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Clinicopathological correlation of caruncular lesions: a 22-year report from the Middle East

Abdulrahman Alfarhan[1*], Yazen Bajaeifer[2], Nawaf Almeshari[3], Muhannad A. Alnahdi[4,5,6], Azza Maktabi[7] and Naif AlSulaiman[1]

Abstract

Introduction Caruncular lesions are uncommon and diverse, making accurate clinical diagnosis challenging. Discrepancies between clinical and histopathological diagnoses are frequent, and malignant lesions can metastasize early. The lack of substantial regional data necessitates a detailed study of the clinical and histopathological characteristics of these lesions.

Methods A retrospective study was conducted over a 22-year period, including 52 patients with caruncular lesions. Clinical presentations, demographic data, and histopathological findings were recorded. All lesions underwent biopsy and histological examination to correlate clinical and pathological diagnoses.

Results A total of 52 patients with caruncular lesions were included, with a mean age of 48 years. The majority presented with unilateral lesions, and six patients had bilateral involvement. The most common presenting complaints were pigmented or enlarging masses. Histopathological examination revealed 13 distinct lesion types, with inflammatory lesions (25%) and melanocytic tumors (23%) being the most common. Malignant lesions were identified in 11.5% of cases. The clinicopathological correlation was accurate in 23% of cases.

Conclusion Caruncular lesions present significant diagnostic challenges due to their rarity and histopathological diversity. This study underscores the importance of histopathological examination for accurate diagnosis and highlights the need for regional data to better understand the epidemiology of these lesions. The findings also suggest that while most lesions are benign, a high index of suspicion for malignancy should be maintained, particularly in cases of rapid growth or atypical presentation.

Keywords Caruncle, Conjunctiva, Clinicopathologic correlation, Lesions, Nevus, Tumor, Benign, Malignant

*Correspondence:
Abdulrahman Alfarhan
amzalfarhan@gmail.com
[1] Oculoplastic and Orbit Division, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia
[2] College of Medicine, King Saud University, Riyadh, Saudi Arabia
[3] Anterior Segment Division, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia
[4] Department of Ophthalmology and Vision Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, Canada
[5] Department of Ophthalmology, King Abdulaziz Medical City, Riyadh, Saudi Arabia
[6] College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[7] Department of Pathology and Laboratory Medicine, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia

Introduction

The caruncle is a soft, ovoid body located medial to the plica semilunaris. It is widely exposed in the palpebral fissure, making any changes in its shape or color easily noticeable to patients. However, cases of caruncular lesions are rare in the literature, and the varying nature of these lesions is attributed to the diversity of their histopathological components, which makes their clinical diagnosis challenging. A study spanning 25-years that included more than 500 patients reported a discrepancy between the clinical and histopathological diagnosis in 50% of their cases [1]. Yvon et al. also described that 33% of the preoperative diagnoses of caruncular lesions were not accurate [2]. Additionally, it has been reported that malignant lesions involving the caruncle seem to metastasize early [3]. All of these factors highlight the need for a better understanding of the clinical and microscopic features of lesions involving this anatomic location. Race, geographic location, and other demographic features can also affect the frequency and incidence of the different pathologies involving the caruncle [4, 5]. Hence, our 22-year study aims to describe the clinical and histopathological identification of caruncular disorders in the Middle East. To the best of our knowledge, no such study has been conducted to review these lesions in this region.

Materials and methods

This retrospective study was conducted at the King Khaled Eye Specialist Hospital (KKESH), the region's largest ophthalmic tertiary referral center. The study reviewed clinical records from 1999 to 2022, focusing on patients treated at the Ophthalmic Pathology Laboratory. Data were collected on patient demographics, affected eye, suspected clinical diagnosis, gross appearance, tumor dimensions, histopathological findings, and postoperative complications. Cases were identified through the hospital's digital pathology software and clinical logbooks maintained by the head ophthalmic and oculoplastic consultant. Inclusion criteria were strictly caruncular lesions, excluding lesions from surrounding structures such as the plica semilunaris and conjunctiva. A biopsy was performed on each lesion, with histopathological analysis performed on paraffin sections stained with hematoxylin and eosin. To reduce interobserver variation in interpretation, the histopathology slides were reviewed by two independent pathologists, as identified by the hospital records, before a final diagnosis was established. Ethics approval for this study was granted by the local ethics review committee at King Khaled Eye Specialist Hospital. This study adheres to the principles of the Declaration of Helsinki. Categorical variables were presented in the form of frequencies and percentages [No. (%)], while continuous variables were presented as mean (± SD), range [min – max]. The inferential analysis was conducted using Chi^2 for associations between diagnostic discrepancies, and statistical significance was defined as a p-value < 0.05.

Results

A total of 52 patients with caruncular lesions were included in the study. The mean age was 48 ± 24 (range: 4–93 years), with a modest female preponderance (29 females, 55.7%). The majority of patients presented with unilateral lesions, with the right and left eyes equally involved, while only six patients had bilateral lesions.

In 54% of the cases, patients reported symptoms at the time of presentation, with pigmented or enlarging masses being the most common complaints. These caruncular lesions were identified through symptomatic presentation rather than incidental discovery. Overall, 12 (23%) caruncular lesions were pigmented, and most were benign (88.5%). The mean duration of follow-up was 4 years. Baseline characteristics are summarized in Table 1.

All caruncular lesions underwent biopsy and were submitted for histological examination. Our case series revealed the presence of thirteen distinct histopathological types of lesions. The most commonly observed lesion was inflammatory in origin (25%), followed by melanocytic (23%), myeloproliferative (19%), vascular (9.5%), surface epithelial (8%), adnexal (7.5%), and epithelial cyst (2%). Two cases had normal histological tissue (4%), and one had non-specific histological changes (2%).

A total of six cases (11.5%) were confirmed to be malignant. Of these, four were diagnosed as lymphoma, while the remaining two were identified as squamous cell carcinoma (SCC) and basal cell carcinoma (BCC).

Overall, the clinical diagnoses correlated with histopathological findings in only twelve cases (23%). The

Table 1 Demographic and lesion characteristics ($N = 52$)

Variable	Category	No. (%)
Age	Mean (± SD), [Min – Max]	48 (24), [4–93]
Gender	**Male**	23 (44.3)
	Female	29 (55.7)
Incidental	**Yes**	24 (46)
	No	28 (54)
Pigmented	**Yes**	12 (23)
	No	40 (77)
Nature of the lesion	**Benign**	46 (88.5)
	Malignant	6 (11.5)
Dration of follow-up (Months)	Mean (SD)	4.0 (2.0)

All values are frequency (%) unless stated otherwise

most frequently proposed clinical diagnosis was melanocytic nevi (12 cases, 23%), followed by pyogenic granuloma (8 cases, 15.3%) and caruncular cyst (3 cases, 5.7%). In ten out of twelve cases (83%), the clinical diagnosis of melanocytic nevi was confirmed by pathological examination. However, in the remaining two cases, histological analysis revealed benign lymphoid hyperplasia and chronic inflammation. Additionally, although eight lesions were initially diagnosed clinically as pyogenic granuloma, histopathological confirmation was achieved in only one case. The other lesions were found to have different histopathological diagnoses (Table 2).

