PRIMARY INTRAOCULAR OSTEOSARCOMA WITH PULMONARY METASTASIS IN A GUINEA PIG (*CAVIA PORCELLUS*)

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Abstract

A 3-year-old male guinea pig (*Cavia porcellus*) presented to the UNAM Exotic Pet and Wildlife Teaching Hospital. Clinical signs included hyphema, buphthalmos, goniosynechiae, anterior uveitis, and hypopyon of the ventral iridocorneal angle of the right eye. The right globe was enucleated and submitted for histopathology and the histopathologic findings were consistent with osteosarcoma. Thoracic radiographs did not reveal evidence of other primary tumors or metastasis. Four months later, the patient had pleural friction rub sounds upon auscultation of the lung fields and prescapular lymphadenomegaly. Radiographic evaluation revealed a radiopaque mineral-dense structure in the right caudal pulmonary lobe, suggestive of osteosarcoma metastasis. The presumptive diagnosis was confirmed at necropsy. This is the first report of a primary intraocular osteosarcoma in a guinea pig.

Key words: osteosarcoma; intraocular; eye; guinea pig; *Cavia porcellus*; heterotopic bone

INTRODUCTION

The anatomy of the guinea pig eye is commonly reported as similar to that of humans and other rodents. The primary difference from the human eye is that guinea pigs have paurangiotic retinal vasculature, in which the retinal vessels extend only for a short distance toward the periphery from the optic disc.[1,2] In guinea pigs, the rest of the retina depends on choriocapillaris vasculature. Guinea pigs also lack a trochlea of the superior oblique muscle.[3]

Although the ophthalmological approach in guinea pigs does not differ from that performed in other species such as the dog, there are few published studies on ophthalmic diseases in this species. In a study performed on 1000 guinea pigs from research centers, shelters, homes, and exhibitions, 55% presented without ophthalmological abnormalities, while 45% exhibited a variety of ocular medical concerns. The most frequent pathologies were the ones that affected the lens: cataracts (17.4%), nuclear sclerosis (10.5%), and nuclear rings (8.1%). Other pathologies reported in this study were conjunctivitis (4.7%), keratitis (3.6%), lipid deposits in the conjunctiva (2.3%), trauma (2.2%), microphthalmia (0.8%), trichiasis (0.8%), heterotopic bone formation (0.8%), whitish ocular discharge (0.4%), corneal lipidosis (0.4%), dry keratoconjunctivitis (0.3%), prolapse of the nictitating gland (0.5%), and anophthalmia (0.1%).[4] Other reports describe ophthalmic pathologies in guinea pigs including dermoid cysts,[5] entropion, and retinal degeneration.[2]

Heterotopic bone formation or osseous choristoma is a histologically normal osseous tissue presenting in an aberrant site. The heterotopic bone formation in the eye is reported in humans (epibulbar, choroidal, and vitreoretinal)[6,7] and guinea pigs (ciliary body).[8]

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This alteration is reported as common finding in older guinea pigs and, if it is a normal aging or a pathological process is unknown.[4,8,9]

At least 25 different neoplasia types have been reported in guinea pigs, involving practically in all systems, either spontaneously or induced.[10-25] Although the anterior chamber of the guinea pig's eye has been used for the experimental growth of tumors of various origins (human, bird, and mouse),[22-27] only 3 cases of spontaneous neoplasias with ophthalmic manifestations (conjunctival lymphosarcoma,[28] corneal T-cell lymphoma,[29] and palpebral liposarcoma[30]) have been reported.

