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Case Report

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Meibomian Gland Adenocarcinoma in a Captive Indian Leopard (*Panthera pardus fusca*)

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ABSTRACT

Isolated and comparative studies describing the incidence of neoplasia in free-ranging or captive leopards have been reported infrequently, amongst which ocular or extraocular tumour cases are extremely rare. A 21-year-old captive, female Indian leopard (*Panthera pardus fusca*) at Manikdoh Leopard Rescue Centre was evaluated for the development of multiple proliferative irregular growths on lateral and medial canthus of the left eye along with purulent discharge and corneal irritation. Radical excision of the growth was performed. It was found that masses originating from the eyelid, nictitating membrane, and conjunctival areas had histopathological features consistent with rare and malignant meibomian gland adenocarcinoma; characterized by irregular neoplastic cellular islands from meibomian glands (modified sebaceous gland) subdivided into lobules by fibrovascular connective tissue with presence of basaloid cells, intracytoplasmic lipid vacuoles, nuclear hyperchromasia, pleomorphism, necrosis with inflammatory cellular infiltration. The present case is a foremost report of meibomian gland adenocarcinoma in leopards with comprehensive documentation of its prevalence diagnostic characteristics, limitations, and available options for treatment.

Keywords: Leopard; *Panthera pardus fusca*; Meibomian gland adenocarcinoma; Surgical excision; Tumor

INTRODUCTION

As the population of leopards in captivity shows a steady rise across the globe, retrospective studies reveal positive correlations between this growing captive population and rising incidences of neoplasms in these big cats. Increased neoplastic processes can be attributed to factors like longer lifespans as a result of better health management and husbandry practices at the rescue centers, zoological parks, etc., and also higher exposure to environmental carcinogens [1,2] (Owston et al., 2008, Lombard and Witte, 1959).

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Neoplastic developments have been observed in Indian leopards, the cases reported include squamous cell carcinoma by [3,4] (Quintard et al., 2017, Kesdangsakonwut et al., 2014), mammary gland adenoma [5] (Nakamura et al., 2018), thyroid carcinoma [6], skin lipoma [7] (Baquir et al., 2014), benign gastric neuroendocrine tumor [8] (Dobson et al., 2013), and uterine leiomyoma [9](Willott et al., 2005). Some novel neoplastic incidences like cystic trichoblastoma, pheochromocytoma, meningioma, and bronchiolar adenoma were also reported in leopards. The retrospective study of neoplasia occurrence in members of *Panthera* species [10] (Kloft et al., 2019). A recent study published in 2020, analyzed the epidemiological neoplastic distribution and studied its prevalence in 195 cases across 16 species of *Panthera* versus non-*Panthera* species of non-domestic felids in-captivity. The data found was conclusive that *Panthera* species not only had a higher prevalence rate of neoplasms than non-*Panthera* felids (52.5%; vs. 13.0% respectively); but also, were at a greater risk of developing malignant forms of the neoplasms. Amongst these, *Panthera pardus* was one of the species found to be more susceptible to malignant neoplasia of the reproductive system [11] (Moresco et al., 2020). When compared to their domestic counterparts, the occurrence of cutaneous neoplasia of epithelial origin is quite common in cats (domestic felines), frequently observed in form of squamous cell carcinoma (SCC), the most malignant tumor in the species [12] (Morris et al., 2001). However, tumors of eyelids and adnexal structures like sebaceous glands are infrequent in cats, yet extensively reported in dogs.

Sebaceous gland tumors are rare, specific epithelial neoplasms arising from sebaceous glands (which are adnexal structures distributed throughout the skin at the base of hair follicles); and can be broadly categorized into sebaceous gland adenoma, sebaceous epithelioma, sebaceous gland carcinoma as well as perineal adenoma/adenocarcinoma [13] (Stanley, 2016). Sebaceous gland tumors are one of the most common cutaneous epithelial tumors especially sebaceous adenoma cases are observed in dogs [14] Scott and (Anderson, 1990), but rarely in cats; and its malignant counterpart (sebaceous gland carcinoma or adenocarcinoma) is uncommon in both dogs and cats [14,15] Scott and (Anderson, 1990), (Vali and Withrow, 2007). Although, there are no reports or studies available on the sebaceous adenocarcinoma of any extraocular or periocular origin in *Panthera pardus*.

