



A Survey and Treatment of Ocular Carcinomas in Iraqi Dairy Cows from (1987- 2012)

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Abstract:

The purpose of this study was to survey and describe the Iraqi dairy cows population underwent eye enucleation, referring to possible complications that may be happened, the type and pathomorphological features of ocular neoplastic growths. During a study period of (25) years. A total of (12000), cows were examined. Of these 500 cows (4.17%) of different ages (3 to 12) years suffer from ocular tumors. Some of these cows were in various pregnancy stages. All animals under investigation were (local and cross breed) and from five dairy farms around Baghdad province. The majority of the cases 174 (34.8%) observed in Alrathwanya. The mostly affected age ranged between (7-8) years, the number reached 185 (37%). According to the seasons of the year, summer recorded the highest number of affections, 260 (52%). The Lesions were present in the right eye 256 cases (51.2%), in the left eye 244 cases (48.8%). There were significant differences between non-pregnant, 425 (85%) and pregnant cows, 75 (15%). Using standard procedures, the tumors were excised surgically under the effect of local anesthesia (lidocaine 2%) with or without sedation. The major surgical complications were hemorrhage in (7%) of the cases. Swelling of pre-orbital region were observed in (15%). Orbital infections were noticed in (3%) of the cases. Partial dehiscence of the suture line was happened in (4%) of the treatment cases. Two cases (0.04%), showed transitory serosanguineous or bloody unilateral nasal discharge. Four cases (0.08%) developed recurrent tumors. Only one pregnant cow was aborted. Two cows were culled, two years post-surgery. Finally two cows were died from causes not related to surgery. The removal lesions had a nodular or cauliflower-like appearance and were varied in size from a few centimeters (12 %) to several centimeters (88%). Over a quarter (25%) of tumor lesions were ulcerated and bled easily. Microscopical appearances showed (well differentiated squamous cell carcinoma), characterized by formation of keratin pearls appear as red onion-like structures surround by inflammatory cells infiltration. The neoplastic cells showed mitotic figures, some of these cells have nucleus with prominent nucleoli. In conclusion, eye enucleation will remain an inexpensive, safe and viable treatment option for ocular diseases, in addition it increase the longevity of the cows within the herd.

Key words: Ocular carcinomas, Enucleation, Cows.

احصاء وعلاج سرطانات عيون الابقار الحلوب العراقية من (1987-2012)

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الخلاصة:

هدفت الدراسة الى احصاء ووصف اعداد الابقار الحلوب العراقية التي خضعت لاستئصال العين والتطرق للمضاعفات وتحديد نوع الورم السرطاني (عيانيا ومرصيا). تم فحص 12000 بقرة خلال (25) سنة حيث اظهرت 500 بقرة تراوحت اعمارها بين 3-12 سنة اصابات بسرطان العين وشكلت نسبة (4.17%) وكان قسما منها حوامل في مراحل حمل مختلفة. الحيوانات المفحوصة كانت محلية ومضرته متواجدة في خمس حقول في مناطق محيطه ببغداد. لوحظت اغلب الحالات المصابة 174 (34.8%) في منطقة الرضوانية. اما بالنسبة للعمر فقد مثلت الابقار ذات الأعمار 7-8 سنة اعلى اصابه 185 حالة (37%) وخاصة في فصل الصيف 260 (52%). كانت اصابة العين اليمنى 256 حاله بنسبة (51.2%) واليسرى 244 حالة بنسبة (48.8%). لوحظ فرق معنوي بين الابقار غير الحوامل 425 (85%) والحوامل 75 (15%). تمت ازالة الورم بالاسلوب الجراحي وتحت تأثير المخدر الموضعي مع او بدون مهدأ. حدثت بعض المضاعفات الثانوية مثل نزف موضعي في (7%) من الحالات و تورم اعلى العين (15%). وخمج كرة العين في (3%) وفتح قسما من غرز الاجفان في (4%) وظهرت حالتان خروج سوائل من الانف من جهة واحدة واربع حالات (0.08%). سجلت عودة الورم السرطاني واجهضت احد الابقار وتم نبذ حيوانين بعد مضي سنتين من اجراء العملية واخيرا نفقت بقرتين لاسباب لا تعود للجراحة. كان الورم المزال شبيه بالقرنبيط واختلف في حجمه من بضعة سنتيمترات (12%) الى عدة سنتيمترات (88%). كان حوالي (25%) من الأورام السرطانية متقرح وينزف بسهولة. اظهر الفحص المجهرى بأن الورم داخل العين هو من النوع الحارشي وتميز بتكوين عدة طبقات حمراء من الكرياتين الشبيه بالبصل محاطه بخلايا التهابية. لوحظ انقسامات خيطيه في الخلايا السرطانية حيث احتوت النواة على نويه واحده او اكثر. يمكن الاستنتاج بأن عملية استئصال العين هي تقنيته امينه واقتصاديته وتعد علاج حيوي لأغلب امراض العين بالإضافة الى انها تزيد من عمر البقرة ضمن القطيع.