Osteosarcoma is an infrequently reported neoplasm in guinea pigs.[20,31-36] Reports include both primary osteosarcoma, as well as soft tissue origin (extra-skeletal osteosarcoma). Osteosarcomas are characterized by a high metastatic potential.[20,31-34,36] The diagnosis is based on histopathology; however, in some cases, immunohistochemistry may be necessary for confirmation.[37-39] There are no reports of treatment of osteosarcoma in guinea pigs. However, surgical resection, radiotherapy, and chemotherapy have been described in humans, dogs, and cats.[37,38,40-42]

CASE REPORT

A 3-year-old male guinea pig with history of several linear proliferative white iridocorneal angle lesions in both eyes 1 year prior was presented to the UNAM Exotic Pet and Wildlife Teaching Hospital of the Veterinary and Husbandry College from the National Autonomous University of Mexico (FMVZ-UNAM), for the presence of exophthalmos and hyphema in the right eye for 1 month prior the consultation. During the ophthalmic examination, the right eye exhibited hyphema with a clot in the ventral portion of the cornea, scleral vasodilatation, exophthalmos (Fig. 1A), goniosinechiae, and anterior uveitis with hypopyon in the iridocorneal angle. The left eye exhibited only scleral vasodilatation and proliferative white tissue in a straight line in the iridocorneal angle (Fig. 1B). Intraocular pressure was measured with a digital applanation tonometer (reference ranges 18.27 ± 4.55 mm HG)[43] and the intraocular pressure of the right eye (18 mm Hg) was elevated compared to the left eye (13 mm Hg). No other abnormalities were found in the general physical examination.

As presumptive diagnoses, uveitis with hypopyon in the right eye and heterotopic bone formation for the white proliferative tissue in the left eye were considered. A systemic antibiotic, nonsteroidal anti-inflammatory therapy and enucleation of the right eye was indicated and recommended, but the owner declined and elected to administer the nonsteroidal anti-inflammatory only. Meloxicam at 1.5 mg/kg PO was prescribed as palliative therapy every 24 hours for 7 days (Metacam oral suspension, 1.5 mg/mL, Boehringer Ingelheim). The owner reported that it had no clinical effect when he returned 5 months later. There was no change in patient condition. Enucleation of the right eye was performed.

The eye was preserved in 10% formaldehyde and submitted to the FMVZ-UNAM Pathology Laboratory for histopathology. The cut surface of the eye was solid and gritty. The newly formed white, hard tissue surrounded the lens and replaced the inner structures, the vitreous and aqueous humors of the anterior and posterior chambers (Fig. 2). Microscopically (Fig. 3), it consisted of a large deposit of extracellular amorphous eosinophilic material (osteoid), surrounded by osteoblasts, many of them with normal and atypical mitotic figures. This material surrounded the lens and replaced much of the choroid, retina, and ciliary body. The neoplasia also invaded the entire thickness of the sclera near the sclerocorneal angle and extended extraocularly to the insertion

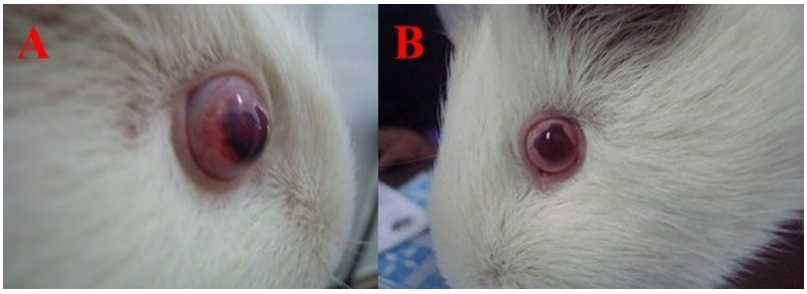

FIGURE 1. Guinea pig at presentation for evaluation and consultation in the UNAM Exotic Pet and Wildlife Teaching Hospital. (A) Right eye of the patient showing exophthalmia, scleral vasodilatation and the ventral hyphema. (B) Left eye of the patient in which the neoformation tissue (red narrows) is observed in the iridocorneal angle.

