

Clinical and Histopathological Evaluation of Bovine Ocular and Periocular Neoplasms in 15 Cases in Sanliurfa Region

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Summary

The present study was conducted to evaluate the clinical and histopathological characteristics of bovine ocular and periocular neoplasms and the results of the therapeutic procedures. The study materials were 15 cattle with ocular-periocular neoplasms, which were housed at modern farm premises or family holdings and either referred to the surgery clinic or treated on-site, between 2008-2011. Treatment was performed by local tumour extirpation in 5 cases and ocular extirpation in 10 cases. In the post operative period, routine controls and wound care were performed on a weekly basis for a one month period in all of the cases. Furthermore, efforts were made to obtain information from the animal owner up to the 6th month post-operation. Based on the histopathological examination of the extirpated neoplastic tissues, 11 of the cases (73%) were diagnosed with ocular squamous cell carcinoma, whilst 1 case (7%) each was diagnosed with trichoepithelioma, solid apocrine ductal carcinoma, apocrine carcinoma, and fibrosarcoma. Until the 6th month post-operation no finding that would suggest the recurrence or possible metastasis of the neoplasms has been observed. In one of the cases, swelling of the parotid lymph node, which lasted for one month, was encountered, whilst another case presented with orbital infection that responded to treatment. During the follow-up period, it was observed that, the therapeutic procedures succeeded in all 15 cases, and decreased milk yields and weight loss improved to a large extent. In conclusion, local tumour extirpation and total extirpation of the eye performed for the treatment of various neoplasms that occur in ocular and periocular tissues are readily applicable and inexpensive methods with low complication risk. Furthermore, these methods are considered feasible as they maintain the economic life of animals and minimize economic losses through the relief of chronic pain.

Keywords: Bovine, Ocular neoplasm

Şanlıurfa Yöresinde Sığır Oküler ve Perioküler Tümörlerinin Klinik ve Histopatolojik Olarak Değerlendirilmesi: 15 Olgu

Özet

Sunulan çalışmada; sığırlarda tespit edilen göz tümörlerinin klinik ve histopatolojik karakterleri ile uygulanan sağaltım sonuçlarının değerlendirilmesi amaçlandı. Çalışmanın materyalini cerrahi kliniğine 2008-2011 yılları arasında getirilen veya mahallinde müdahalesi yapılan, modern çiftlik ya da ev ahırlarında barındırılan oküler-perioküler tümörlü 15 sığır oluşturdu. Tedavi amacıyla, 5 vakada lokal tümör ekstirpasyonu, 10 olguda göz ekstirpasyonu uygulandı. Post operatif dönemde tüm vakaların, bir ay süreyle haftalık kontrolleri ve yara bakımları yapıldı. Post operatif, ortalama 6. aya kadar telefonla hasta sahibinden bilgi alınmaya çalışıldı. Uzaklaştırılan 15 tümöral kitlenin histopatolojik muayeneleri sonucunda; 11 (%73)'inin yassı hücreli göz kanseri, 1 (%7)'inin trikoepitelyom, 1 (%7)'inin solid tip apokrin duktal karsinom, 1 (%7)'inin apokrin karsinom ve 1 (%7)'inin de fibrosarkom olduğu tespit edildi. Post operatif 6. aya kadar tümörlerin nüks etmesi veya muhtemel bir metastaz ile ilgili net bir bulguya rastlanılmadı. Bir vakada bir ay süren parotit lenf bezi şişkinliği ve 1 vakada tedaviye cevap veren orbital enfeksiyon gözlemlendi. Belirtilen takip süresi içerisinde, uygulanan tedavilerin 15 vakada başarılı olduğu, önceden belirtilen süt ve kilo kaybının da büyük oranda düzeldiği gözlemlendi. Sonuç olarak; sığırların oküler-perioküler dokularında oluşan değişik karakterdeki tümörlerinde uygulanan lokal tümör rezeksiyonu veya total göz ekstirpasyonu gibi tedavilerin, kolay uygulanabilir, az komplikasyon riskli ve düşük maliyetli olduğu söylenebilir. Aynı zamanda, kronik ağrıyı ortadan kaldırması sonucu, hayvanların ekonomik ömrünün uzaması ve dolayısıyla ekonomik kayıpların minimize edilmesi nedeniyle uygun bir yöntem olabileceği düşüncesine varıldı.

