Original Article

Clinical and histopathological profile of primary caruncular lesions

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Purpose: To provide a retrospective analysis of lesions of the caruncle which have been very rarely reported in the literature. **Methods:** A retrospective review of all the caruncular lesions between January 2000 and January 2020 was done at a single tertiary eye care hospital. The lesions were classified as benign and malignant lesions. Clinicopathological correlation was done for the excised lesions. **Results:** A total of 87 caruncular lesions were included in the study. Males (59%) were affected more than females (41%). The mean age at presentation was 44 ± 20 years. The mean duration of complaint was 36 ± 62 months. A total of 36 patients underwent surgical excision whereas the rest opted for conservative management. Recurrence was noted in five patients. Fifteen different types of lesions were identified histopathologically. Benign lesions (78%) were far more common than malignant ones (22%). Epithelial inclusion cyst was the most common benign lesion and sebaceous gland carcinoma was the most common malignant lesion. Correct clinicopathological correlation was seen in 52.7% of the cases. Caruncular tuberculosis, oncocytoma, and basosquamous cell carcinoma were some of the rare lesions. **Conclusion:** Caruncular lesions are uncommon and very diverse, which makes clinical diagnosis challenging. Epithelial inclusion cyst and sebaceous gland carcinoma were the most common benign and malignant lesions respectively. Correct clinicopathological correlation was seen in more than half of the cases.

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Caruncular lesions are uncommon, the vast majority being benign. Malignant lesions have also been rarely reported.[1] The lesions of the caruncle have been found to constitute about 1% of the total excised conjunctival lesions.[2] Albrecht von Gräfe reported the first series of lesions of the caruncle in 1854,[3] following which a few more investigators have subsequently reported their series on the spectrum of this otherwise rare group of lesions, though no such study has been reported from India till date. There was a need to fill these lacunae in the literature and provide the Indian perspective. We did a retrospective review of all the caruncular lesions presented to our institute over the past 20 years. To the best of the authors' knowledge this is the first such study from the Indian subcontinent.

Methods

A retrospective review of all the caruncular lesions between January 2000 and January 2020 was done from the electronic medical record. The data analyzed included demographic details, nature of the lesion, clinical and histopathological diagnoses, and management outcome. The lesions were classified as benign and malignant tumors and inflammatory lesions. Secondary caruncular involvement by the lesions arising from the surrounding eyelid, conjunctiva, and orbit were excluded. The institutional review board approved the study and it adhered to the tenets of the Declaration of Helsinki. Clinicopathological correlation for the excised lesions was calculated and the incorrectly diagnosed lesions were further analyzed for their correct diagnosis and the possible cause for the incorrect diagnosis.

Results

There were a total of 87 cases out of which 36 underwent surgery. There was a slight male preponderance [Male: 51 (59%), Female: 36 (41%)]. Right side was involved in 41 cases (47%) while the left-sided lesion was seen in 44 (51%). Two patients had bilateral involvement. Seven patients (8%) had congenital lesions, while 80 (92%) were acquired cases. Mean age at presentation was 44 ± 20 years (range: 4–79 years). Nine (10.3%) cases were in the pediatric range while 78 (89.6%) were adults. The demographic details of the patients who underwent surgery have been summarized in Table 1.

The mean duration of the complaint was 36 ± 62 months (range: 1–360 months). Thirty-six patients (41.3%) opted for surgery while the rest preferred not to be operated and be under observation and regular follow up. Benign lesions (28, 78%) were far more common than the malignant ones (8, 22%).