Introduction:

Bovine ocular squamous cell carcinoma is more commonly referred to in the cattle industry as "cancer eye" (1) as well as the most frequently diagnosed ocular tumor in the bovine (2). It is less frequent in sheep, goat, horses, dogs and cat (3, 4). This disease is of extreme economic importance to the cattle producer as it accounts for nearly (12%) of carcass condemnation. The etiology of the disease is multifactorial. There is a predisposition towards cattle with non-pigmented eyelids and conjunctiva (white faced cattle). Prolonged exposure to sunlight (ultraviolet light) also seems to be a driving force for the disease (5). The tumors generally develop in cattle over the age of seven years and rarely in cattle less than three years. Indications for eye enucleation include chronic panophthalmitis, chronic glaucoma, intraocular neoplasms and trauma of the eyeball leading to irreversible damage of the eye and intra-ocular contents (6).

Enucleation involves the removal of the eye with para-orbital structures. This type of enucleation is typically referred to as extirpation or exenteration of the eyeball, and this technique would be associated with few post-operative complications such as bleeding, infection and recurrence of the tumor (7, 8). The purposes of this study was to survey and describe the Iraqi cows population underwent enucleation, complications, the type and pathomorphological features of ocular neoplastic growths in cows.

Materials and Methods:

1- Animals:

During a study period of (25) years extending from April 1987 to April 2012. A total of (12000) cows were examined. Of these 500 cows (4.17%) of different ages and weights suffer from ocular squamous carcinomas (figures 1,2). Some cows were in various pregnancy stages. All

animals under investigation were (local and cross breed) and from five dairy farms around Baghdad. Animal age, clinical signs and symptoms, climatic conditions, breeds, pregnancy status and any changes related to the tumors were recorded. Using standard procedures the tumors were

excised surgically under the effect of local anesthesia with or without sedation. Then examined grossly and microscopically. The following tables (1 to 5) show's the informations about the cows suferred of ocular tumor.

Table: 1- Number of the affected cows according to the areas around Baghdad.

Areas	No. of animals
Alrathwanya	174
Alyousfyia	102
Abograb	95
Almahmodya	73
Altajii	56
Total	500

Table: 2- Number of the affected cows according to the ages.

Age (year)	No. of animals
3-4	39
5-6	141
7- 8	185
9-10	113
11-12	22
Total	500

Table: 3- Number of the affected cows according to the seasons of the year.

N0. of animals	Summer	Autumn	Spring	Winter
500	260	94	77	69

Table: 4- Number of the affected cows according to their location in the eye.

No. of animals	Right eye	Left eye
500	256	244

Table: 5- Number of the affected cows according to pregnancy status.

No. of animals	Non-pregnant	Pregnant
500	425	75

2- Surgical Interventions: For treatment of ocular squamous cell carcinoma, eye extirpation (enculation) was performed as follows:

A- Pre-operative Considerations:

The animal was restrained in a squeeze crush with its head secured to one side with a halter. The para-ocular surgical sites were clipped and aseptically prepared.