Such tumors usually associated with extraocular structures like eyelids; either as a result of malignancy or having a primary origin from adnexal or ocular structures, leads to visual impairment of the animal due to inflammation, secondary glaucoma, and ulcerations in ocular structures, thus, compromising on its quality-of-life [16] (Hauck et al., 2012).

This case report is a brief description of the history, presentation, surgical treatment and post-surgical management of a Leopard (*Panthera pardus*) diagnosed with Sebaceous adenocarcinoma also known as the Meibomian gland adenocarcinoma on eyelids, nictitating membrane (third eyelid), and conjunctiva.

CASE PRESENTATION AND CLINICAL FINDINGS

A 21-year-old, female Indian Leopard (*Panthera pardus fusca*) was rescued from Chalisgaon, Maharashtra, and rehabilitated in captivity at Manikdoh Leopard Rescue Centre, Junnar from 26th December 2004, microchip number: 00063B3F95. In recent times, the leopard gradually began to develop two proliferative cauliflower-like growths on the medial and lateral canthus of the left eye, profuse unilateral ocular discharge, and congested conjunctiva of the affected eye. The leopard's aggressive behavior was a major limiting factor for complete physical examination to aid the diagnosis. It was decided that the animal would require to be operated for excision of the growths from eyelid under general anesthesia.

Hematological and serological analysis

Blood was sampled from lateral tail vein, collected into vacutainer tubes containing EDTA (ethylenedianinetetraacetic acid) and clot activator for pre-operative haematological and serological examination, respectively. Significant changes were recorded as mentioned in (Table 1). Observations included marginal elevated hemoglobin; mild leukocytosis associated with neutrophilia; thrombocytosis; azotemia with elevated BUN; mild elevated creatinine; marginal elevated AST; increased total protein; mild increase in globulin (all tests performed for parameters undermentioned were done on automated hematology and biochemistry analyser.). Hematological abnormalities were attributed to mild dehydration and stress-induced leukocytosis which is most likely to occur during the restraining procedure in the captive wild felids [19,20] (Stella et al., 2013, Davis et al., 2008). The elevated renal profile is associated with the aging factor.

Table 1: Preoperative Hematological and Biochemical values of 21-year-old female leopard (*Panthera pardus*).

PARAMETER	RESULT	UNIT	REFERENCES RANGE
Haemoglobin	16.1	g/dl	8.4-14
Total WBC count	14	$\times 10^3/\mu l$	1.6-13.7
	DIFFERENTIAL COUNT		
Neutrophil	72	%	64-70
Lymphocytes	20	%	19-28
Monocytes	01	%	3-6
Eosinophil	07	%	2-7
Basophil	00	%	0-1
	RBC INDICES		
RBC Count	8.6	$\times 10^6/\mu l$	6.5-15.5
Haematocrit	43.8	%	35-45
MCV	51	*fl*	45-72
MCH	18.7	pg	12-20
MCHC	36.7	%	28-38
	PLATELETS INDICES		
Platelets Count	292	$\times 10^3/\mu l$	140-250
MPV	10.2	*fl*	6-10
	SERUM BIOCHEMISTRY INDICES		
Serum urea	99.09	mg/dl	19-60
Serum creatinine	3.21	mg/dl	0.24-2.35
Serum uric acid	1.20	mg/dl	2.2-4.5
Calcium	8.79	mg/dl	5.5-11
Phosphorus	13.59	mg/dl	2.5-6.5
Cholesterol	196.10	mg/dl	160-260
Total Bilirubin	0.72	mg/dl	0.4-1.6
Direct Bilirubin	18	mg/dl	up to 25
Indirect Bilirubin	0.05	mg/dl	0-0.8
SGPT	38.30	IU/L	7-56
SGOT	48.85	IU/L	15-35
Alkaline Phosphatase	31.33	IU/L	12.7-88.5
Total Protein	9.99	g/dl	5.5-7.8
Albumin	3.05	g/dl	2.8-6.4
Globulin	6.94	g/dl	1.5-5.7

Management

The leopard (body weight 50kg) was fasted for 24 hours before physical examination and subsequently; was immobilized with a dart using a combination of Ketamine (3mg/kg) and Xylazine (1mg/kg). Following 20 minutes of darting, the tranquilization depth was reviewed by checking for ear flick and touch reflexes. Glycopyrrolate (@ 0.01 mg/kg with presentation of 0.2 mg/ml) was administered as pre-anesthetic anticholinergic agent subcutaneously.