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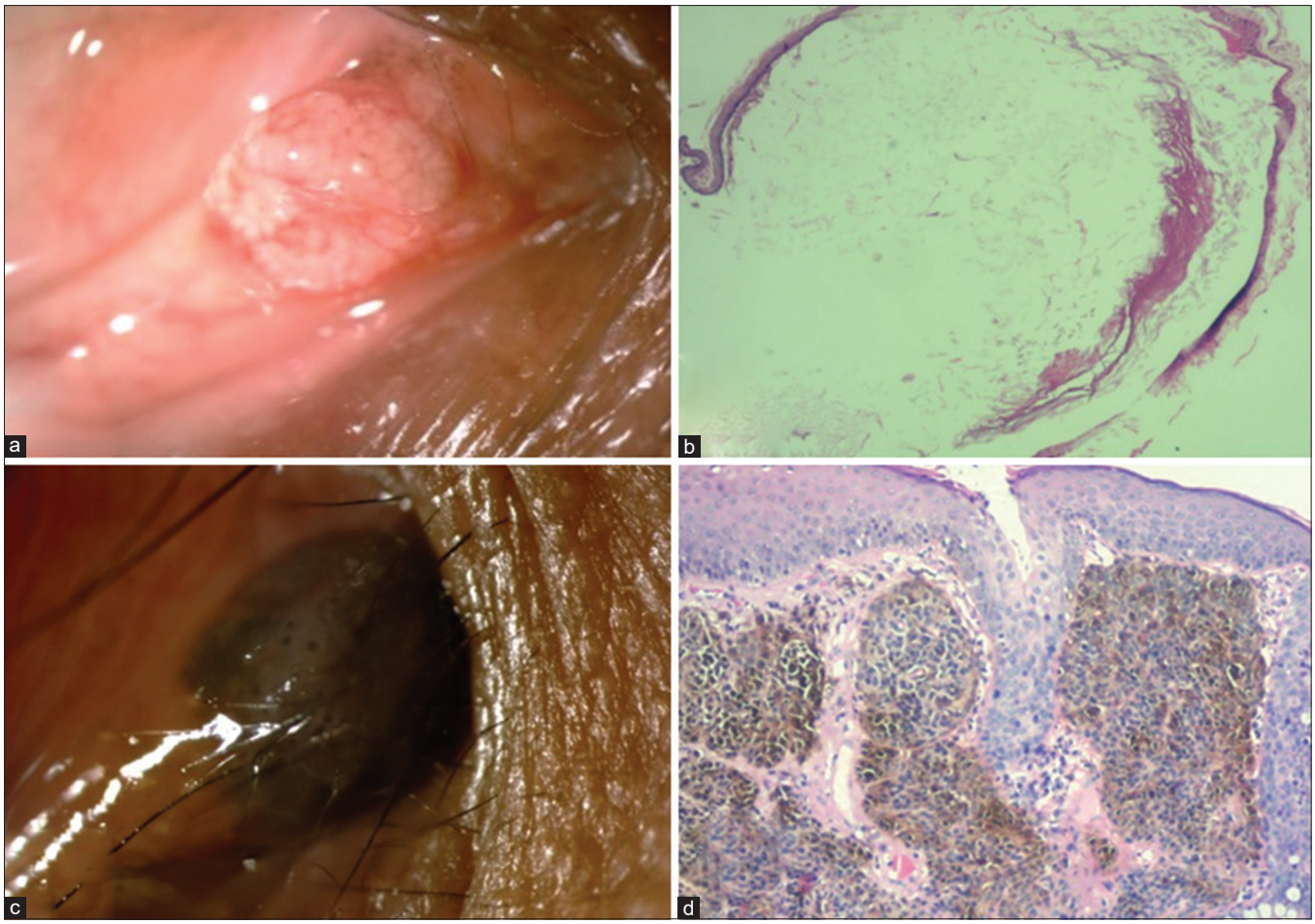

Figure 1: (a) Slit-lamp photograph showing a yellowish caruncular mass; (b) Microphotograph of the excised lesion showing a cyst wall lined with non-keratinized epithelium and sebaceous glands. The lumen contains sebaceous material. Findings suggestive of epidermoid cyst; (c) Slit-lamp photograph showing a pigmented caruncular mass with hairs protruding from it; (d) Microphotograph of the excised mass shows portions of epithelium and dermis along with matured nevus cells

Among benign lesions, 20 cases (71.4%) were neoplastic, 7 (25%) were inflammatory, while 1 (3.5%) was degenerative.