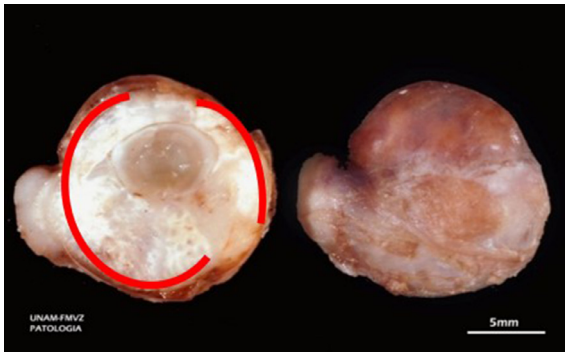

FIGURE 2. Macroscopic cross-section of the right eye of the patient, where bone tissue can be observed surrounding the lens and displacing the eye structures (red lines).

point of the extraocular muscles. Neoplastic cells were pleomorphic with well-defined and angulated cytoplasmic borders. Few cells are binucleated with oval and hyperchromatic nuclei and finely granular chromatin with 1 to 2 evident nucleoli (Fig. 4). Seven atypical mitoses were seen in 10 random fields at 40×. Coagulative necrotic areas, cell debris, hemosiderophages, and a hemorrhage were observed among the neoplastic cells. No neoplastic cells were found at the surgical borders. However, the lumen of the blood vessels of the retrobulbar region of the eye contained osteosarcoma cells. The previously described features are consistent with an osteosarcoma in the right eye.

After the histopathology diagnosis, a full-body radiographic study was performed, and there was no radiographic evidence suggesting primary neoplasia or metastasis (Fig. 5). Two radiopaque

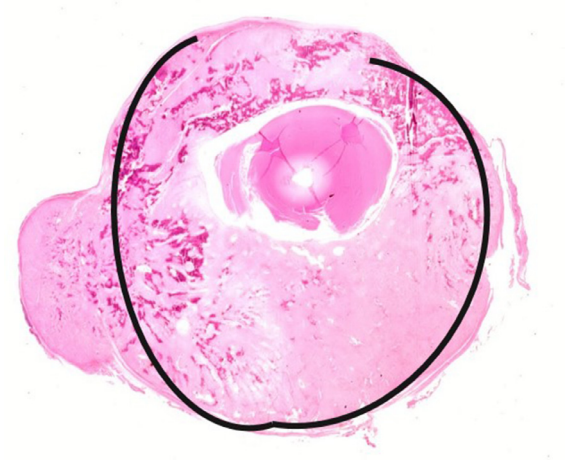

FIGURE 3. Microphotography of the histological section of the right eye (H/E Stain, 4×). The newly formed tissue is seen surrounding the crystalline and replacing the choroid, retina, and ciliary body, invading the sclera and infiltrating the periorbital muscle tissue (delineated by the black lines).

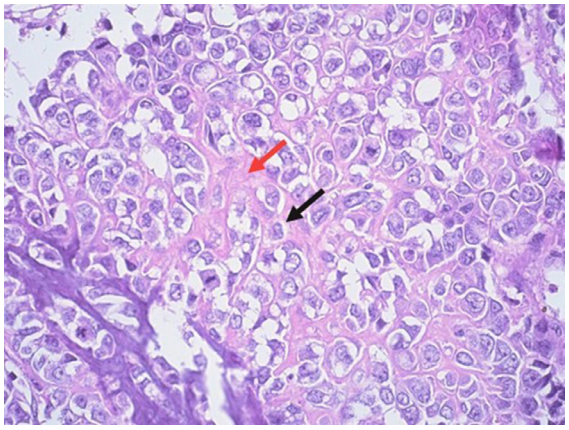

FIGURE 4. Microphotography of the right eye showing neoplastic tissue and neoplastic cells (black arrow) with a vacuolated cytoplasm, round nucleus, prominent and prochromatic nucleoli, thick-face chromatin and the presence of bone matrix (red arrow). H/E staining (40×).

structures with mineral density were present in the left anterior ocular chamber and coincided with the possible heterotopic bone (Fig. 6).

Based on the histopathological and radiographic results, lesions of the right eye were consistent with primary ocular osteosarcoma. Gross and radiographic changes in the left eye were consistent with heterotopic bone formation.