Figure 1: Tumorous growth on the Left eye of the captive female leopard. ((C) WildlifeSOS-MLRC)

The surgery was performed successfully while the leopard's anesthesia was maintained on diluted intravenous ketamine to effect. Close ocular examination during surgery revealed multiple proliferative masses on eyelids and conjunctiva of the left eye (Figure 1); suspected to be of neoplastic origin. The surgery involved removal of upper eyelid mass by full-thickness deep wedge incision including an appropriate size rim of normal unaffected eyelid tissue followed by eyelid reconstruction i.e., blepharoplasty [17] (Crispin, 2005). The gap was closed by an advancing skin flap, thus minimizing the possibility of undue distortion of eyelid margin. The conjunctival and dermal defect were sutured in separately. Besides, four additional masses were excised from the third eyelid and conjunctiva. During the surgery, all vital parameters of this geriatric leopard were critically monitored (temperature, CRT, color of mucus membranes, SPO2 levels, electrocardiogram, heart rate, respiratory rate, and pulse rate at frequent intervals. A multimodal approach to control hemorrhages was adopted which included topical infiltration of adrenaline, ligation of blood vessels, and intra-operative administration of ethamsylate @ 15 mg/kg (intramuscular). Post-operatively, the animal was administered with long acting enrofloxacin @ 1 ml / 10 kg, dexamethasone @ 0.5 mg/kg, meloxicam @ 0.25 mg/kg, and yohimbine @ 0.2 mg/kg (intramuscular) as a reversal for xylazine. The leopard was shifted to a smaller cage in the vicinity of its enclosure to closely monitor its recovery. The surgical wound healing was unremarkable in the post operative period; without any visible distortion of the eyelid [17,18] (Crispin, 2005, Aquino, 2007).

Histopathological findings

Tissue samples of masses excised during surgery were preserved in routine 10% formalin for histopathological examination (Figure 2: A-D).

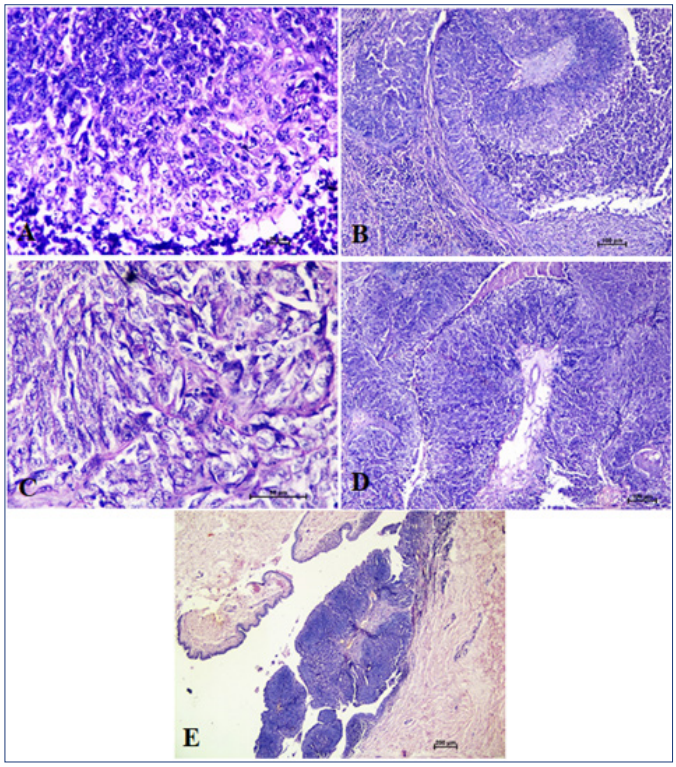

Figure 2: (A) Hematoxylin and eosin stain sections from the eyelid of the leopard shows a cluster of tumor cells showing pleomorphic changes, intracytoplasmic lipid vacuoles, hyperchromasia of a nucleus with one or two dark-stained nucleoli H&EX400, Bar 20µm. **(B)** Section from eyelid shows a Cluster of tumor cells showing pleomorphic changes, intracytoplasmic lipid vacuoles, hyperchromasia of a nucleus with one or two dark-stained nucleoli. Irregular island of neoplastic meibomian glandular tissue subdivided into lobules by thin layers of fibrous connective tissue. H&EX100. Bar 100µm. **(C)** Section from the third eyelid shows small lobules of tumor cells separated by fine trabeculae or connective tissues. H&EX400, Bar 20µm. **(D)** In the expanded version Tumor cells showing anisocytosis, hyperchromatic pleomorphic nuclei, and prominent nucleoli. Intracytoplasmic lipid vacuoles can be observed. H&EX100, Bar 100µm. **(E)** Growth removed from conjunctiva observed and it reflects Foci of conjunctival tissue exhibiting growth similar to the meibomian gland tissue with pleomorphic cellular changes, suggestive of metastasis. H&EX100, Bar 100µm.