Inflammatory lesions

Chronic inflammatory lesions are the most prevalent lesions in this series (13 cases, 25%). Four were detected incidentally, two were presented as pigmented lesions over a duration of 5 and 3 months, respectively, while the complaints of the remaining cases were not specified.

These lesions were diagnosed clinically as thickened caruncle (3 cases), pyogenic granuloma (3 cases), nevus (1 case), and the remaining 2 cases were not specified. Microscopically, the lesions showed acanthotic epithelium along with pseudocysts formation surrounded by inflammatory cells such as lymphocytes and plasma cells.

Melanocytic lesions

Melanocytic tumors were the second most prevalent histological diagnosis in this series (23%). Among the melanocytic tumors, nevus was the most common (10 cases, 19%), followed by primary acquired melanosis (PAM) with atypia (2 cases, 4%). There was a male predominance (70%), with the majority of patients having unilateral involvement (80%). All lesions with a histopathological diagnosis of nevi had accurate clinical diagnoses. Four patients presented complaining of pigmented lesions, one patient noticed an enlarging caruncular mass, and the remaining lesions were discovered incidentally. Lesions were highly variable in size and dimensions. Clinically, eight lesions appeared as pigmented mole-like spots, while the other two were non-pigmented (Fig. 1A). Histopathologically, the lesions demonstrated numerous melanocytic nevus cells with pigmentation in the subepithelial layers (Fig. 1B). Additionally, PAM with atypia was detected in two cases. Both lesions were surgically removed due to the potential risk of progression to malignant melanoma.

Surface epithelial lesions

We encountered one case of BCC in a 56-year-old male. The lesion was progressively enlarging and extending

Table 2 Top three inaccurate clinical diagnoses

Proposed diagnoses	No. (%)	Acurate pathological diagnosis (12; 23%)	Inacurate pathological diagnosis (42; 77%)	*p-value*
Melanocytic nevus	12 (23)	10 (83)	2 (17)	
Pyogenic granolma	8 (15.3)	1 (12.5)	7 (87.5)	
Crancular cyst	3 (5.7)	1 (33.3)	2 (66.7)	
				(0.001)*

All values are frequency (%) unless stated otherwise * *P*-value < 0.05

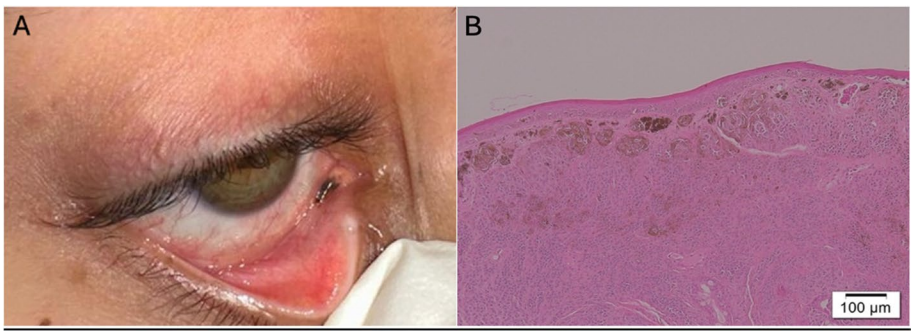

Fig. 1 Melanocytic Nevus. **(A)** A clinical photograph depicts a smooth, well-demarcated, brown pigmented lesion overlying the caruncle. **(B)** The histopathology shows unremarkable epidermis. The dermis is infiltrated by islands of mature nevus cells. [hematoxylin–eosin stain × 100]

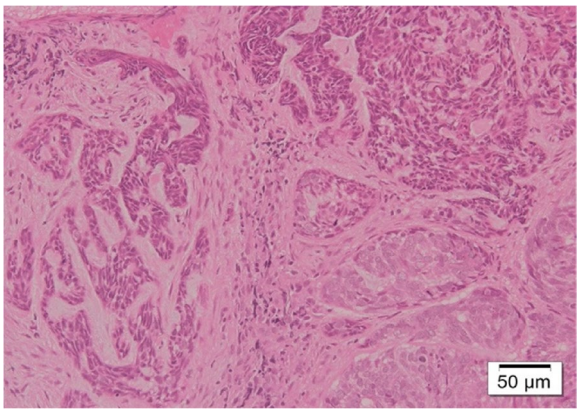

Fig. 2 Basal cell carcinoma. The histopathology shows islands of abnormal malignant cells that has a feature of basal cell carcinoma—sclerotic subtypes. [hematoxylin–eosin stain × 200]

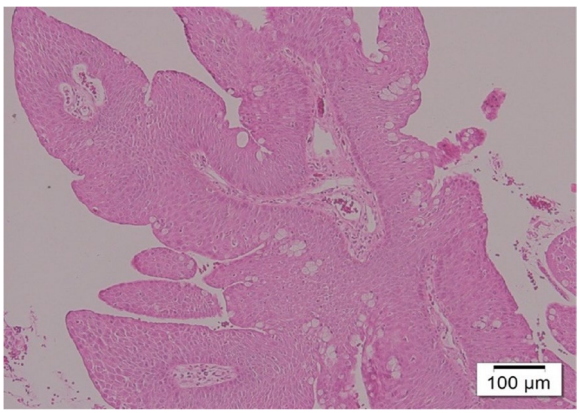

Fig. 3 Benign squamous papilloma. The histopathology shows fronds of benign looking conjunctival epithelium with central vascular core. [hematoxylin–eosin stain × 100]

over the lower fornix toward the conjunctiva. A contrast-enhanced computed tomography scan (CT) of the orbit revealed the orbital extension of the lesion, and the diagnosis was confirmed by pathological evaluation, which showed abnormal malignant cells with features suggestive of BCC (Fig. 2).

A SCC was detected in an elderly female who primarily complained of pain and limited eye movement over 3 months. Imaging showed orbital extension of the lesion. Pathological evaluation confirmed the diagnosis of well-differentiated SCC.

Squamous papilloma accounted for 4% of the cases in this series. The lesion was pedunculated and associated with itchiness. Histopathologically, the lesions exhibited a pronounced papillary growth pattern in the epithelium, with numerous mucus glands and goblet cells (Fig. 3).

Myeloproliferative disorders

Myeloproliferative disorders comprised 20% of the cases, including benign lymphoid hyperplasia (6 cases, 11.5%) and lymphoma (4 cases, 7.5%). The mean age at biopsy was 37.3 years, and more males were affected than females (60% vs. 40%, respectively). Half of the cases were discovered incidentally. Clinically, the lesion appeared pink, fleshy, pedunculated, and non-tender (Fig. 4A). All the cases had an incorrect preoperative clinical diagnosis. Reactive lymphoid hyperplasia displayed numerous mature lymphocytic infiltrates with lymphoid follicles and irregular germinal centers (Fig. 4B,C,D). In contrast, lymphoma cases showed lymphocytic infiltration with pleomorphism and histiocytes containing tangible bodies in their cytoplasm.