Anahtar sözcükler: Sığır, Göz tümörü



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INTRODUCTION

Ocular and periocular neoplasms, which cause major economic losses, are frequently encountered in the Veterinary profession. These tumours display species-dependent differences, which affect the biological behaviour and prognosis of the neoplasms. In cases, where ocular and periocular tissues are the primary target of the tumour, primary ocular and periocular neoplasms are encountered, whilst in cases, where these tissues are the target of metastatic diseases, secondary ocular and periocular neoplasms are encountered. Furthermore, orbital invasions of tumours originating from the nose and sinuses may also be observed. Ocular and periocular neoplasms may involve the orbit, eyelids, conjunctiva, cornea and intraocular tissues¹⁻⁴.

Ocular and periocular neoplasms have been reported in several farm animals, the most in cattle^{2,5-11}. Previously reported bovine ocular and periocular neoplasms include lymphosarcoma (secondary intraocular tumour)¹², haemangio-endothelioma, adenoma of the Meibomian and Moll's glands, fibrosarcoma¹³, papilloma, melanoma and ocular squamous cell carcinoma (OSCC), the latter being the most common^{3,6,8,9,11,14}. The present study was conducted to evaluate clinical and histopathological characteristics of bovine ocular and periocular neoplasms and the results of the therapeutic procedures.

MATERIAL and METHODS

Fifteen cattle, housed at modern farm premises and family holdings in Sanliurfa province and its vicinity (38° 47' E, 37° 9' N; altitude 547 m), which were either referred to the Surgery Clinics of Faculty of Veterinary Medicine Harran University, between the years 2008 and 2011 or treated on-site, constituted the material of the study (Table 1).

The anamnesis of the cases revealed the presence of red or pink-coloured abnormal ocular masses and swellings persisting on average for 2-12 months, which emerged as slightly protuberant lesions and displayed progressive enlargement over time, associated with lacrimation of varying character, decreased milk yield and weight loss.

Physical and ocular examinations suggested that these abnormal tissue proliferations could be neoplastic (Fig 1-A/B/C), tentative local tumour extirpation (at a peripheral distance of 3-4 mm to the lesion) without obtaining pre-operative biopsy specimen was performed in 5 cases, 1 of which was associated with blepharoplasty of the lower eyelid, such that the eye ball was not harmed and vision was maintained, whilst total extirpation of the eye (exenteration) was performed in the remaining 10 cases (Table 1). All surgical operations were performed in compliance with previously described standard surgical

procedures^{6,15,16} under combination of sedation and local anaesthesia, such that an electrocauter was used when required and the animals were maintained in lateral recumbent position. During the post operative period, in all cases, routine check and wound care were performed on a weekly basis for one month. Furthermore, efforts were made to obtain information from the animal owner up to the 6th month post-operation.

The masses extirpated by surgical intervention were sent to the pathology laboratory for histopathological examination. After fixing in 10% buffered formaldehyde solution, tissue samples were subjected to routine tissue processing and were embedded in paraffin blocks. Five-micron-thickness sections were cut from the blocks and stained with haematoxylin-eosin (H&E) and examined under a light microscope.

Descriptive statistics were used in the Minitab software for the analysis. Data were given in percentile rates (%).

RESULTS

The clinical and histopathological characteristics of the ocular and periocular neoplasms diagnosed in 15 cattle, the therapeutic procedures applied and the results of these procedures are summarized in Table 1. Of the bovine diagnosed with ocular and periocular neoplasms, 10 (67%) were of the Holstein breed, 3 (20%) Simmentals and 2 (13%) Simmental crosses; whilst 13 (87%) female and 2 (13%) male. The ages of the animals were determined as 4 years in 3 (20%), 5 years in 6 (40%), 6 years in 3 (20%), 7 years in 2 (13%) and 8 years in 1 (7%) of the cases. It was ascertained that the affected eyes were the right eye in 10 (67%) of the animals and the left eye in 5 (33%) of the animals.