The hematoxylin and eosin staining of these tissue sections that neoplastic cells originated from the meibomian glandular tissue of eyelids having neoplastic differentiation. They were surrounded by irregular islands of round to oval-shaped basophilic cells with; further subdivided by thin fibrovascular connective tissue trabeculae. Multiple foci revealed the cells having typical intracytoplasmic lipid vacuoles in different amounts; indicating the varying degrees of ongoing cytoplasmic lipidization process within these tumor cells. Cellular nuclei were large, hyperchromatic with prominent and dark stained nucleoli, exhibiting a moderate degree of pleomorphism. The normal structure of sebaceous glands was seen in a single focus of the microscopic field. Multiple mitotic figures observed in other high-power fields in each specimen submitted were indicative of malignancy. Interstitial presence of basaloid epithelial cells with large ovoid nuclei, whose proliferative phase was evident due to the associated basophilia and hyperchromasia. Some areas had acinar lumens lined by spindle-shaped cells with eosinophilic deposits; instead of normal vertically arranged holocrine acini. Few areas of dermal infiltration by inflammatory cells like lymphocytes and macrophages were observed along with hyper melanosis in the basal layer. Additionally, (Figure 1: E) the conjunctival epithelial layers exhibited areas of congestion, degeneration, and necrosis as a result of diffuse infiltration of inflammatory cells. Metastasis was confirmed in the conjunctival section following the observation of meibomian gland tissue clusters in association with basophilia and hyperchromasia.

Immunohistochemical investigations was performed for identification of malignant nature of neoplastic cells using CK as tumor marker. Immunohistochemical staining for cytokeratin yielded a strong positive reaction in the neoplastic tissue masses indicated proliferative cells in the meibomian glandular tissue of eye (Figure 3).

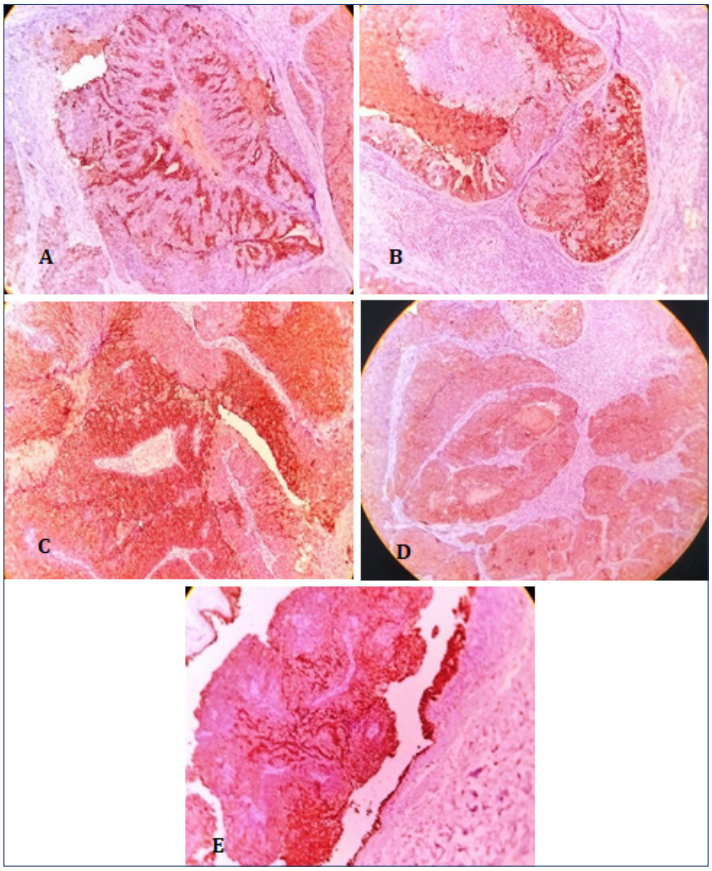

Figure 3: IHC for CK: Note positive expression of CK marker for neoplastic endothelial cells as brownish pigment. ×100 (Immunohistochemistry was performed on 4-µ sections for Cytokeratin markers (CK) using routine IHC protocol as suggested by the manufacturer (Dako-Agilent, Denmark)).