Recommendations included semiannual clinical examination and thoracic radiographic follow-up to detect possible metastases, along with monthly ophthalmic evaluation to monitor intraocular pressure in the remaining eye and to evaluate the progression of the proliferative heterotopic bone lesion. However, the owner did not adhere to the recommendations.

Four months later, the patient returned depressed, hypothermic (35°C, reference range 37.2°C to 39.5°C),[44] demonstrating pain upon abdominal palpation, with abundant gas in the intestinal loops, pleural friction upon pulmonary auscultation, and prescapular lymphadenomegaly. A radiographic study of the thorax was performed, and a radiopaque structure with mineral density was observed in the right caudal lobe (Fig. 7) suggestive of pulmonary metastasis. Abdominal radiographs showed gastric dilation occupying a large area of the cranial abdomen and the middle part of the left side, with the displacement of the other abdominal structures. Due to the previous diagnosis, the patient's condition, and overall poor prognosis, the owner elected euthanasia.

Necropsy was performed at the FMVZ-UNAM Pathology Laboratory. The reported findings included multiple irregular plaques consisting of neoplastic cells (osteoblasts) with moderate

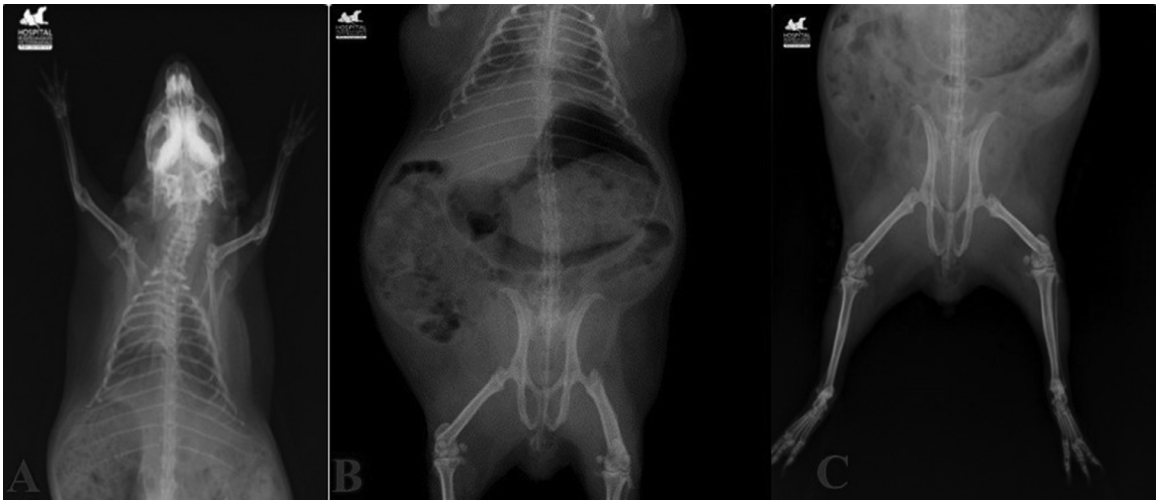

FIGURE 5. A full-body radiographic study in which no changes are observed in the bone structures. (A) Dorsal-ventral projection of the thorax. (B) Ventrodorsal abdomen projection. (C) Comparative cranial-caudal views of the pelvic limbs.

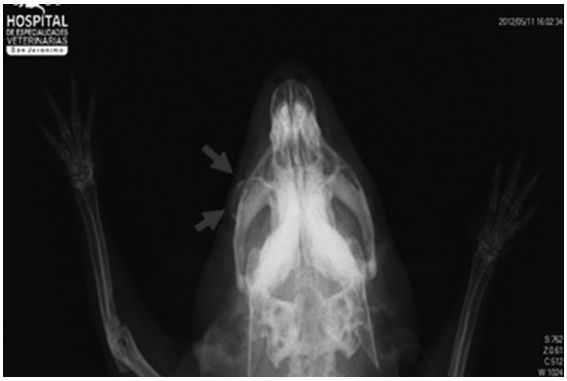

FIGURE 6. Skull radiographic study (dorsal-ventral view), where there is no evidence of periocular bone reactions; also, radiopaque zones with bone density in the left anterior eye (arrows) are observed.