B- Anesthesia:

Sedation were used in (60%) of the cows which included the administration of xylazine hydrochloride 2% at a dose rate of 0.05mg/kg., B.W. injected IM in the thigh muscles. To desensitize the eye, local anesthesia with 2% lidocaine hydrochloride was used. In (60%) of the cases, anesthesia was accomplished by

sub-cutaneous infiltrating of the anesthetic drug around the intended line of the skin incision in the upper and lower eyelids (5ml/lid). Also Peterson's technique was used to block the five nerves that supply the eye (10-15ml) of local anesthetic. In (40%) of the cases, local anaesthesia was performed by four-points retrobulbar block. A slightly curved, 8-10cm; 20 gauge needle was inserted through the dorsal eyelid towards the apex of the orbit where the nerves emerge from the orbital foramen. This was repeated through the ventral eyelid and the medial and lateral canthi. About 10 ml of local anaesthetic was injected for each site. Approximately 40 ml of lidocaine was used in total. A successful block was indicated by exophthalmus, corneal anaesthesia and mydriasis (9).

C- Surgical Technique:

The eyelids were sutured together with simple continuous pattern by non-absorbable suture material (silk size 2) with the ends of the suture left long (to form loop like-appearance) to minimize contamination of the surgical field and help the surgeon during dissection. An incision was made through the skin of both upper and lower lids (5 - 10) mm from the lid margins. These incisions meet beyond the medial and lateral canthus. Care was taken not to damage the branches of the angular vein adjacent to the medial canthus. Then blunt dissection to separate the ocular muscles and other structures from the bony orbit, once this had been

achieved, curved hemostat was introduced to grasp the optic nerve. The eyeball was removed by introducing curved surgical scissor in front of the hemostat to cut it. Bleeding was carefully arrested either with hemostat if it is minor or via ligation of the bleeder with fine dissolvable suture material such (cat gut 3-0). In most cases bleeding was controlled by forceful packing of the orbit with swabs or gauze for a short time. Sterile gauze soaked in eye ointment (tetracycline) introduced to fill the orbital cavity and this was changed (2 to 3) times each 48 hours. The upper and lower eyelids were restitched by interrupted horizontal mattress pattern with non-absorbable suture. Broad spectrum antibiotic represented by penicillin 20,000 I.U., and streptomycin 10mg/kg B.W., injected IM for (5 to 7) consecutive days. The skin stitches were taken off in (10 to 14) days post-surgery, if secondary complications were not encountered.

D- Histopathological Examination:

The whole tumor mass was removed and examined grossly then cut into pieces and fixed in (10%) neutral buffer formalin. The tissue specimens were processed in a tissue processor, paraffin blocks were made; (5- 6) μ m thick sections were cut with a microtome and stained with Hematoxylin and Eosin dyes (10). Then stained slides were examined under light microscope.

3- Statistical Analysis: All data concerning the affected cows were expressed as a percent (%).



Figure: 1- Show's cow with ocular squamous cell carcinoma of the left eye.



Figure: 2- Show's cow with ocular squamous cell carcinoma of the right eye.

Results:

A- Clinical Findings:

Environmental conditions in the areas where the dairy farms are located are warm and dry in summer and autumn and relatively cold in winter. Fluctuation of temperature of this area is in the range of (0 to 50) degree centigrade. Mean daily sunlight period over the year is (9 to 14) hours. Approximately 500 (4.17%) cases out of 12000 cases, suffered from tumors that were located in the entire eyeball. The majority of the cases 174 (34.8%) observed in Alrathwanya when compared with the remaining areas. The mostly affected cows aged between (7-8)years, the number reached 185 (37%). In contrast younger ages reflected low rate of affections, 39 cases (7.8%). According to the seasons of the year, summer recorded the highest number of the cases 260 (52%), while winter cases were the lowest, 69 cases (13.8). Lesions were present on the right eye in 256 cases (51.2%), on the left eye in 244 cases (48.8%). There were significant differences between non-pregnant cows, 425 (85%) and pregnant cows, 75 (15%).