The observed microscopic lesions by histopathoogy and immuohistochemistry of the tumor masses were suggestive of malignancy and the tumor was diagnosed as Meibomian gland Adenocarcinoma.

DISCUSSION

The meibomian glands, also called tarsal glands are located in the tarsus portion near eyelid margins; which are responsible for the production of lipid-based secretion 'meibum' through its ductal openings, that form an oily layer over the preocular tear film above the cornea [21] (Gelatt et al., 2021). These glands can be described as holocrine acinar, modified sebaceous glands found in most mammals including domestic and non-domestic felids [21,22] (Gelatt et al., 2021, Maggs et al., 2008). This explains why some authors prefer to use the term Sebaceous glands while referring to Meibomian glands [23] (Shields et al., 2005). The ductal openings of these sebaceous glands (meibomian glands) are lined by keratinized stratified squamous epithelial cells. The number of these glands vary, and family Felidae has been known to have these glands more developed in the upper eyelids, hence rendering them more susceptible to neoplastic alternations [21,22] (Gelatt et al., 2021, Maggs et al., 2008).

The neoplastic cases documented in Indian leopard (*Panthera pardus*) includes squamous cell carcinoma, mammary gland adenoma, thyroid carcinoma, skin lipoma, uterine leiomyoma, malignant reproductive tract tumors, and benign gastric neuroendocrine tumor [3-10](Quintard et al., 2017, Kesdangsakonwut et al., 2014, Nakamura et al., 2018, [3-5]., 2014, Baquir et al., 2014, Dobson et al., 2013, Willott et al., 2005, Kloft et al., 2019). However, there exists no evidence or report of meibomian gland carcinoma in leopards, with regards to which a comparative study is conducted based extensively on the features of sebaceous adenocarcinoma (meibomian adenocarcinoma) cases reported in domestic cats and dogs, as well as few other wild animals.

Adenomas, epitheliomas, and other benign tumors of primary origin from eyelids are common in dogs, occasional in cats, and rarely observed in any other non-domestic species [17,24] (Crispin, 2005, Conceicao et al., 2010). From June 1999 to June 2008, a ten-year retrospective study was conducted at the University of Tennessee in 43 domestic cats; which eventually identified squamous cell carcinoma, mast cell tumor, hemangiosarcoma, adenocarcinoma, peripheral nerve sheath tumor, lymphoma, apocrine histiocytoma, and hemangioma as most prevalent eyelid tumors contributing to almost 30% of all eyelid tumors in cats [25] (Newkirk and Rohrbach, 2009). Furthermore, another eight-year study was conducted in 1986, in a population of 200 dogs, to estimate various types of palpebral tumor cases. The study concluded that 88% of the dogs under evaluation revealed incidences of benign neoplasms like sebaceous gland adenomas, melanomas, and papillomas; on the other hand, malignant neoplasms accounted for only 12% in form of melanoma, adenocarcinoma, basal cell carcinoma, mast cell tumor, squamous cell carcinoma, hemangiosarcoma, and myoblastoma [26] (Roberts et al., 1986). This was consistent with another research of the year 2007, suggesting that neoplastic developments in geriatric canines are usually benign; whereas those observed in geriatric felines are malignant [18] (Aquino, 2007).