The most commonly observed lesions were of epithelial origin (n = 17). Of these, epithelial inclusion cyst was the most common, representing 35% (6 of 17) of the epithelial lesions. The mean age at presentation for this group was 32 years (10–44 years) and there was a male preponderance with a male–female ratio of 1.75:1. We had a total of 22 lesions which were clinically diagnosed as epidermoid cyst; however, histopathologically, there were only two such cases since a majority of them did not opt for surgery. Clinically, an epidermoid cyst appeared as a slow growing, non-tender, ovoid mass with a smooth surface possessing a yellowish tinge [Fig. 1a]. Histopathologically, a cyst wall lined by stratified squamous epithelium without keratinization of inner layers was observed [Fig. 1b]. Other benign epithelial lesions included sebaceous hyperplasia (n = 4), epidermoid cyst (n = 2), sebaceous adenoma (n = 2), papilloma (n = 1), dermoid (n = 1), pterygium (n = 1), and oncocytoma (n = 1).

Papilloma clinically appeared as a typical cauliflower-like mass [Fig. 2a]. Histologically, the tumor was composed of fibrovascular fronds covered by acanthotic conjunctival

Table 1: Demographic details of the patients undergoing surgery

Parameters studied	Numbers and Percentage
Sample size	36
Eye involved	Right: 19, 52.7% Left: 15, 41.6% Bilateral: 2, 5.5%
Sex	Male: 24, 66.6% Female: 12, 33.3%
Mean age (years)	44±20 (Range: 4-79)
Mean duration of complaint (months)	36±61 (Range: 1-360)
Age-wise distribution	Pediatric: 4, 11.1% Adult: 32, 88.8%
Onset of lesion	Congenital: 2, 5.5% Acquired: 34, 94.4%
Nature of lesion	Benign: 28, 77.7% Malignant: 8, 22,2%
Clinicopathological correlation	53% (19/36)
Recurrences	5, 13.8%
Mean duration of follow up (in months)	13±16.5 (Range: 1 month-5 years)

