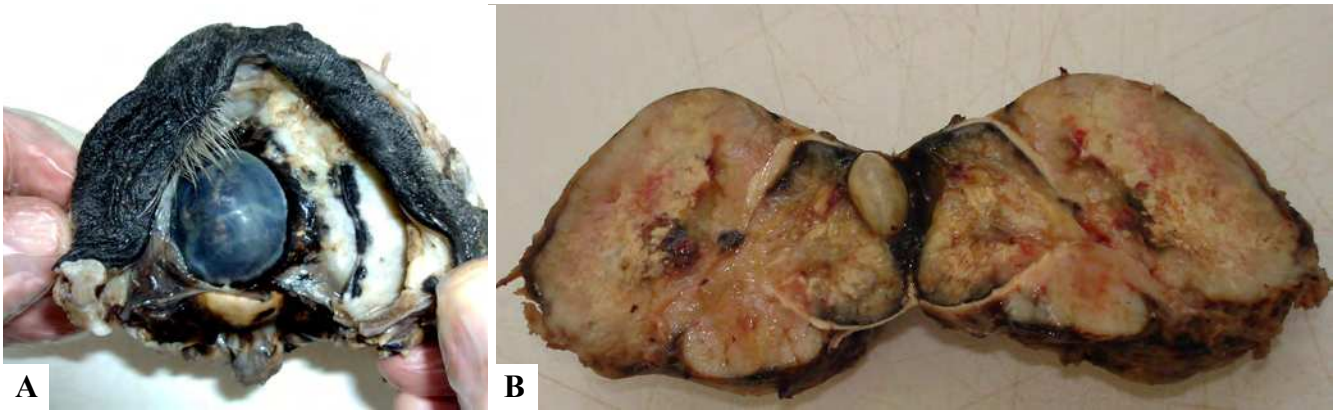


Figure 2. Gross evaluation of the surgical piece of the left eye and the neoplastic mass that is infiltrated and adjacent to the ocular globe, infiltrated by all the sclera area and replacing all the choroid plexus and retina. **A.** Whole piece. **B.** Sectioned piece.

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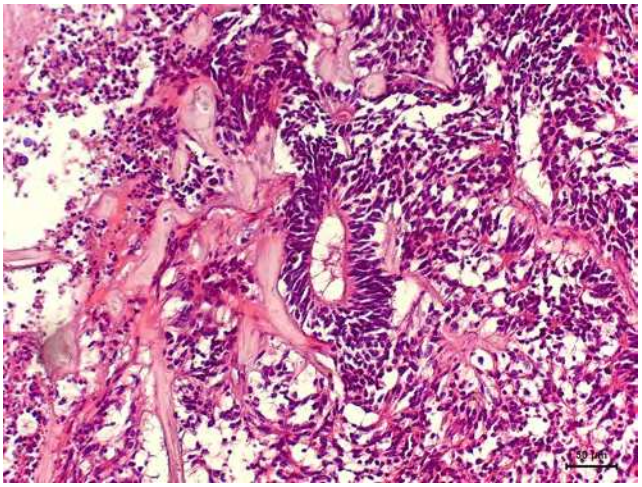


Figure 3. Histologic evaluation of the ocular neoplastic mass, showing neoplastic neuroepithelial cells arranged in tubules and on Flexner-Wintersteiner rosettes. (400x HE).

plexus, retina, ciliary body, iris and lens. The intraocular neoplasia contained discrete areas of hemorrhage, which were located mainly perivascularly within the stromal septa and extended between neoplastic cells. Neoplastic cells in the metastatic foci infiltrated in a multifocal manner and replaced the parenchyma of the organs in question.

Six months after the surgical procedure, a further increased volume was noted in the left orbit from which the ocular globe and the tumor were previously removed, a process compatible with a recurrence case. In approximately three weeks there was a very rapid growth of the mass, deforming the face of the animal. The patient was referred for clinical care, presenting with epistaxis, difficulty breathing, ocular-nasal discharge and was not eating. The animal died during the clinical examination before any intervention was performed.

At necropsy, the left orbit was filled by a lobulated tumor that was friable, with reddish-white color that infiltrated and filled the left maxillary sinus and nasal cavity, causing compression of the turbinated bones of the region. In the left orbit, an increased volume was observed with a neoplastic mass of 21 x 26 cm, infiltrating the eye orbit and nasopharynx region. The rostral portion of the left mandibular bone was expanded and replaced by neoplastic tissue. There was observed an increased volume of the left submandibular lymph node. The neoplasm was infiltrated in the nasal duct and obstructed the nasopharynx region. When the brain was removed, the bone destruction of the left parietal leaflets was observed, in communication with the skullcap, and the limitation of this region was not preserved, only the membranes of the meninges separated the brain from the affected area. Was observed cerebral and cerebellar blood vessels congested and the heart right ventricle dilated. The pulmonary and hepatic parenchyma had multiple white-gray nodules measuring one to two centimeters of diameter, demonstrating macroscopic characteristics similar to those mass of ocular neoplastic tissue.