In the post-operative period, neither during the weekly on-site controls performed until the 30th day nor during the 6-month follow-up period was any finding suggestive of either the recurrence or possible metastasis of the neoplasms encountered. Furthermore; eye examination using ophthalmoscope in locally extirpated 5 and totally extirpated, histopathologically examined 10 cases intra-ocular metastasis or any tumoral mass were not determined. However, case 3 presented with a parotid lymph node swelling that was detected on post-operative 15th day and lasted for a month, whilst case 5 suffered from an orbital infection that developed during the wound healing. The therapeutic procedures applied produced success in the follow-up period in all 15 cases, and it was observed that decreased milk yields and weight losses had improved to a large extent.

Based on histopathological examination, the animals were diagnosed with ocular squamous cell carcinoma in 11 (73%) cases (Fig 1-B), and with trichoepithelioma

Table 1. Signalement of the 15 cases constituting the study material, the clinical and histopathological characteristics of the tumours detected in these cases, the therapeutic procedures applied and their results (OSCC: ocular squamous cell carcinoma), Duration*: According to anamnesis (months). °: Vision was normal. -: Loss of vision
Tablo 1. Çalışma materyalini oluşturan 15 olgunun; eşkı, tümörlerin klinik ve histopatolojik karakterleri ile yapılan tedavi şekli ve sonuçları, OSCC: oküler skuamöz hücreli karsinoma, Duration*: Anamneze dayalı süredir (ay). °: Görüş normal. -: Görme kaybı

Case No	Breed, age (years), sex, perocular pigmentation status of animal	Tumour Location	Affected Eye and Vision Status		Duration* and Clinical Appearance of Neoplasm	Histopathological Diagnosis	Surgical Intervention	Postoperative Result (average follow up period 6 months)
			Right	Left				
1	Simmental, 5, ♀ Unpigmented	Lower eyelid and its conjunctiva	-°	+°	6, Haemorrhagic; Nodular	Trichoepithelioma	Local tumour extirpation, blepharoplasty of the lower eyelid	No recurrence, normal wound healing
2	Holstein, 6, ♀ Pigmented	Nictitating membrane (third eyelid)	+°	-°	8, Nodular	OSCC	Local tumour extirpation, partial resection of the nictitating membrane	No recurrence, normal wound healing
3	Holstein, 6, ♀ Pigmented	Upper and lower eyelids and upper and lower palpebral conjunctivae, entire bulbus oculi	+•	-°	12, Nodular with purulent discharge and accompanied by foul odour	OSCC	Total eye extirpation	No recurrence, normal wound healing, detection of swelling of the right parotid lymph node lasting 1 month, on the 15 th day post operation
4	Simmental, 7, ♀ Pigmented	Entire bulbus oculi	+•	-°	9, Nodular with purulent discharge and accompanied by foul odour	OSCC	Total eye extirpation	No recurrence, normal wound healing
5	Holstein, 6, ♀ Pigmented	Entire bulbus oculi and periocular tissues	+•	-°	12, Lobular with purulent discharge	Apocrine ductal carcinoma (solid type)	Total eye extirpation, resection of the periocular neoplastic tissue	No recurrence, opening of the sutures on the 10 th day post-operation due to orbital infection, normal wound healing 30 days after the revision of the wound
6	Holstein, 4, ♂ Pigmented	Entire bulbus oculi and periocular tissues	-°	+•	4, Lobular with purulent discharge and accompanied by foul odour	Apocrine carcinoma	Total eye extirpation	No recurrence, normal wound healing
7	Holstein, 5, ♀ Pigmented	Retrolbulbar	-°	+•	5, Exophthalmos	Fibrosarcoma	Total eye extirpation Deep orbital debridement	No recurrence, normal wound healing
8	Holstein, 5, ♀ Pigmented	Nictitating membrane	+°	-°	2, Nodular two plaques	OSCC	Local tumour extirpation	No recurrence, normal wound healing
9	Holstein, 7, ♀ Pigmented	Lower palpebral conjunctiva, nictitating membrane	+°	-°	5, Lobular with purulent discharge	OSCC	Local tumour extirpation	No recurrence, normal wound healing
10	Holstein, 5, ♀ Pigmented	Lower palpebral conjunctiva, nictitating membrane	-°	+°	6, Nodular with purulent discharge	OSCC	Local tumour extirpation	No recurrence, normal wound healing
11	Holstein, 5, ♀ Pigmented	Upper and lower palpebral conjunctivae, nictitating membrane	-°	+•	3, Lobular with purulent discharge, panophthalmia purulenta	OSCC	Total eye extirpation	No recurrence, normal wound healing
12	Simmental cross, 5, ♀ Pigmented	Entire bulbus oculi	+•	-°	8, Haemorrhagic	OSCC	Total eye extirpation	No recurrence, normal wound healing
13	Simmental, 4, ♂ Pigmented	Entire bulbus oculi	+•	-°	9, Panophthalmia purulenta, purulent discharge	OSCC	Total eye extirpation	No recurrence, normal wound healing
14	Holstein, 8, ♀ Pigmented	Cornea, limbus	+•	-°	5, Lobular with purulent discharge, panophthalmia purulenta	OSCC	Total eye extirpation	No recurrence, normal wound healing
15	Simmental cross, 4, ♀ Pigmented	Upper eyelid and bulbar conjunctiva	+•	-°	9, Lobular with purulent discharge	OSCC	Total eye extirpation	No recurrence, normal wound healing