Sebaceous gland tumors originate from the modified sebaceous glands, that is meibomian glands of the eyelid; nearly contribute to 6.8% to 7.9% and 2.3% to 4.4% of all the skin tumors in dogs and cats, respectively; thus, indicating its rarity in the feline counterparts [14,16] (Scott and Anderson, 1990, Hauck et al., 2012). Sebaceous adenocarcinoma, also known as the Meibomian gland adenocarcinoma is a malignant adnexal tumor usually seen on the head, neck, or perineum as local infiltration in form of gross cauliflower-like masses [27] (Goldschmidt and Hendrick, 2002). These are locally invasive and grow aggressively. The reports of distant metastases are infrequent but if present, then it occurs via lymphatic routes; quite often associated with ulcerated and inflamed gross lesions [16] (Hauck et al., 2012). The histomorphologic location of this carcinoma when traced back to meibomian glands is the primary factor for its identification. Histopathologically, the tumors of meibomian (sebaceous) gland origin share common morphological features depending on the extent of glandular cell differentiation and pleomorphism; based on which they can be identified as a meibomian adenoma (well-differentiated sebocytes with mild mitotic activity) to meibomian adenocarcinomas (multilobulated masses with anaplasia and a high degree of mitotic activity) [27,28] (Goldschmidt and Hendrick, 2002, Gross et al., 2015). This tumor is predominantly associated with old cats and dogs without any proof of sex predilection [13,14] (Stanley, 2016, Scott and Anderson, 1990).

In our case, as presented above, the grossly proliferative

cauliflower-like, bright pink to red-tinged mass near the eyelid margin was distinctly demarcated from surrounding normal tissue. Such masses near the eyelid margin are commonly associated with alternations of eyelid functions; thus, leading to secondary ocular complications like epiphora, conjunctivitis, blepharospasms, corneal irritation, and ulceration. Microscopic evaluation of hematoxylin & eosin stained sections revealed irregular islands of neoplastic cells from meibomian glands with the presence of typical basaloid cells, anisocytosis and pleomorphic nuclei associated with hyperchromasia, intracytoplasmic lipid vacuoles, sebocytic differentiation, and proliferative changes following the inflammatory cellular infiltration [27,28] (Goldschmidt and Hendrick, 2002, Gross et al., 2015); essentially led to the confirmatory diagnosis of meibomian gland adenocarcinoma of the eyelid in this leopard under study. The findings of our case were consistent with those described in sebaceous and meibomian gland adenocarcinomas of dogs and cats.

Sebaceous adenocarcinoma has also been confirmed and reported in submandibular salivary glands [29] (Sozmen et al., 2002) and external auditory canal [30] (Kapakin and Hazirogul, 2008) of domestic felids. Two cases reports were evaluated describing the gross and microscopic lesions of this malignancy in cattle; one in form of perineal gland carcinoma in the perineum and vulva of a Friesian cow [31] (Matovelo et al., 2005) and another identifier as meibomian carcinoma of an eyelid in a Simmental cow [32] (Gokhan et al., 2010). A unique case of concurrent sebaceous carcinoma was also diagnosed in an African hedgehog with primary fibrosarcoma of the foot [33] (Heatley et al., 2005). This tumor has to be differentially diagnosed from liposarcoma due to the involvement of cytoplasmic lipid vacuoles and sebaceous hyperplasia may be seen as an initial microscopic lesion, precursor to its development into the malignant variant [16] (Hauck et al., 2012).

Due to the lack of additional data or research on sebaceous carcinoma in wild animals and non-domestic felids, an exact etiological factor of this neoplasm continues to be unknown. Surgical excision of well-formed tumor mass is the treatment of choice in this case, yet this treatment alone is limited by increased recurrence for locally invasive tumors. However, if the excision is performed completely, adenocarcinoma resections have a good prognosis [26] (Roberts et al., 1986). Grafting procedures may be done post-excision, for such eyelid neoplastic masses to ensure the integrity of eyelid margins and retain its normal physiological function [34] (Stades and Gellat, 2008). Local radiation therapy warrants a limited success rate ought to the higher risks associated with irreversible damage to delicate ocular structures; except in cases of enucleation or exenteration [22] (Maggs et al., 2008). The major constraint lies in limited knowledge available on chemotherapy and radiosensitivity of the neoplastic cells [12] (Morris et al., 2001). Other advanced treatments available in ophthalmic surgeries for neoplasia in human and domestic animals include the use of systemic drug combinations for chemotherapy or cryosurgery [18,34,35] (Aquino, 2007, Joshi et al., 2012, Stades and Gelatt, 2008). Promising results have been observed with the use of the latest innovative intralesional therapy by administration of bevacizumab in combination with surgical excision of sebaceous adenocarcinoma in Amur tiger (*Panthera tigris altaica*) attributed to its antiangiogenic properties that inhibit vascular endothelial growth factor (VEGF) [36] (Edelmann et al., 2013). Similar successful attempts have been recorded in neoplasia treatment of Southern white rhinoceros (*Ceratotherium simum simum*) and Pacific walrus (*Odobenus rosmarus divergens*) [37] (Hanley et al., 2008) with bevacizumab. Topical use of antineoplastic drugs like mitomycin C for superficial carcinomas has also been reported [38] (Shields et al., 2002).