B- Post-surgical Complications:

The major surgical complication were hemorrhage into the orbit in (7%) of the cases obscuring the surgical field. This problem was anticipated and largely overcome by care in dissection within the orbit, avoiding trauma to intraorbital soft tissue and special attention to the ligation

or crushing of the optic nerve and Forceful packing of the orbit with gauze for a short time. Swelling of pre-orbital region were noticed in (15%), this problem was transient lasted for the first (2-3) days post-surgery and resolved without any treatment. Orbital infection was noticed in (3%) of the cases, 5- 8 days following surgery manifested by discharge from the skin suture line. It was treated by creating a drainage pathway by blunt probing of the orbit, irrigation with sterile normal saline 0.9% and evacuating the contents by massage. This was followed by curetting, removal of infected tissue and suture materials and finally sterile gauze soaked in tincture iodine 5% was introduced which changes when it is necessary. Partial dehiscence (opening of few stitches) of the suture line was happened in (4%) of the treatment cases. Affected cows were treated by suture removal, debridement, wound lavage and administration of systemic antibiotics in then resutured the skin. Two cases (0.04%) had noted transitory serosanguineous or bloody unilateral nasal discharge in week following enucleation, animals were restless and tilted their head toward the affected side, treatment was initiated with systemic antibiotic (penicillin-streptomycin) for five days, thus animal should be checked twice daily for 48 hours to detect any signs of sinusitis. There were only four cases (0.08%) developed

recurrent tumors (2-3) years after the initial surgery. These cows were culled from the herd without further treatment. Only one case which was pregnant in the eight month was aborted. The remaining (34) pregnant cows were raised a calf (1-7 month) following surgery. Two cases were culled, 2 years post-surgery due to reproductive failure and were sold. Finally two cases were died from causes not related to surgery. The first cow died due to black leg and the second due to dystocia. Most cattle were re-evaluated at the time of suture removal (10 to 14) days after surgical excision of the eye.

C-Macroscopical Findings:

Lesions were present in the right eye in 256 cases and in the left eye in 244 cases. Many lesions had a nodular or cauliflower-like appearance (figure 3), and were varied in size from a few centimeters (12 %) to several centimeters (88%). Over a quarter (25%) of tumor lesions were ulcerated and bled easily. When the eyelids were closed they caused increased lacrimation and sometimes discharge of pus and the cornea was opaque. Neoplastic tissue had invaded and destroyed the entire orbital contents, ocular adnexa, other soft tissue. In (5%) of the cases the surrounding bones were involved. Interestingly optic nerve among the multiple irregular

neoplastic tissues was intact, though it was slightly compressed with tumor mass.

D-Microscopical Findings:

Microscopical appearance of tumor mass of eye cows showed malignant neoplastic cells (well differentiated squamous cell carcinoma). The neoplastic cells consisting of elongated cords of stratum sponunusum layers of epidermis projecting toward the dermis and subcutaneous tissue with formation of corner pearls appears as red onion-like structures which consist of laminated keratin layer with inflammatory cells infiltration (figure 4). Vascular degeneration with connective tissue septa were noticed and the cancer cells contained large, rounded and pyknotic nucleus (figure 5). Large number of inflammatory cells mainly esonophils which have numerous spherical eosinophilic granules that fill the cells. Also there are many lymphocytes also present in the stroma of the tumour (figure 6). There were hypertrophy of the muscular layer of blood vessels with vascular degeneration of tunica intema and proliferation of endothelial cells toward the lumen (figure7). The neoplastic cells with mitotic figures, some of these cells contained nucleus with prominent nucleoli (figure 8).



Figure- (3). The macroscopical apperances of the excisional ocular tumor.

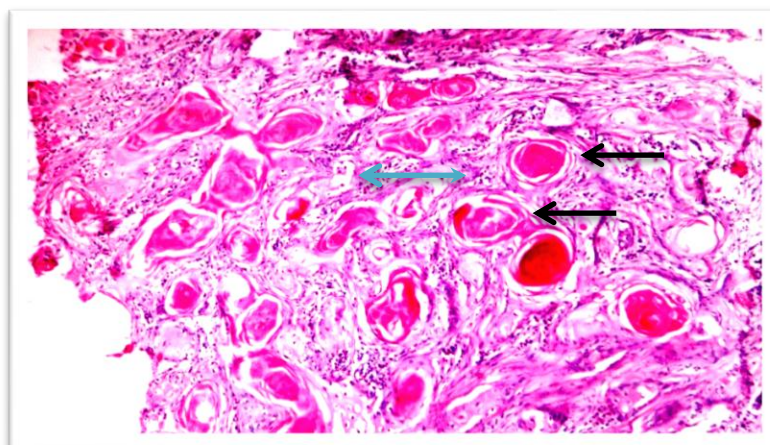


Figure- 4. Histopathological section of tumor mass of eye cow show's, laminated keratin pearls appears as red onion-like structures (black arrows) with inflammatory cells infiltration (blue arrow). (H & E X100).