(Fig. 1-A), solid apocrine ductal carcinoma (Fig. 1-C), apocrine carcinoma and fibrosarcoma, each in 1 case (7%) (Table 1). In general, the microscopic examination of these tumours demonstrated that, in the OSCC cases, ulcerous and inflammatory areas were scattered along the cut surface and in the dermis. The neoplastic masses were composed of concentric cell proliferations and tumour cells with eosinophilic cytoplasm encapsulated by stroma, containing cancer pearls in the centre. In the neoplastic areas, light microscopic examination at x400 magnification demonstrated the presence of 1-3 mitotic figures (Fig. 1-D). In the solid apocrine ductal carcinoma, the mass was composed of tubules surrounded by two or more epithelial layers, enclosed by an apparent stromal layer, with dark coloured eosinophilic secretion in the centre. Light microscopic examination at x400 magnification demonstrated the presence of 1-2 mitotic figures. In the apocrine carcinoma, the mass was composed of tubular structures comprising single or double epithelial layers enclosed by fibrous stroma. Under x400 magnification, 0-1 mitotic figures were observed in the neoplastic mass. In the trichoepithelioma, the dermis contained tumour islets, which were composed of basal cells of the hair follicle epithelium that were surrounded by connective tissue. In the fibrosarcoma, a great many pleomorphic fibroblasts and less dense fibrocyte proliferation were

observed between the collagen fibres. Light microscopic examination at x400 magnification demonstrated the presence of 1-2 mitotic figures in the neoplastic areas.

DISCUSSION

The diagnosis of OSCC in 11 out of 15 cases (73%) in the present study (Table 1) was in agreement with the high rates reported in previous studies^{14,17}. However, in a health screening conducted by Isler et al.¹⁸ for ocular diseases in 9967 cattle raised in Hatay province and its vicinity, although 1012 cattle were diagnosed with 14 different ocular diseases, ocular or periocular neoplasms were detected in neither of the animals. The etiology of OSCC, which originates from the eyelids, bulbar conjunctiva and orbital bone, remains unclear. The localization site of OSCC in several animal species, including primarily cattle and horses, is the ocular organs such as the orbit, eyelids, conjunctiva and limbus (border between the cornea and sclera). OSCC emerges as a neoplasm of benign character, which later progresses into a neoplasm of malign character. Initial plaque-like proliferations evolve into papillomas. Following the *in situ* stage, the carcinoma acquires an invasive character. OSCC leads to necrosis, haemorrhages and ulcerations in the tissues where it is located, resulting in production losses (milk, meat, fertility),



Fig 1. **A-** Clinical appearance of the left eye of case 1 diagnosed with trichoepithelioma, **B-** Clinical appearance of the right eye of case 3 diagnosed with OSCC, **C-** Clinical appearance of the right eye of case 5 diagnosed with apocrine ductal carcinoma (solid type), **D-** Histopathological view of the same case in Fig 1-B, note the specific cancer pearl (arrows), (H&E x400)

Şekil 1. **A-** Çalışmanın 1. olgusunu oluşturan trikoepitelyomalı ineğin sol gözünün klinik görünümü. **B-** Çalışmanın 3. olgusunu oluşturan OSCC'li ineğin sağ gözünün klinik görünümü, **C-** Çalışmanın 5. olgusunu oluşturan apokrin duktal karsinomlu ineğin sağ gözünün klinik görünümü, **D-** Şekil 1-B'deki olgu 3'ün histopatolojik kesitinde spesifik kanser incisinin görünümü (oklar), (H&E x400)

increased costs due to treatment, and economic losses arising from the condemnation and destruction of the carcasses of affected animals at slaughterhouses^{1,8,14,15,19}. In the present study, anamnesis and clinical examination revealed the occurrence of similar economic losses and it was determined that the treatment applied reduced these losses to a large extent.