Adnexal tumors

All cases of sebaceous gland hyperplasia were identified incidentally. Microscopically, the epithelium exhibited parakeratosis, and the subepithelial tissue contained multiple prominent and hyperplastic sebaceous glands (Fig. 5).

Oncocytoma was incidentally discovered in an 81-year-old female, initially diagnosed with caruncular enlargement. Pathology revealed a cystoadenomatous tumor within the stroma consisting of glandular epithelial cells with eosinophilic cytoplasm. Although the lesion was surgically removed, it recurred over the subsequent follow-up visits (Fig. 6).

Vascular lesions

Pyogenic granuloma (PG) represented 5.5% (3 cases) of the whole series. There were two female and one male patients. Two of the three PG cases were associated with ocular surgery; one underwent ocular decompression, and the other occurred after dacryocystorhinostomy with Jones tube placement. Clinically, all lesions presented unilaterally and were discovered incidentally during clinical evaluation (Fig. 7). A correct clinical diagnosis was only made in one case, while the other two were diagnosed as caruncular cysts and melanocytic nevus. The microscopic features of PG included an irregular piece of granulation tissue with edematous stroma containing moderately thick-walled vessels with capillary proliferation and infiltration of chronic inflammatory cells.

Capillary hemangioma was observed only in female patients. The clinical presentation varied between the two cases. One patient reported an enlarging mass over three months, characterized by a keratinized, crusty edge that was initially diagnosed as a papilloma. The other case was discovered incidentally during a routine clinical evaluation. On histological evaluation, the specimens

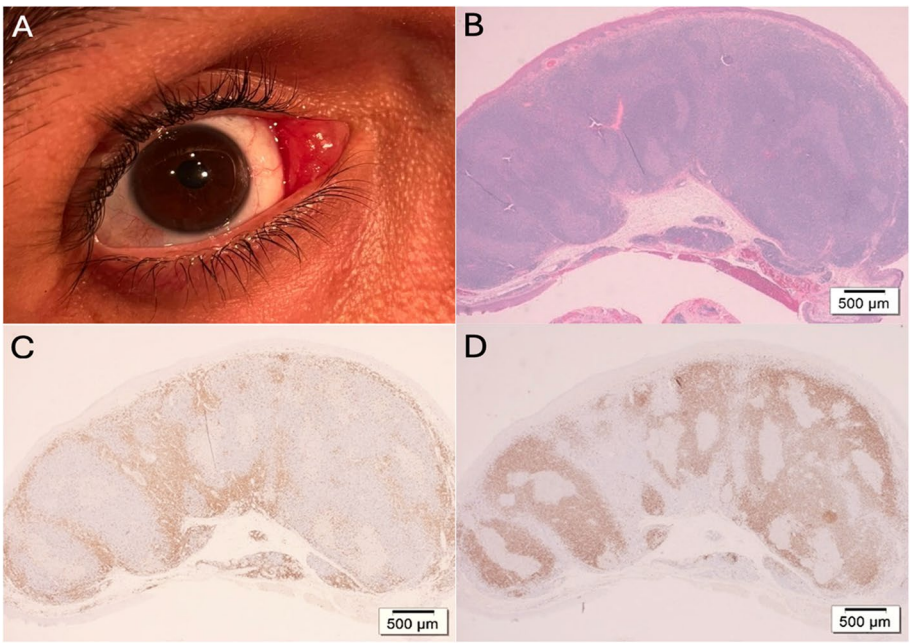

Fig. 4 Benign reactive lymphoid hyperplasia. **(A)** A clinical photograph shows a pink, smooth-surfaced caruncular lesion in a 41-year-old male. The histopathology shows soft tissue lined by unremarkable epithelium. The underlying substantia propria shows diffuse proliferation of mature lymphocytes with formation of lymphoid follicles with germinal centers **(B)** hematoxylin–eosin stain ×20, **(C)** CD 5 × 20, **(D)** CD 23 ×20,)

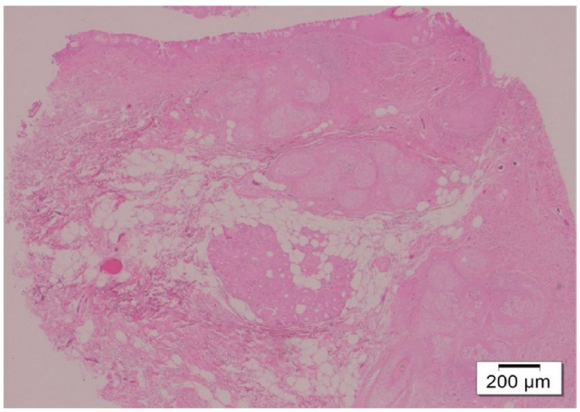

Fig. 5 Sebaceous hyperplasia. The histopathology shows soft tissue lined by unremarkable epithelium. Subepithelial tissue shows increased number of sebaceous glands. [hematoxylin–eosin stain ×40]

revealed multiple lobules of proliferating capillary-like blood vessels, separated by thin fibrous tissue septae in the underlying substantia propria. Additionally, larger sinusoidal endothelial-lined vascular spaces are noted.

Cysts

Only one case of epithelial inclusion cyst was reported in a 70-year-old female. The diagnosis of a caruncular cyst was confirmed through histopathology, which showed an incomplete cystic cavity within the dermis containing keratin in a multilayered arrangement.

Discussion

The lacrimal caruncle, located in the lacus lacrimalis at the medial angle of the eye, is a small, reddish, smooth structure measuring about 5 mm in height and 3 mm in width [6]. Though it is regarded as a cutaneous structure, the caruncle features unique modifications. Its surface consists of non-keratinized stratified squamous epithelium, differentiating it from typical skin tissue. Reflecting its developmental origins, the caruncle contains hair follicles with sebaceous glands (ectodermal structures), as well as connective tissue and fat (mesodermal structures). Horner's muscle is also present within its stroma, and goblet cells are found at the junction with the conjunctiva. The caruncle is supplied by the superior medial palpebral arteries, its lymphatics drain into the submandibular lymph nodes, and it is innervated by the infratrochlear nerve it [6].