CONCLUSION

The present case is a pioneering and unique report of meibomian gland adenocarcinoma in a 21-year-old geriatric Indian leopard (*Panthera pardus fusca*) at Manikdoh Leopard Rescue Centre, Junnar, and Maharashtra. The aim of designing this literature is to contribute all features of this malignancy to the scientific and wildlife community. Surgical removal of the masses from the eyelid margin, third eyelid, and conjunctiva with a simple wedge resection of the eyelid was the treatment of choice in this case. The recovery and healing were unremarkable without any post-operative complications. Exploring other treatment options was practically not possible about the lack of necessary amenities and considering the temperament as well as the age of the animal under treatment.

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REFERENCES

1. Owston MA, Ramsay EC, and Rotstein DS. (2008). Neoplasia in felids at the Knoxville Zoological Gardens, 1979–2003. J Zoo Wildl Med. 39(4): 608-613.
2. Lombard LS and Witte EJ. (1959). Frequency and types of tumors in mammals and birds of the Philadelphia Zoological Garden. Cancer Res. 19(2): 127-141.
3. Quintard B, Greun EM, Lefaux B, Lemberger K, and Leclerc A. (2017). Squamous cell carcinoma in two snow leopards (uncia uncia) with unusual auricular presentation. J Zoo Wildl Med. 48(2): 578-580.
4. Kesdangsakonwut S, Sanannu S, Rungsipipat A, and Banlunara W. (2014). Well-differentiated squamous cell carcinoma in a captive clouded leopard (Neofelis nebulosa). The Thai Journal of Veterinary Medicine. 44(1): 153.
5. Nakamura M, Yoshida T, Eguchi A, Inohana M, Nagahara R, et al. (2018). Intermediate-grade mammary gland adenocarcinoma in an 18-year-old female black leopard (Panthera pardus) with acute pancreatic necrosis and chronic interstitial nephropathy. J Vet Med Sci. 80(2): 337-340.
6. Malmlov A, Campbell T, Monnet E, Miller C and Miceli B. (2014). Diagnosis, surgical treatment, recovery, and eventual necropsy of a leopard (Panthera pardus) with thyroid carcinoma. Case Reports in Veterinary Medicine. 2:1-5
7. Baqir S, Al Azri H, Al Rasbi K, Mastromonaco G, and Gartley C. (2014). Skin lipoma in an Arabian leopard (Panthera paradus nimr). Acta Scientiae Veterinariae. 42: 1-6.
8. Dobson EC, Naydan DK, Raphael BL, and McAloose D. (2013). Benign gastric neuroendocrine tumors in three snow leopards (Panthera uncia). J Zoo Wildl Med. 44(2): 441-446
9. Siegal-Willott JL, Henrikson T, Carpenter JW, and Andrews GA. (2005). Chronic obstipation in a leopard (Panthera pardus) caused by intrapelvic uterine leiomyoma compression of the distal colon. J Zoo Wildl Med. 36(3): 534-537.
10. Kloft, HM, Ramsay EC, and Sula MM. (2019). Neoplasia in captive Panthera species. J Comp Pathol. 166: 35-44
11. Moresco A, Muñoz KE, Gutiérrez F, Arias-Bernal L, and Yarto-Jaramillo. (2020). Taxonomic Distribution of Neoplasia Among Non-Domestic Felid Species Under Managed Care. Animals (Basel). 10(12): 2376
12. Morris J, and Dobson JM. (2001). Small animal oncology (Vol. 567). Oxford: Blackwell science.
13. Stanley R. (2016). BSAVA manual of canine and feline ophthalmology, 3rd edn. Edited by D Gould and G McLellan. BSAVA, UK, 2014. 350 pages. ISBN: 9781905319428. 94(3):80-80.
14. Scott DW and Anderson WI. (1990). Canine sebaceous gland tumors: a retrospective analysis of 172 cases. Canine practice. 15(1): 19-27.
15. Vail DM and Withrow SJ. (2007). Tumors of the skin and subcutaneous tissues. Small Animal Clinical Oncology. 4a ed. Saunders. United States. 375-401.
16. Hauck ML, Withrow S J, and Vail DM. (2012). Tumors of the skin and subcutaneous tissues. Withrow & MacEwen's small animal clinical oncology. 375-401.
17. Crispin Sheila M. (2005). Notes on veterinary ophthalmology.
18. Aquino SM. (2007). Management of eyelid neoplasms in the dog and cat. Clin Tech Small Anim Pract. 22(2): 46-54.
19. Stella J, Croney C, and Buffington T. (2013). Effects of stressors on the behavior and physiology of domestic cats. Appl Anim Behav Sci. 143(2-4): 157-163.
20. Davis AK, Maney DL, and Maerz, JC. (2008). The use of leukocyte profiles to measure stress in vertebrates: a review for ecologists. Functional Ecology. 22(5): 760-772.
21. Gelatt KN, Ben-Shlomo G, Gilger BC, Hendrix DV and Kern TJ. (Eds.). (2021). Veterinary ophthalmology. John Wiley & Sons.
22. Maggs D, Miller P and Ofri R. (2017). Slatter's Fundamentals of Veterinary Ophthalmology E-Book. Elsevier Health Sciences.