Predisposing factors reported for OSCC^{2,3,11,15,19}, include high altitude, geographical proximity to the equator, high mean temperatures, exposure to intense solar radiation due to prolonged grazing under the sun, prolonged grazing in dusty and dry atmosphere, all exist in the Sanliurfa province, from which the study material originated. Moreover, the Sanliurfa province ranks first among other provinces with a mean daily sunlight period of 8.3 hours, and the average annual number of sunny day is 327^{20,21}.

It has been reported that, when left untreated, OSCC metastasis primarily to the parotid lymph node and secondarily to the salivary glands, lungs, liver and kidneys²²; and occasionally invades the brain²³. In the present study, excluding the swelling of the right parotid gland (suspected of being a metastasis) in case 3, which emerged during the follow-up period but later disappeared (*Table 1*), no clear finding of metastasis was detected. However, in a study conducted in animals diagnosed with OSCC, Klein et al.²⁴ reported that, of the animals displaying swelling of the parotid lymph node (61%), 21% suffered from metastasis to the regional lymph nodes with 6 also having metastasis to the lungs. The metastasis and invasion of OSCC further causes economic losses resulting from the death and slaughter of animals, as well as the condemnation and destruction of tumour-bearing carcasses considered to be unfit for human consumption. Nevertheless, based on slaughterhouse data, it has been indicated that, when treated appropriately, the rate of metastasis could be reduced by 30%^{15,19}.

Several researchers^{1-3,13,25,26}, have reported orbital neoplasms invading the retrobulbar cavity, such as lymphosarcoma and fibrosarcoma, among the causes of unilateral exophthalmos in cattle. In the present study, case 7 displayed unilateral exophthalmos. A retrobulbar mass was suspected upon resistance to the pushing of the eye ball. Operative and histopathological procedures proved the mass to be fibrosarcoma.

The ocular and periocular neoplasms detected in the present study display a distributional pattern similar to that reported in previous literature^{3,5,14,15,27,28}, in terms of breed, sex, age, affected eye, and location of the tumour.

In recent years, it has been recommended that OSCC and other ocular and periocular neoplasms could be treated by surgical extirpation, cryotherapy, hyperthermia, immunotherapy, chemotherapy and radiotherapy or by the combination of these methods^{5,15,28}. However, these

techniques are relatively complicated, require the use of specific equipment and the achievement of success depends on the clinical experience of the practitioner. In a study conducted in 17 cattle, Hirsbrunner et al.²⁹ reported bulbar extirpation to be adequate for the treatment of OSCC. In the present study, small, localized neoplasms with no effect on the bulbus oculi and no loss of vision were treated by local surgical extirpation, whilst large and invasive neoplasms resulting in loss of vision were treated by extirpation/exenteration, thus, the bulbus oculi and all other ocular anatomical structures were removed. The authors consider the therapeutic procedures applied to have produced successful outcome. In the present study, although no clear findings were determined in the post-operative 6-month follow-up period that would suggest recurrence of the tumours; some researchers^{30,31} reported that in cases with no swelling of the parotid lymph node, surgical extirpation produced a success rate of 90% as well as a recurrence rate of 37-45%. Furthermore, Schulz and Anderson¹⁷ reported a recurrence rate of 5%. On the other hand, in cases characterized by the invasion of the neoplasm to the orbital bone, sinuses, oral cavity and brain, Brown¹ do not recommend the performance of surgical extirpation due to unfavourable prognosis. In the present study, the neoplasms did not invade the regions indicated by Brown¹.

In conclusion; local extirpation and total bulbar extirpation for the treatment of various neoplasms that develop in bovine ocular and periocular tissues are applicable and inexpensive methods with low complication risk. These methods are also effective to relieve chronic pain, and may maintain the economic life of the animals and minimize economic losses.

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