During embryonic development, the lacrimal caruncle forms after the eyelids fuse, typically around the third month of gestation. One theory suggests that this formation involves the detachment of a part of the medial aspect of the lower eyelid margin during the development of the inferior lacrimal canaliculus [6, 7]. Another theory posits that the lacrimal caruncle arises from the

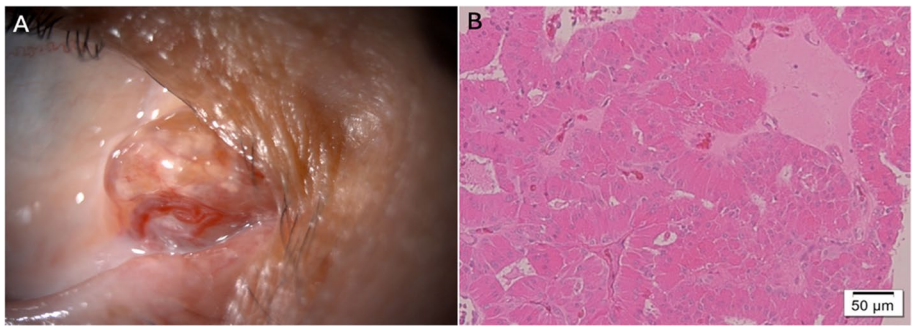

Fig. 6 Oncocytoma. **(A)** A clinical photograph shows a caruncular mass with prominent vessels. **(B)** The histopathology shows cords of benign tall cells with eosinophilic granular cytoplasm. [hematoxylin–eosin stain ×200]

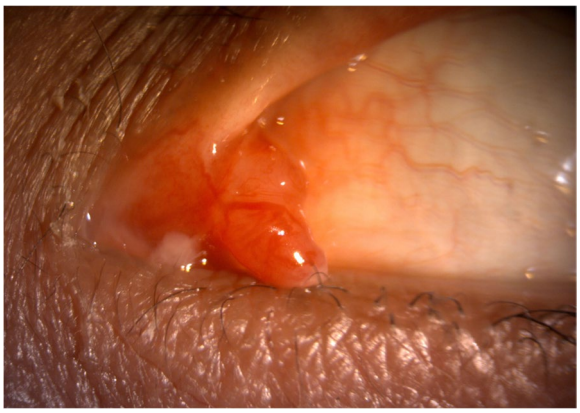

Fig. 7 Pyogenic granuloma. A clinical photograph illustrates a pedunculated, reddish caruncular lesion with a smooth surface in a 49-year-old female

cellular proliferation of the epithelium on the posterior surface of the nasal lower eyelid [7].

The diverse composition of the caruncle gives rise to a wide range of lesion types, making the histopathological examination of the lesion essential to accurately identify the lesion and aid in guiding the treatment plan. In this series, we identified 13 different categories of caruncular lesions based on their histopathological findings. Our findings indicate that caruncular lesions were more prevalent in females compared to males (55% vs 45%, respectively). However, gender distribution varies across different studies; some have reported a higher incidence in females [8–10], while others found a predominance in males [2, 11]. The majority of the lesions in our study (46 out of 52, or 88.5%) were benign, aligning with existing literature [10–12].

The most common lesions identified in this study were chronic non-granulomatous inflammation (13 cases, 25%), followed by melanocytic nevi (10 cases, 19%). This outcome aligns with several papers that have reported melanocytic nevi as a prevalent caruncular lesion along with papillomas [1, 10, 12, 13]. Table 3 compares the types and frequencies of caruncular lesions in our study with those reported in the literature.

Our study showed an accurate clinicopathological correlation in 19.5% (10/52 cases) of the instances. Melanocytic nevi were more likely to have an accurate clinicopathological correlation ($P=$ 0.001), likely due to their distinctive gross features. This rate is lower than those reported in previous literature [2, 8, 10, 12, 14]. For example, Santos et al. examined 113 lesions and reported an accurate preoperative diagnosis in 50% of the lesions. In their study, the most frequently proposed clinical diagnosis was nevi, with 32 out of 38 confirmed through histological evaluation [10].

Melanocytic lesions

Nevi were the most commonly encountered melanocytic lesion and the second most common type of caruncular lesion in our case series. These findings agree with the literature, with reported rates ranging from 34 to 60% [1, 10, 12–14]. Clinically, it typically presents in young patients around puberty as a brown to black pigmented lesion, although it can also be non-pigmented [7, 14]. Melanocytic nevi are typically diagnosed correctly due to their distinct clinical features, setting them apart from other lesions [7, 10]. Histologically, nevi manifest as clusters of benign melanocytic cells, which can occur in the epithelium and substantia propria (compound nevus), at the interface of the epithelium and substantia propria (junctional nevus), or as isolated clusters in subepithelial tissues (subepithelial nevus) [10]. Most of the lesions in this series were removed for cosmetic reasons, with only one lesion excised to rule out malignancy. As reported by Shields et al., excision is recommended when there are changes in size, color, or vascularity to rule out malignancy [7].

PAM typically affects patients in their forties and appears as poorly defined flat pigmented lesions. This

Table 3 Relative frequency of caruncular lesions: comparative literature review[a,b,c]

Pathologic diagnosis	Comparison of surveys	Shields et al. (1977–1985) (*n* = 57)	Santos et al. (1957–1990) (*n* = 113)	Kaeser et al. (1979–2005) (*n* = 192)	Levy et al. (1990–2007) (*n* = 42)	Solari et al. (1993–2008) (*n* = 42)	Kapil et al. (1991–2009) (*n* = 59)	Yvon et al. (2004–2020) (*n* = 31)	Alam et al. (2000–2020) (*n* = 36)	Present study (2000–2023) (*n* = 52)
Surface epithelial Lesions										
Squamous cell papilloma		**31.5**	26	15	7	9.5	8.5	22.5	3	4
Squamous cell carcinoma		2	-	-	-	-	-	-	3	2
Basal cell carcinoma		2	-	2	2.5	2.5	2	3	3	2
Caruncular cyst										
Epithelial inclusion cyst		-	12	7	-	-	-	6.5	17	2
Hidrocystoma		-	-	-	-	-	-	-	-	-
Steatocystoma		-	-	0.5	-	-	-	-	-	-
Melanocytic tumours										
Melanocytic nevus		25	**34**	**47**	**60**	21	**41**	**26**	8	19
PAM* without atypia		-	-	-	-	-	-	5	-	-
PAM with atypia		-	-	0.5	-	-	-	-	-	4
Malignant melanoma (in situ and invasive)		-	4	0.5	-	-	3	7	-	-
Adnexal tumours										
Sebaceous hyperplasia		-	4	8	2	2	2	-	11	5.5
Sebaceous adenoma		2	2	1	2	1	-	-	5.5	-
Sebaceous carcinoma		-	1	0.5	-	-	-	-	**17**	**-**
oncocytoma		3.5	-	4	7	7	5	6.5	3	2
Myeloproliferative disorders										
Benign lymphoid hyperplasia		-	3	-	2	2	-	-	14	11.5
Lymphoma		2	1	0.5	-	2	3	3	-	7.5
Vascular lesions										
Pyogenic granuloma		9	3	1.5	-	-	-	-	3	5.5
Capillary haemangioma		-	-	1	-	-	-	-	-	4
Neural tumours										
Neurofibroma		-	-	-	-	-	-	-	-	-
schwannoma		-	-	-	-	-	-	-	-	-
Inflammatory process										
Chronic inflammation		4	1	6	5	**29**	7	10	-	**25**
Lipogranuloma		2	-	-	-	-	-	-	-	-
Normal tissue		3.5	-	1	-	**-**	-	-	-	4
Non-specific changes		-	-	2.5	-	**-**	-	-	-	2

[a] All values are percentages

[b] Percentages may not total 100% due to rounding

[c] Lesions with the highest frequency in each study are highlighted in bold

[*] Primary Acquired Melanosis

condition is further classified based on the presence or absence of atypia (abnormal cellular features) [15, 16].