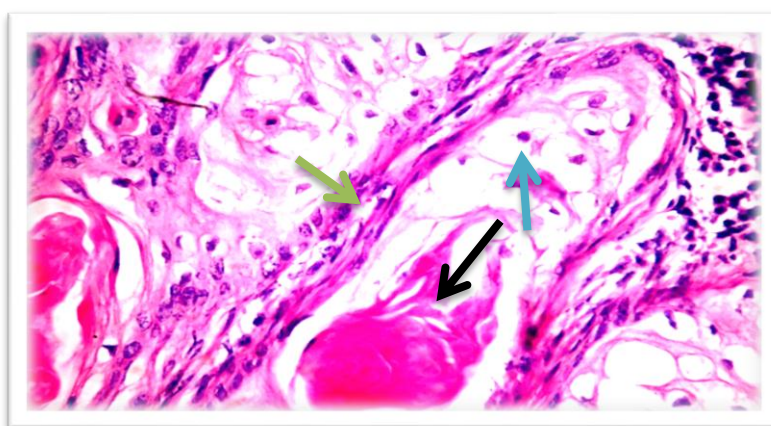


Figure- 5. Histopathological section show's, neoplastic cells forming keratin layers (black arrow). Vacuolar degeneration with connective tissue septa (green arrow). Cancer cell contained large, rounded and pyknotic nucleus (blue arrow). (H & E X100).

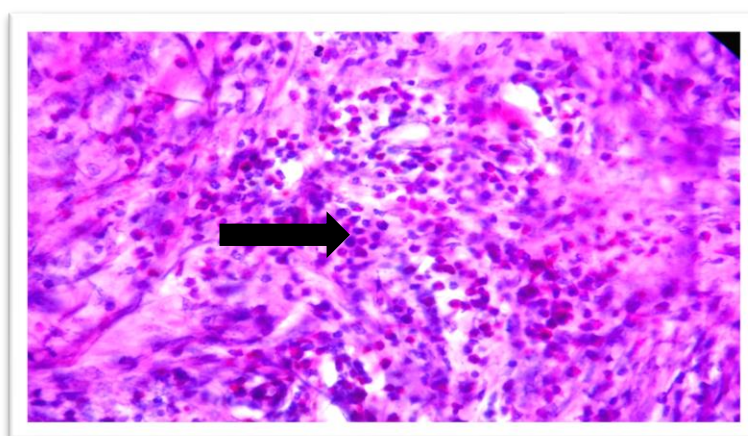


Figure - 6. Histopathological section show's, large number of inflammatory cells mainly eosinophils and lymphocytes (arrow). (H & E X100)

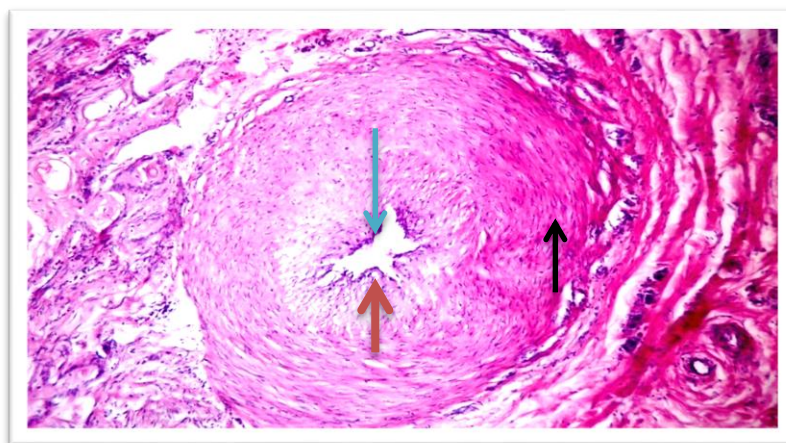


Figure -7. Histopathological section show's, hypertrophy of the muscular layer of blood vessels (black arrow), with vascular degeneration of tunica intima (brown arrow) and proliferation of endothelial cells toward the lumen (blue arrow). (H & E X100).