cytoplasm, round to oval nucleus, eosinophilic nucleoli, open-face chromatin, mitosis (5 to 7 per 10,400 × high field power), and abundant bone matrix (Fig. 8) in the visceral pleura of the lung, which were compatible with pulmonary metastasis of osteosarcoma. Macroscopic and microscopic inspection of the periphery of the enucleation site and surrounding tissues of the eye did not reveal the presence of the neoplasm. Macroscopic findings included a white circular area in the left iris which was not further investigated. The prescapular enlarged lymph nodes with hyperplasia evidence only.

DISCUSSION

This is the first report of a primary intraocular osteosarcoma in a guinea pig. Osteosarcomas have been previously reported in guinea pigs in other anatomical regions: 1 in the humerus,[35] 2 in the tibia,[33,34] 1 in the femur,[32] 2 in the lumbar vertebrae,[20] and 1 extra-skeletal.[31]

In this case, it was not necessary to perform an immunohistochemistry to confirm the diagnosis, since the osteosarcoma reported here presented all the histopathological elements to confirm it. The tissue was inconsistent with chondrosarcoma, fibrosarcoma, or an osteosarcoma due to the limited production of tumoral osteoid.[37-39]

Reports of primary intraocular osteosarcomas are scarce. They include dogs and an umbrella cockatoo (*Cacatua alba*).[39,46,47] Signs such as hyphema, increased of the sclera vascularity, glaucoma, hypopyon, and uveitis observed in this patient are consistent with those reported for other species.[40-42,44-47] Fordham, Rosenthal, and Durham (2010)[40] reported a case of intraocular osteosarcoma in a white cockatoo (*Cacatua alba*), which could have its origin in the scleral ossicles that birds possess; however, they did not perform histological analysis of the entire eye in order to confirm it. From the reports of primary intraocular osteosarcomas in humans and dogs,[47-47] bone metaplasia caused by chronic ocular diseases or trauma has been proposed as the origin, but in none of the cases was the cause definitively determined.

Except for the white proliferative tissue (possible heterotopic bone formation) identified in this patient, no data on previous ophthalmic pathologies or traumas were available. In this case, the histopathology diagnosis of heterotopic bone formation in the left eye could not be confirmed by technic problems with the eye, but based on what has been reported in the literature (clinical signs

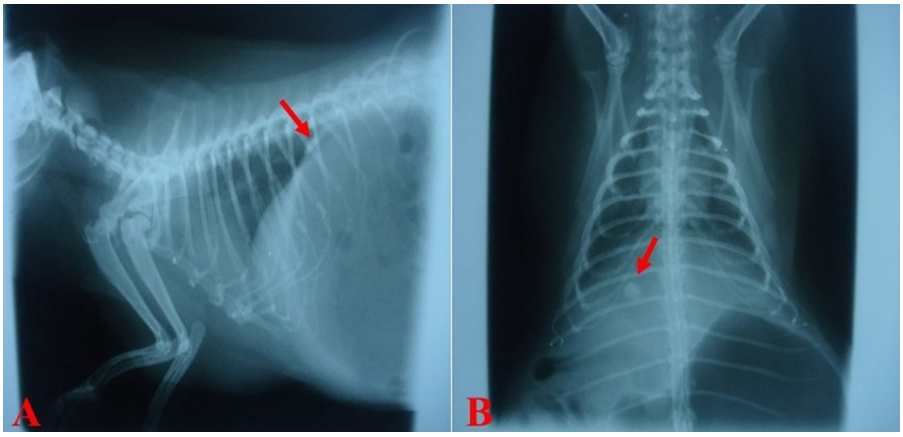

FIGURE 7. Radiographic study of the thorax. (A) Right lateral-left lateral view showing a radiopaque zone with bone density at the pulmonary caudal level (arrow), suggestive of osteosarcoma pulmonary metastasis. (B) Ventrodorsal view in which the same radiopaque area with bone density is observed at the right caudal lobe level (arrow).