PAM without atypia has numerous melanocytic cells without other cellular irregularities, such as nuclear hyperchromasia or prominence of the nucleoli. However, PAM with atypia is characterized by the proliferation of various types of cells, including small polyhedral cells, spindle cells, large dendriform melanocytes, or epithelioid cells. These cells may remain confined to the basilar region (basilar nests), form nests at all levels of the epithelium, or spread individually to all levels of the epithelium (pagetoid extension) [16].

Diagnosing PAM with atypia can be challenging as it may resemble a junctional nevus. Both lesions share histological features, such as intraepithelial proliferation of polyhedral cells, and exhibit common growth patterns such as basilar hyperplasia, basilar nesting, and intraepithelial nesting. However, pagetoid extension is not commonly associated with junctional nevus [16]. While histological similarities exist, the clinical context, such as patient age, often plays an essential role in distinguishing between the two lesions, as junctional nevi are more common in childhood [16]. Fortunately, the PAM without atypia has almost no risk of progressing to malignant melanoma. However, the risk increases to 13% for PAM with atypia. In such cases, surgical excision is recommended [17].

Surface epithelial lesions

Squamous papilloma is a benign growth and is often reported as a frequent finding on the caruncle in multiple studies [1, 2, 7]. However, it only accounted for 4% of all caruncular lesions in our series. It typically appears as either a pedunculated or sessile cauliflower-like mass [2, 7].

Previous literature has established a connection between conjunctival papilloma and human Papillomavirus (HPV), particularly strains 6 and 11 [18]. While a report from the Middle East estimated the HPV infection rate to be 2.5% [19] this rate is notably low compared to findings from other regions [20]. Excision of the papilloma is the preferred treatment approach to establish the diagnosis and rule out malignancy. In cases where the papilloma recurs or persists, topical α-interferon and mitomycin-C may be considered [21–23].

Although BCC predominantly arises in tissue exposed to the sun, it rarely develops directly in the caruncle [24, 25]. Instead, caruncular BCC is more likely to develop secondarily from an adjacent lesion [26]. Given that BCC is the most common eyelid malignancy, it is important to recognize that the caruncle can serve as a potential site for extension or recurrence [27]. Histologically, BCC appears as basaloid cells that resemble normal basal cells of the epidermis. However, BCC cells are larger and have a high nuclear-to-cytoplasmic ratio [28]. Excision of caruncular BCC with clear margins can often be challenging due to the intricate anatomical structure and proximity to essential ocular tissues. Achieving complete removal while preserving normal tissue is crucial but difficult with traditional surgical methods due to the complex anatomy and proximity of vital eye structures. Mohs micrographic surgery has emerged as a superior technique in these cases, offering lower recurrence rates and better conservation of surrounding healthy tissue compared to conventional excision methods [29]. In complex cases, additional radiation therapy after the surgery may be recommended to ensure clear margins and reduce the risk of BCC recurrence [30].

SCC of the caruncle is also rare. Østergaard et al. and Santos et al. examined 574 and 113 lesions, respectively, but did not detect any cases of SCC [1, 10]. In contrast, Shields reported 2 cases of SCC out of 57 lesions [7]. While SCC commonly occurs in older age groups, it may also affect younger individuals, particularly those with underlying skin disorders or genetic predispositions such as xeroderma pigmentosum, epidermodysplasia verruciformis, and albinism [31, 32]. Additionally, factors such as chronic sun exposure, radiation, and infections like HIV and HPV are implicated in the development of SCC [33–37]. Caruncular SCC can present in various ways, ranging from being completely asymptomatic to causing decreased vision, burning sensation, photophobia, or diplopia if the extra-ocular muscles are involved [38, 39]. Caruncular SCC is managed by the same principles as periocular SCC and ocular surface squamous neoplasia (OSSN). Periocular SCC is treated with margin-controlled surgical excision and postoperative radiation therapy in cases of perineural invasion, while OSSN is managed with 2- to 3-mm margin surgical excision combined with cryotherapy or adjuvant therapy (Mitomycin C, 5-fluorouracil, Topical interferon) [40–42].

Vascular lesions

Pyogenic granuloma manifests as fleshy vascular polypoid mass with a tendency to bleed. While the exact etiology of pyogenic granuloma is unknown, trauma is a well-known predisposing factor. It is thought that trauma initiates an aberrant healing response marked by the overproduction of granulation tissue [7, 43]. Its pathogenesis also involves an increased neovascular response to an angiogenic stimulus, resulting in predominant pericyte growth with less effect on endothelial cells [43]. It could be associated with other conditions such as port wine stain, psoriasis, and eczematous dermatitis, which can be linked to the hypervascular response related to this condition [43]. Although Shields et al. accurately

diagnosed 4 out of 5 cases prior to tissue biopsy, accurate clinical diagnosis in this series was achieved in only one case [7]. Pyogenic granulomas may resolve spontaneously or can be managed with topical corticosteroid or surgical excision [7, 44]. Other vascular lesions reported in the caruncle include capillary and cavernous hemangioma, lymphangioma, and Kaposi sarcoma [12, 45, 46]. Although less common, these lesions highlight the diverse pathology that can affect the caruncle and emphasize the importance of accurate diagnosis.

Capillary hemangioma is a benign congenital condition that primarily affects infants, but it can also occur in older patients [44, 47]. The lesion typically appears as a smooth, red, well-circumscribed mass and is usually asymptomatic. Over the first two years, the lesion may enlarge and then slowly regress [44]. Management often involves observation unless the patient is symptomatic or has developed complications such as amblyopia [44, 48]. Treatment options include topical or systemic corticosteroids, and surgery [44].

Adnexal lesions

Oncocytoma is composed of oncocytes growing in an adenomatous pattern. The development of oncocytoma is believed to arise from either the oncocytic metaplasia of normal cells in the lacrimal or salivary gland within the ocular adnexa, or possibly as a result of the oncocytic transformation of adjacent conjunctival tissue epithelium [49]. It usually appear as a cherry red to brown cystic lesion [49, 50]. We found one case of oncocytoma; in an 81-year-old patient, which is consistent with the literature as oncocytoma mostly affects the elderly [9, 49]. However, Luthra et al. reported a patient in his thirties, highlighting the possibility of oncocytoma in younger individuals [13].