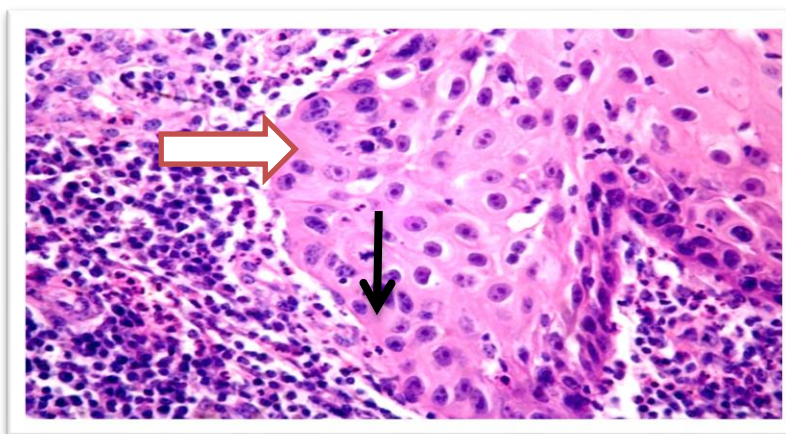


Figure- 8. Histopathological section show's, neoplastic cells with mitotic figures (black arrow), some of these cells contained nucleus with prominent nucleoli (white arrow). (H & E X100).

Discussion:

In this study, age range of the affected cows was (3 to 12) years. High percent (37%) of the tumors were observed in the age (7 to 8) years. The tumors were not common in animals younger than three years and were rare (0%) in animals less than one year of age (no cases were observed). This finding was in accordance with a study by (11), who found that the average age of cattle with ocular squamous cell carcinoma is eight years and the tumors are less common in cattle younger than five years and rare and hardly ever seen in cattle younger than three years.

In Iraq the majority of cases of cows ocular squamous cell carcinomas were observed in areas surrounding Baghdad province, especially in Alrathwanya and during summer. Despite the fact that incidence of cows ocular neoplasms varies geographically in Iraq, this may be attributed to greater exposure to sunlight in warm and dry areas which considered as a predisposing factor in initiation of the tumor. This contention supported by previously publication in Zimbabwe (12), who observed ocular squamous cell carcinoma in Simmental cattle, and

exposure to intense solar radiation has been proposed as the cause, especially when cattle are kept in a sunny and warm climate. According to the results of (13), they found that the season was important in progression of lesions and occurrence of new lesions of ocular tumors, and these were highest during summer and lowest during winter. However (14), were observed that there is a significant association between increasing risks of developing eye tumor and increasing levels of actinic radiation, and cattle exposed to high levels of radiation with longest hours of sunlight per year develop the disease at younger ages. In a research by (15), on 147 adult horses of both sexes. They recognized nine albinos horses had ocular squamous cells carcinomas.

Selective breeding for increased pigmentation in and around the eye protected cattle against the harmful effects of incident Ultra-Violet radiation and developing tumor eye. It is suggested that melanin plays a photo-protective role in epidermal and mucosal surface (16). The distribution of tumors between right (51.2%) and left (48.8%) eyes were approximately equal. In original study in horses (3), the sites of ocular tumours were limbus and cornea (6.25%), conjunctiva, and nictitating membrane (71.88%), and in (21.88%) of cases, the eyeball was destroyed by the tumour. While (17) , found that the most common sites of ocular carcinoma in Hereford cattle, were the lateral (25.7%) and medial (16.5%) corneo-scleral junctions. These findings disagree with my results. The discrepancy between these studies is likely due to two factors, including large population of cows involved in the present study and more detailed follow-up informations .