23. Shields JA, Demirci H, Marr BP, Eagle JrRC and Shields CL. (2005). Sebaceous carcinoma of the ocular region: a review. Surv Ophthalmol. 50(2): 103-122.

24. Conceição LFD, Ribeiro AP, Piso DYT and Laus JL. (2010). Considerations about ocular neoplasia of dogs and cats. Ciência Rural. 40(10): 2235-2242.

25. Newkirk KM and Rohrbach BW. (2009). A retrospective study of eyelid tumors from 43 cats. Vet Pathol. 46(5): 916-927.

26. Roberts SM, Severin GA, and Lavach JD. (1986). Prevalence and treatment of palpebral neoplasms in the dog: 200 cases (1975-1983). J Am Vet Med Assoc. 189(10): 1355-1359.

27. Goldschmidt MH and MJ Hendrick (2002). Tumors of the skin and soft tissues. Tumors in domestic animals. 45-117.

28. Gross TL, Ihrke PJ, Walder EJ and Affolter VK. (2008). Skin diseases of the dog and cat: clinical and histopathologic diagnosis. John Wiley & Sons.

29. Sozmen M, Brown PJ and Eveson JW. (2002). Sebaceous carcinoma of the salivary gland in a cat. J Vet Med A Physiol Pathol Clin Med. 49(8): 425-427.

30. Kapakin KA, Bozkurt F, and Haziroğlu R. (2008). Sebaceous adenocarcinoma in a cat. Acta Veterinaria Brno. 77(1): 123-125.

31. Matovelo JA, Malago JJ and Maselle RM. (2005). Gross and microscopic pathological findings in a sebaceous gland carcinoma of the perineum and vulva in a Friesian cow. Vet Rec. 156(19):612-613

32. Gokhan N, Sozmen M, Ozba B and Gungor E. (2010). CASE REPORT: Meibomian carcinoma of the eyelid in a Simmental cow. Veterinary ophthalmology. 13(5): 336-338.

33. Heatley JJ, Mauldin GE and Cho DY. (2005, July). A review of neoplasia in the captive African hedgehog (Atelerix albiventris). In Seminars in Avian and Exotic Pet Medicine. 14(3): 182-192

34. Stades FC and Gelatt KN. (2008). Diseases and surgery of the canine eyelid. Essentials of Veterinary Ophthalmology. 53

35. Joshi P, Joshi A, Norohna V, Prabhash K and Kane S (2012). Sebaceous carcinoma and systemic chemotherapy. Indian J Med Paediatr Oncol. 33(4): 239-241.

36. Edelmann ML, Utter ML, Klein LV and Wotman KL. (2013). Combined excision and intralesional bevacizumab for sebaceous carcinoma of the eyelid in an Amur tiger (Panthera tigris altaica). Vet Ophthalmol. 16(3): 219-224.

37. Hanley CS, Rosenthal JG, Shellabarger WC, et al. (2008). A new application for endothelial inhibitors: intralesional therapy. In Proceedings of American Association of Zoo Veterinarians. Los Angeles, California, USA.

38. Shields CL, Naseripour M, Shields JA and Eagle Jr RC. (2002). Topical mitomycin-C for pagetoid invasion of the conjunctiva by eyelid sebaceous gland carcinoma. Ophthalmology. 109(11): 2129-2133.