Sebaceous gland is a lipid-producing structure organized in a lobular pattern. Within the periocular structures, the sebaceous gland is located in the meibomian gland, the gland of zies, the brow cilia, and the caruncle. Any sebaceous growth commonly manifests as a yellow lesion due to the presence of lipids [51].

Sebaceous gland hyperplasia has a characteristic history and distinct appearance. The lesion usually affects older age groups and appears as a slow-growing yellow mass, and patients generally present with cosmetic concerns. However, it may cause foreign body sensations, irritation, or tearing. Factors such as actinic exposure or rosacea can be associated with this condition [51, 52]. In our study, all cases were initially misdiagnosed preoperatively, contrasting with the findings of Clemens et al., who reported an 83% accuracy rate in preoperative clinical diagnoses [9]. Distinguishing between sebaceous gland hyperplasia and sebaceous adenoma can be challenging due to their similar clinical presentations. However, histopathological examination reveals that sebaceous gland hyperplasia is characterized by normal cellular maturation sequences, whereas sebaceous adenomas lack this feature [7].

Inflammatory lesions

Our series differs from previous studies [7, 10, 12, 14] by identifying inflammatory lesions as the most prevalent caruncular abnormality, accounting for 25% of the patients investigated. The most commonly documented inflammatory processes are chronic non-granulomatous inflammation, lipogranulomatous inflammation, and foreign body granuloma [7, 8, 10, 13]. Alam et al. reported caruncular tuberculosis, which was successfully treated with anti-tubercular medications [11]. This case emphasizes the possibility of less prevalent inflammatory processes. Other uncommon inflammatory disorders that can affect the caruncle include methicillin-resistant Staphylococcus aureus (MRSA) caruncle abscess, Cytomegalovirus (CMV) infection, molluscum contagiosum, and ocular cicatricial pemphigoid [53–56].

Lymphoproliferative lesions

Lymphoproliferative disease of the ocular adnexa represents a spectrum of conditions ranging from harmless overgrowths (reactive hyperplasia) to malignant lymphomas [57] Although it is considered rare to arise within the ocular adnexa, it accounted for 20% of the cases in this series. Typical clinical presentation is a progressively enlarging, salmon-colored lesion. Reactive lymphoid hyperplasia and lymphoma may mimic each other clinically, and for this reason, pathological examination with immunohistochemistry stains and/or clonal analysis are essential [9].

Lymphomas are malignant lymphoid tissue tumors originating from clonal proliferations of either B-lymphocytes or T-lymphocytes, with less frequent involvement of natural killer (NK) cells [58]. The World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissues categorizes these tumors based on their cell type of origin [59]. Overall, 5% to 15% of all extranodal cases and fewer than 1% of all non-Hodgkin lymphomas (NHLs) are attributed to ocular lymphoma [60, 61]. Local intralesional injections of interferon-alpha have been shown to be an effective alternative to radiation therapy for treating conjunctival mucosa-associated lymphoid tissue lymphoma [62]. Additionally, intralesional interferon injection showed complete resolution of conjunctival NHLs along with multiple beneficial systemic effects [63].

Cyst

Epithelial inclusion cyst, which predominantly affects females, manifests as a smooth, painless lump that transilluminates [10, 11]. However, these are not the only cystic lesions observed in the caruncle, as epidermoid, and dermoid cystic lesions have also been documented [11, 13]. Surgical intervention is typically pursued for cosmesis or to alleviate discomfort. Although spontaneous resolution may occur, there is a risk of recurrence if fluid reaccumulates [7].

Approaching caruncular lesions

The diverse yet rare presentation of caruncular lesions represents a challenging clinical evaluation. Differentiating between benign and malignant lesions is crucial as it significantly influences management strategies. A thorough and detailed patient history is essential. Key elements to focus on include the patient's age, given that malignant lesions are more prevalent in older age groups, and the presenting complaint, with particular attention to lesion progression. Malignant lesions such as BCC and SCC typically exhibit slow growth [64]. A detailed past medical history can provide valuable insights, especially if there is a history of malignancy or conditions such as xeroderma pigmentosum, which increases the risk of squamous cell carcinoma [64]. Risk factors must be considered including sun exposure, which predisposes to BCC or actinic keratoses which increases the risk of SCC. Additionally, exposure to ionizing radiation is a known risk factor for both sebaceous and basal cell carcinoma [64].

During physical examination, the color and morphology of the lesion can provide clues to its nature. For instance, brown-black lesions might indicate nevi, while fleshy pink lesions suggest myeloproliferative lesions. Clinicians should also assess features indicative of malignancy, such as irregular borders, induration, ulceration, and telangiectasia [65]. Malignant lesions have the potential to spread to adjacent structures and lymph nodes, necessitating thorough inspection and palpation.

Despite the importance of history and physical examination, they are unreliable in distinguishing malignant from benign lesions. Therefore, a biopsy is highly recommended to confirm the lesion type and guide the management plan. Throughout clinical visits, both before and after treatment, it is essential to document the lesion's characteristics and progression meticulously, including photographic documentation, to monitor its changes over time and accurately identify the excision site.

This 22-year study provides a comprehensive analysis of caruncular lesions, addressing a significant gap in regional medical knowledge. It highlights the broad pathological diversity of these lesions and underscores the frequent discrepancy between clinical and histopathological diagnoses, reinforcing the critical role of biopsy for accurate assessment. However, as a single-center retrospective study, its findings may not be fully generalizable. Future research should include multi-center studies with extended follow-up periods to enhance understanding of recurrence patterns, treatment efficacy, and long-term patient outcomes.

In conclusion, caruncular lesions are rare and display significant variability, presenting substantial challenges for accurate clinical diagnosis. In our series of 52 patients, a wide age range was observed. We identified 13 different histopathological types, with chronic inflammation and melanocytic nevi being the most frequent findings. Although malignancy was uncommon, clinical diagnoses were accurate in only half of the cases, emphasizing the critical role of histopathological examination. Given the diverse nature of these lesions, any changes in size or color should prompt excision and pathological evaluation. Close collaboration between ophthalmologists and ocular pathologists is advisable in complex cases to ensure precise diagnosis and optimal treatment.

Abbreviations

SCC	Squamous Cell Carcinoma
BCC	Basal Cell Carcinoma
PAM	Primary Acquired Melanosis
CT	Computed Tomography
HPV	Human Papilloma Virus
MRSA	Methicillin-Resistant Staphylococcus Aureus
CMV	Cytomegalovirus
NK	Natural killer cell
WHO	World Health Organization
NHLs	Non-Hodgkin Lymphomas

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Authors' contributions

Abdulrahman AlFarhan: Study Design, Data Collection, Data analysis, Manuscript writing, ethical approval. Yazen Bajaeifer: Manuscript writing, Manuscript review, visualization. Nawaf AlMeshari: Study Design, Data Collection, Data analysis, Manuscript writing. Muhannad A. AlNahdi: Study Design, Data Collection, Manuscript writing. Azza Maktabi: Study Design, Data collection, Manuscript review. Naif AlSuliman: Study Design, Manuscript review

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Data availability

Due to patient privacy regulations, the datasets generated and analyzed in this study are not publicly available. However, de-identified data may be provided upon reasonable request to the corresponding author, Dr. Abdulrahman Alfarhan, at amzalfarhan@gmail.com. All requests will be reviewed by the King Khaled Eye Specialist Hospital Institutional Review Board (IRB) to ensure compliance with ethical guidelines and data protection policies. Approved data sharing will be subject to a formal data-sharing agreement.