Fragments removed from the tumoral structures listed were fixed in 10% formalin solution, processed routinely, and included in paraffin for making histological slides stained with hematoxylin and eosin. The nodules in the maxillary sinus and nasal cavity, lungs, and liver collected during the necropsy consisted as metastases of the primary eye mass and showed similar microscopic characteristics as the medulloepithelioma diagnosed in the first mass removed surgically with the live animal. Further investigations as immunohistochemistry techniques were not possible to be applied due to cost and resource availability issues. Thus, the conclusion of the diagnosis was based on the unique characteristics of the histopathological findings combined with the clinical signs and pathological findings.

The head anatomical piece was dissected and submitted to the cooking maceration procedure and baths in caustic solutions to evidence the intense bone destruction caused by the invasion of the neoplastic mass in the affected region (Fig. 4). Invasion of the left skullcap was observed with destruction of the frontal, zygomatic, lacrimal bones, arch and zygomatic process, maxillary sinus, nasal cavity, and turbinated bones.



Figure 4. Photographic image of an 8-year-old equine skull showing on the left side the destruction of the frontal bones, zygomatic, lacrimal, arch, and zygomatic process, maxillary sinus and nasal cavity and turbinated bones. **A.** Dorsal side view. **B.** Left side view.

Discussion

The main differential diagnoses for intraocular neoplasms are medulloepitheliomas and retinoblastomas. Retinoblastomas are embryonic neoplasms that originate from neuroepithelial cells in the developing retina. Intraocular medulloepitheliomas are derived from the undifferentiated medullary epithelium that lines the optic vesicle, which gives rise to the retina, iris and choroid. They may demonstrate partial differentiation in one to several derivatives of the internal or external medullary epithelium, such as photoreceptor or glial cell differentiation (17). In contrast to medulloepitheliomas, retinoblastomas are mainly composed of sheets of undifferentiated neuroepithelial cells (7, 20). The main histological characteristic of medulloepithelioma is the formation of the Flexner-Wintersteiner rosettes (7), therefore, immunohistochemistry could be performed to confirm the suspicion of medulloepithelioma and exclude the differential diagnoses (23, 29) as the neuroendocrine carcinomas and paragangliomas (26).

Generally, intraocular medulloepitheliomas originate from the ciliary body due to its late development, developing more rarely from the optic nerve (6, 17). This rare tumor has a slow growth (10, 21) and, although it was described as locally aggressive, metastases to distant sites are uncommon (21). This type of neoplasm is commonly classified as malignant with locally aggressive but with rarely metastasis to regional lymph nodes and lungs (8). There is little information about the metastatic potential of this tumor type in animals, and the retrobulbar extension has also been documented in horses (27). In humans, metastasis rarely occur and local invasion in the orbit appears to be the most common form (24). In the reported case, the location of the tumor, the shape and arrangement of the cells provided evidence that the neoplasm should be classified as a non-teratoid medulloepithelioma.

Medulloepitheliomas, originating from the primitive optic vesicle before differentiating into mature tissue, are considered congenital neoplasms. Neoplastic cells have the potential to differentiate into different tissues such as cartilage, skeletal muscle, and brain tissue (20). In the present case, no foci of undifferentiated or differentiated tissue were observed in the aforementioned variants, allowing the conclusion that the neoplasm did not have a teratoid character, been a non-teratoid medulloepithelioma case. The tumor cells in the medulloepithelioma are usually arranged in tubules and rosettes. Such structures were consistently present in the case described here, where cells tended to group together in a columnar or pseudo-stratified neuroepithelium around a central lumen, considered to be the main characteristics of medulloepithelioma (4, 20).

Ocular medulloepitheliomas are usually diagnosed in young individuals in most animal species (1) but in equine is more commonly observed in young adult horses (10) as the horse presented here, an 8-year-old at the time of diagnosis. The intraocular neoplasia was probably congenital and asymptomatic until the development of secondary complications, as in the case described in young horses (18, 29). There are few reports in the literature of intraocular medulloepitheliomas in older horses (15), with two cases diagnosed in 11-year-old mares, cases of teratoid medulloepitheliomas (15, 18) and a 14-year-old gelding horse case of non-teratoid medulloepithelioma (23), all the three cases without metastasis (15, 18, 23). The case reported in this work is a case of non-teratoid medulloepithelioma of an old mare with pulmonary and hepatic metastases and with invasion of the face bones around the primary tumor.

In the medulloepithelioma cases described in horses, the recommended therapeutic procedure is enucleation of the affected eye (15, 18, 23, 29), as was done in this reported clinical case. Although medulloepitheliomas are typically locally invasive and enucleation is usually curative, in rare cases, such as the one presented here, there may be recurrence and lymphatic and/or hematogenic dissemination (28). Due to the difficult to estimate the prognosis after the enucleation of an eye with an medulloepithelioma as well the absence of some clinical proceedings as fine needle lymph node aspirate, thoracic radiographs and abdominocentesis, these could be considered as limitations to detect signs of metastasis (29).

Metastasis of intraocular teratoid medulloepithelioma is possible, and tumor staging is recommended in cases where the diagnosis of teratoid medulloepithelioma is confirmed (18). In this report, invasion of the skullcap without brain involvement was observed, and the dissemination to the cranial bones and brain can occur mainly in cases where the diagnosis is late (6). This reported case demonstrates that ocular medulloepitheliomas in horses can be markedly malignant and aggressive, causing extensive damage and widespread metastasis to visceral organs.

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