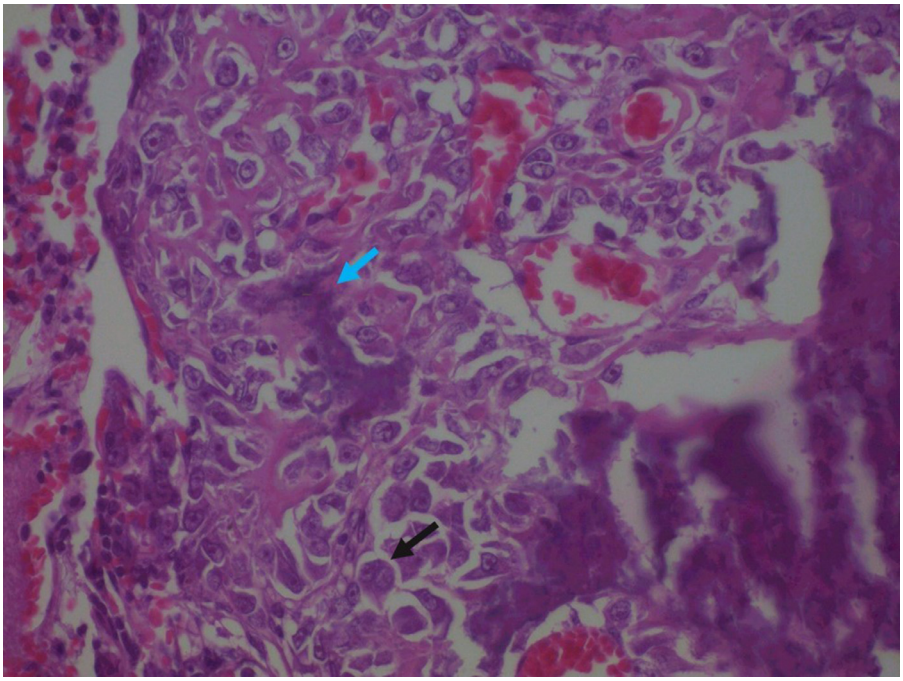

FIGURE 8. Lung microphotographs showing mesenchymal neoformation tissue (bone tissue, red arrow) and neoplastic cells (black arrow) with moderate cytoplasm, and round to oval nuclei. H/E staining (40×).

and evolution)[48,49,8] it was considered the most likely diagnosis. For this patient, the intraocular osteosarcoma possible origin sites would be the choroid and the ciliary body, since both places have been reported in bone origin pathologies for humans[50] and guinea pigs,[49,8] respectively. The heterotopic bone formation suspected on the left eye could also have been present in the right eye and given rise to this neoplasia; however, this could not be confirmed.

Although primary tumor resection/amputation is the most widely used treatment in osteosarcomas, the addition of postoperative chemotherapy increases survival in human and canine patients without gross evidence of metastasis at the time of surgery. In humans and dogs, chemotherapy can suppress the micrometastases, as long as the treatment starts when there are no apparent nodules.[37-39,51,52] Chemotherapeutic protocols have not been described for this condition in the guinea pig.

At the time of the patient's enucleation, there were no radiographic signs suggestive of pulmonary metastasis. However, the retrobulbar blood vessel lumens contained neoplastic cells, so micrometastases could not be ruled out. Metastatic

lesions are often not radiographically detected when the size is less than 6 mm.[37-39,53] In dogs and humans with clinical evidence of osteosarcoma, more than 80% of the patients already have some degree of metastasis, mainly in the lungs.[37-39,53] The primary locations for osteosarcoma metastasis in guinea pigs are the lungs (as seen in this patient), kidneys, and spleen.[20,31-34,36] Metastases to liver, heart, pancreas, testicles, seminal vesicles, subcutaneous tissue, stomach, peritoneal and pleural cavities, and mesentery have also been reported in guinea pigs.[20,31-34,36]

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