Declarations

Ethics approval and consent to participate

This study was approved by the Local Ethics Review Committee at King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia, and conducted in accordance with the principles of the Declaration of Helsinki. The Institutional Review Board (IRB) at King Khaled Eye Specialist Hospital waived the requirement for informed consent in compliance with Article 14 of the National Regulations for Research on Living Creatures, issued by the National Committee of Bioethics (NCBE), King Abdulaziz City for Science and Technology (KACST), Saudi Arabia.

As outlined in Article 25 of the same regulations, which addresses research involving minors, the IRB determined that obtaining informed consent from parents or legal guardians was not required for this study. This decision was based on the study's design and objectives, ensuring full compliance with ethical and regulatory standards.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Østergaard J, Prause JU, Heegaard S. Caruncular lesions in Denmark 1978–2002: a histopathological study with correlation to clinical referral diagnosis. Acta Ophthalmol Scand. 2006;84(1):130–6.
2. Yvon C, Balamurugan T, Bianchi E, Lee HB, Mclean C. Caruncular lesions: a 16-year single centre review in the United Kingdom. Eur J Ophthalmol. 2023;33(2):847–55.
3. Paridaens AD, McCartney AC, Minassian DC, Hungerford JL. Orbital exenteration in 95 cases of primary conjunctival malignant melanoma. Br J Ophthalmol. 1994;78(7):520–8.
4. Norn M. Pigmentation of plica and lacrymal caruncle. Acta Ophthalmol. 1984;62(6):939–43.
5. Wilson RP. Tumours and cysts of the lacrimal caruncle. Trans Ophthalmol Soc N Z. 1959;11:23–32.
6. Wolff E. Anatomy of the eye and orbit: including the central connexions, development, and comparative anatomy of the visual apparatus. 7th ed. Warwick R. Philadelphia: Saunders; 1976.
7. Shields CL, Shields JA, White D, Augsburger JJ. Types and frequency of lesions of the caruncle. Am J Ophthalmol. 1986;102(6):771–8.
8. Solari HP, Ventura MP, Orellana ME, Novais GA, Cheema DP, Burnier MN. Histopathological study of lesions of the caruncle: a 15-year single center review. Diagn Pathol. 2009;4(1):29.
9. Clemens AC, Loeffler KU, Holz FG, Herwig-Carl MC. Clinico-pathological correlation of lacrimal caruncle tumors: a retrospective analysis over 22 years at the University Eye Hospital Bonn. Graefes Arch Clin Exp Ophthalmol. 2022;260(4):1415–25.
10. Santos A, Gómez-Leal A. Lesions of the lacrimal caruncle. Ophthalmology. 1994;101(5):943–9.
11. Alam MS, Pal SS, Krishnakumar S. Clinical and histopathological profile of primary caruncular lesions. Indian J Ophthalmol. 2022;70(6):1975–81.
12. Kaeser PF, Uffer S, Zografos L, Hamédani M. Tumors of the caruncle: a clinicopathologic correlation. Am J Ophthalmol. 2006;142(3):448-455.e2.
13. Luthra CL, Doxanas MT, Green WR. Lesions of the caruncle: a clinicohistopathologic study. Surv Ophthalmol. 1978;23(3):183–95.
14. Levy J, Ilsar M, Deckel Y, Maly A, Pe'er J. Lesions of the caruncle: a description of 42 cases and a review of the literature. Eye. 2009;23(5):1004–18.
15. Folberg R, McLean IW, Zimmerman LE. Primary acquired melanosis of the conjunctiva. Hum Pathol. 1985;16(2):129–35.
16. Jakobiec FA, Folberg R, Iwamoto T. Clinicopathologic characteristics of premalignant and malignant melanocytic lesions of the conjunctiva. Ophthalmology. 1989;96(2):147–66.
17. Shields JA, Shields CL, Mashayekhi A, Marr BP, Benavides R, Thangappan A, et al. Primary acquired melanosis of the conjunctiva: risks for progression to melanoma in 311 eyes. Ophthalmology. 2008;115(3):511-519.e2.
18. Sjö NC, Heegaard S, Prause JU, von Buchwald C, Lindeberg H. Human papillomavirus in conjunctival papilloma. Br J Ophthalmol. 2001;85(7):785–7.
19. Human Papillomavirus and Related Cancers, Fact Sheet 2023. Human Papillomavirus (HPV) Information Centre. Available from: https://www.hpvcentre.net/. Cited 2024 Dec 10.
20. Wang R, Guo XL, Wisman GB, Schuuring E, Wang WF, Zeng ZY, et al. Nationwide prevalence of human papillomavirus infection and viral genotype distribution in 37 cities in China. BMC Infect Dis. 2015;15(1):257.
21. De Keizer RJW, De Wolff-Rouendaal D. Topical α-interferon in recurrent conjunctival papilloma. Acta Ophthalmol Scand. 2003;81(2):193–6.
22. Schechter BA, Rand WJ, Velazquez GE, Williams WD, Starasoler L. Treatment of conjunctival papillomata with topical interferon Alfa-2b. Am J Ophthalmol. 2002;134(2):268–70.
23. Yuen HKL, Yeung EFY, Chan NR, Chi SCC, Lam DSC. The use of postoperative topical mitomycin c in the treatment of recurrent conjunctival papilloma. Cornea. 2002;21(8):838–9.
24. Marzuka AG, Book SE. Basal cell carcinoma: pathogenesis, epidemiology, clinical features, diagnosis, histopathology, and management. Yale J Biol Med. 2015;88(2):167–79.
25. Larsen A. Conjunctival malignant melanoma in Denmark: epidemiology, treatment and prognosis with special emphasis on tumorigenesis and genetic profile. Acta Ophthalmol. 2016;94(A103):1–27.
26. Meier P, Sterker I, Meier T. Primary basal cell carcinoma of the caruncle. Arch Ophthalmol. 1998;116(10):1373–4.
27. Deprez M, Uffer S. Clinicopathological features of eyelid skin. Tumors a retrospective study of 5504 cases and review of literature. Am J Dermatopathol. 2009;31(3):256–62.
28. Margo CE, Waltz K. Basal cell carcinoma of the eyelid and periocular skin. Surv Ophthalmol. 1993;38(2):169–92.
29. Lindgren G, Lindblom B, Larkö O. Mohs' micrographic surgery for basal cell carcinomas on the eyelids and medial canthal area. II. Reconstruction and follow-up. Acta Ophthalmol Scand. 2000;78(4):430–6.
30. Rossman D, Arthurs B, Odashiro A, Saraiva V, Burnier M. Basal cell carcinoma of the caruncle. Ophthalmic Plast Reconstr Surg. 2006;22(4):313–4.
31. Donaldson MJ, Sullivan TJ, Whitehead KJ, Williamson RM. Squamous cell carcinoma of the eyelids. Br J Ophthalmol. 2002;86(10):1161–5.
32. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum. Cutaneous, ocular, and neurologic abnormalities in 830 published cases. Arch Dermatol. 1987;123(2):241–50.
33. Kwa RE, Campana K, Moy RL. Biology of cutaneous squamous cell carcinoma. J Am Acad Dermatol. 1992;26(1):1–26.
34. Van De Put MAJ, Haeseker BI, De Wolff-Rouendaal D, De Keizer RJW. Squamous cell carcinoma of the lacrimal caruncle: case reports. Eur J Ophthalmol. 2014;24(3):441–5.
35. Maclean H, Dhillon B, Ironside J. Squamous cell carcinoma of the eyelid and the acquired immunodeficiency syndrome. Am J Ophthalmol. 1996;121(2):219–21.
36. Johnson TM, Rowe DE, Nelson BR, Swanson NA. Squamous cell carcinoma of the skin (excluding lip and oral mucosa). J Am Acad Dermatol. 1992;26(3):467–84.
37. Meyer D, Smit DP. Eyelid and orbital involvement in HIV infection – An African perspective. Ocul Immunol Inflamm. 2020;28(7):1022–30.
38. Cervantes G, Rodríguez AA, Gómez LA. Squamous cell carcinoma of the conjunctiva: clinicopathological features in 287 cases. Can J Ophthalmol. 2002;37(1):14–20.
39. Lee GA, Hirst LW. Retrospective study of ocular surface squamous neoplasia. Aust N Z J Ophthalmol. 1997;25(4):269–76.
40. Sagili S, Yin V, Esmaeli B, O'Donnell B, Eckstein R, Malhotra R. Squamous cell carcinoma of the caruncle. Ophthalmic Plast Reconstr Surg. 2015;31(4):e80–2.
41. McNab AA, Francis IC, Benger R, Crompton JL. Perineural spread of cutaneous squamous cell carcinoma via the orbit. Ophthalmology. 1997;104(9):1457–62.
42. Galor A, Karp CL, Oellers P, Kao AA, Abdelaziz A, Feuer W, et al. Predictors of ocular surface squamous neoplasia recurrence after excisional surgery. Ophthalmology. 2012;119(10):1974–81.