The study reported herein reflected hemorrhage in (7%) of the cases. This problem was anticipated and largely overcome by care in dissection within the orbit, avoiding trauma to intraorbital soft tissue and special attention to the ligation

or crushing of the optic nerve and forceful packing of the orbit with guaze for a short time. Swelling of pre-orbital region were noticed in (15%), this complication was transient, lasted for the first (2 to 3) days post-surgery and resolved without any treatment. These two health problems documented by (12) in cattle.

Orbital infection was noticed in (3%) of the cases. This phenomena is common in cows having enucleation performed under field conditions. Cows with post-operative orbital infections represented a wide variation in severity, with most cases having mild purulent discharge noted in the period between surgery and sutures removal (10 to 14) days post-surgery. Although all cases responded to medical therapy, the high rate of post-operative infection emphasizes the need to perform aseptic preparation of the surgical site, utilize optimal surgical technique including proper tissue handling, and perform follow-up care. A prospective randomized experiment, (18) referred that, the severity and nature of the disease compromised by tissue pathology are expected to be associated with post-operative complications despite the circumstances under which the surgery is performed. One of the advantages to the enucleation procedure is that it can be done under varying circumstances and differing peri-operative protocols.

Antibiotics time and routes of administration varied between clinicians. I administered broad-spectrum antibiotic IM., 30 minutes prior to surgery to produce its effect and minimized the rate of contamination and continued for five days post- surgery. On other hand, (19) were injected antibiotics at time of surgery due to orbital infection evocated from eye enucleation. The same authors noticed that additional intraorbital infusion of antibiotics did not appear to affect the orbital infection rate but limits the degree of infection.

Two cases (0.04%), had been suffered of transitory serosanguineous or bloody unilateral nasal discharge in week following enucleation which disappeared spontaneously in a short period. A scientific paper in dogs (20), had been reported minor bloody discharge from the nostril on the same side of the surgery in one dog. This sign resolved within 48hrs., without any treatment.

Only one pregnant cow in the eight month was aborted, this may be due to the effect of xylazine hydrochloride which may cause relaxation of birth canal and facilitate abortion, thus small dose of sedation must be used as preanesthetic especially in advanced pregnancy stage to overcome this problem. This finding was in accordance with previous study (14), who reported abortion in two buffalos resulted from xylazine administration.

In macroscopical examination, lesions were present in the right eye 256 and 244 left eye. It had a nodular or cauliflower-like appearance and were varied in size from a few centimeters to several centimeters. The tumor lesions were ulcerated and bled easily because it is highly vascular, and sometimes discharge of pus and the cornea was opaque. A retrospective randomized trial by (15), who detected five ocular tumors affected right eye and four in the left eye which differed in their sizes and appeared as a growth destroyed the entire orbital contents, ocular adnexa, other soft tissues and the surrounding bones. The growth was cauliflower-like, ulcerated and easily bled. This observation corroborated by (21), who indicated that most ocular carcinomas accompanied by secondary changes, such as necrosis, ulceration and bleeding.

In the present study, microscopical examination of the ocular tumor masses revealed (squamous cell carcinoma), characterized by excess keratin, known as "hyperkeratosis," including keratin pearls or whorled nests of keratin which is

visible as an amorphous pink material within and surrounding the cytoplasm of the cells. Some of the cells appeared in irregular cords and there was mild fibroplasia of the stroma. Similar histopathological features were observed by other several authors (7, 8) in cattle and small animals (22). The tumor invasion was almost always accompanied by an intense visible immune cells composed of variable types of inflammatory cells including neutrophils, lymphocytes or a mixed infiltrate this may be due to response of the host to tumor antigens. In addition numerous eosinophils were also present. In a research on buffalo (2), stated that extensive infiltration of eosinophils to stroma of the ocular squamous cell carcinomas is a rare finding. The real reason for this phenomenon is not defined, but may result from spontaneous tumor regression.

The cell's nucleus appears as enlarged, hyperchromatic and contained of one or more nucleoli. Cells displayed mitotic figures which means that the nuclei were in the process of division. This picture is similar to different retrospective studies in dairy cattle (7), equine (24) and in dogs (25). In conclusion enucleation remains an inexpensive, safe and viable treatment option for many types of severe ocular pathology in cows and the animal can be retained to original reproduction within few weeks, in addition to increase longevity of the cows within the herd.

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