43. Patrice SJ, Wiss K, Mulliken JB. Pyogenic granuloma (Lobular Capillary Hemangioma): a clinicopathologic study of 178 cases. Pediatr Dermatol. 1991;8(4):267–76.
44. Shields JA, Mashayekhi A, Kligman BE, Kunz WB, Criss J, Eagle RC, et al. Vascular tumors of the conjunctiva in 140 cases. Ophthalmology. 2011;118(9):1747–53.
45. Kafil-Hussain N, Khooshabeh R, Graham C. Superficial adnexal lymphangioma. Orbit. 2005;24(2):141–3.
46. Hirsch C, Holz F, Tetz M, Völcker H. Klinik und Histopathologie von Karunkeltumoren. Klin Monbl Augenheilkd. 1997;210(03):153–7.
47. Murphy BA, Dawood GS, Margo CE. Acquired Capillary Hemangioma of the Eyelid in an Adult. Am J Ophthalmol. 1997;124(3):403–4.
48. Fernández-Vega Cueto L, Tresserra F, de la Paz MF. Crecimiento de novo de un hemangioma capilar conjuntival. Arch Soc Esp Oftalmol. 2014;89(3):127–9.
49. Biggs SL, Font RL. Oncocytic lesions of the caruncle and other ocular adnexa. Arch Ophthalmol. 1977;95(3):474–8.
50. Østergaard J, Prause JU, Heegaard S. Oncocytic lesions of the ophthalmic region: a clinicopathological study with emphasis on cytokeratin expression. Acta Ophthalmol. 2011;89(3):263–7.
51. Massry GG, Holds JB, Kincaid MC, Patrinely JR. Sebaceous gland hyperplasia of the caruncle. Ophthalmic Plast Reconstr Surg. 1995;11(1):32–6.
52. Browning DJ, Proia AD. Ocular rosacea. Surv Ophthalmol. 1986;31(3):145–58.
53. Koo L, Chang EL. Methicillin-resistant staphylococcus aureus caruncle abscess. Ophthalmic Plast Reconstr Surg. 2007;23(2):160–1.
54. España-Gregori E, Vera-Sempere FJ, Cano-Parra J, Ramos-Fernandez V, Navea-Tejerina A, Diaz-Llopis M. Cytomegalovirus infection of the caruncle in the acquired immunodeficiency syndrome. Am J Ophthalmol. 1994;117(3):406–7.
55. Vannas S, Lapinleimu K. Molluscum contagiosum in the skin, caruncle, and conjunctiva. Acta Ophthalmol. 1967;45(3):314–21.
56. Murube J, Chenzhuo L, Murube E, Rivas L, Shalaby O. Measuring the Lacunar Sulci as a New Indicator of Shrinkage of the Ocular Surface. Eur J Ophthalmol. 2001;11(3):227–32.
57. Coupland SE, Krause L, Delecluse HJ, Anagnostopoulos I, Foss HD, Hummel M, et al. Lymphoproliferative lesions of the ocular adnexa. Ophthalmology. 1998;105(8):1430–41.
58. McGrath LA, Ryan DA, Warrier SK, Coupland SE, Glasson WJ. Conjunctival lymphoma. Eye (Lond). 2023;37(5):837–48.
59. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, de Araujo IBO, Berti E, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022;36(7):1720–48.
60. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer. 1972;29(1):252–60.
61. Oh DE, Kim YD. Lymphoproliferative diseases of the ocular adnexa in Korea. Arch Ophthalmol. 2007;125(12):1668–73.
62. Blasi MA, Gherlinzoni F, Calvisi G, Sasso P, Tani M, Cellini M, et al. Local chemotherapy with interferon-α for conjunctival mucosa-associated lymphoid tissue lymphoma. Ophthalmology. 2001;108(3):559–62.
63. Ross JJ, Tu KL, Damato BE. Systemic remission of non-Hodgkin's lymphoma after intralesional interferon alpha-2B to bilateral conjunctival lymphomas. Am J Ophthalmol. 2004;138(4):672–3.
64. De Imus GC, Arpey CJ. Periorbital skin cancers: the dermatologist's perspective. Focal points. Am Acad Ophthalmol. 2006;24(1):1-5.
65. De la Garza AG, Carter KD, Kersten RC, Purdy EP. Evaluation and treatment of benign eyelid lesions. Focal points. Am Acad Ophthalmol. 2010;28(5):1-2.

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