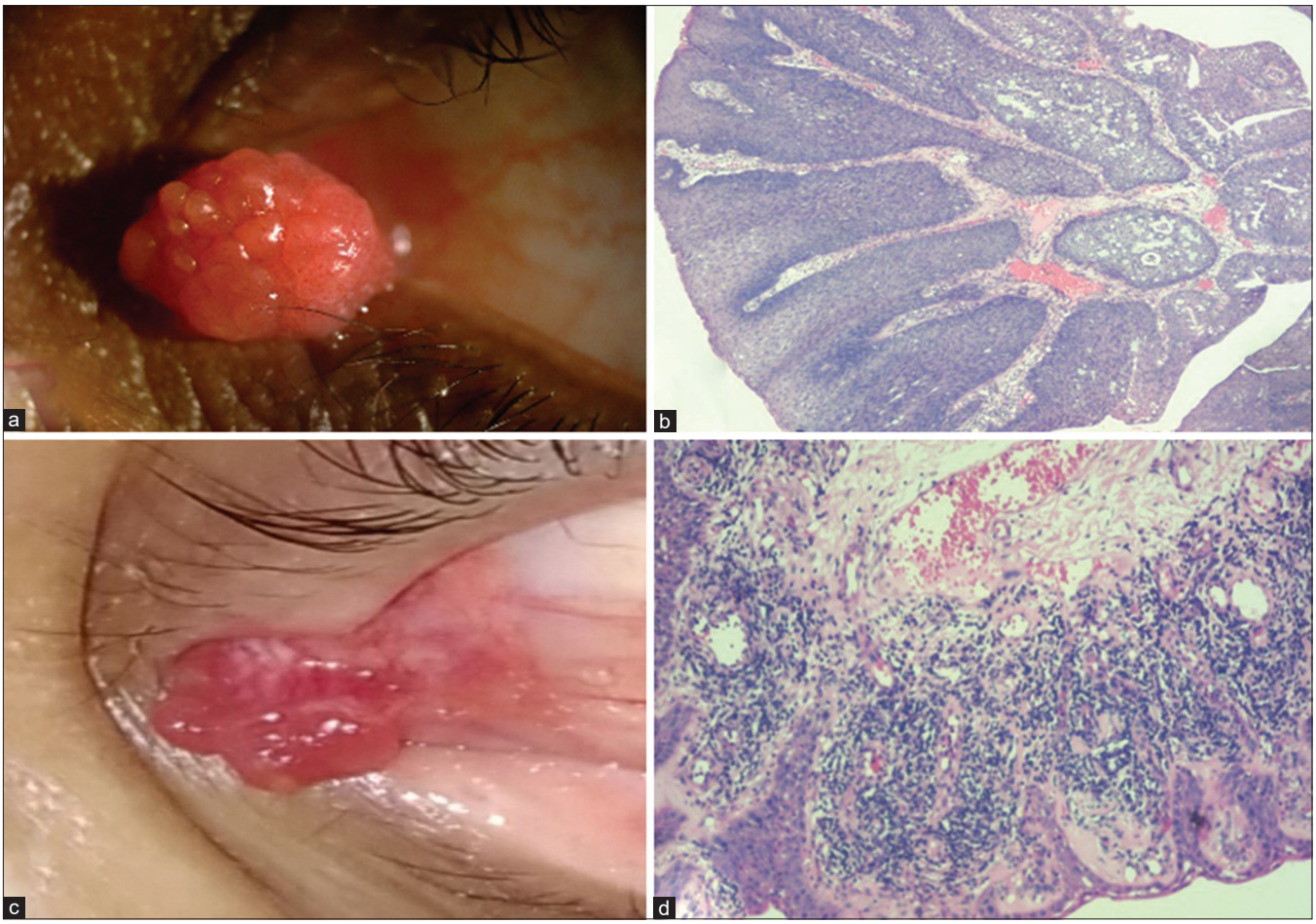

Figure 2: (a) Slit-lamp photograph showing a papillomatous caruncular mass; (b) Microphotograph showing multilayered thickening with acanthosis. There are scattered clumps of goblet cells with neutrophils showing exocytosis. No atypia is seen, suggestive of mucoepidermoid papilloma; (c) Slit-lamp photograph showing a vascular caruncular mass; (d) Microphotograph showing irregular thickening of the conjunctival epithelium. There is subepithelial lymphocytic infiltrate and multiple vascular channels with degraded collagen, suggestive of pyogenic granuloma

epithelium [Fig. 2b]. Sebaceous gland adenoma appeared as a greasy, yellowish tumor. Histology revealed mature sebaceous lobules around a central duct.

There were a total of eight malignant epithelial lesions, out of which six were sebaceous gland carcinoma (SGC) [Fig. 3a and b], and one each was squamous cell carcinoma and basosquamous cell carcinoma [Fig. 3c and d]. All of these patients underwent a metastatic workup which turned out to be negative.

SGC had a slight female preponderance in the ratio of 2:1 and the mean age was 62 years (range: 49–73 years). Five of these patients were treated by complete excision. Four patients had a recurrence and three had to undergo re-excision. One patient had a diffuse pagetoid spread of the lesion and underwent exenteration.

A total of 20 lesions were diagnosed as melanocytic lesions clinically; however only 3 patients opted for surgery. Nevus was the most common melanocytic lesion. Nevi clinically appeared as fleshy lesions with varying amount of pigmentation with or without hairs protruding out from it [Fig. 1c and d]. The mean age at presentation for melanocytic lesions was 42 years (range: 4–67 years) with a slight female preponderance (55%).

Inflammatory lesions, inflammatory tumor-like lesions and non-specified lesions together accounted for eight cases (22.2%). Five lesions were classified as lymphoid tissue hyperplasia while one each was pyogenic granuloma [Fig. 2c and d], tuberculosis, and pterygium [Table 2].

The histopathological diagnosis of the lesion was available for 36 excised cases. A positive clinicopathological correlation was seen in 19 of these cases (52.7%) [Table 3]. Correct histopathological diagnosis of the clinically misdiagnosed lesions has been provided in Table 3. Eight lesions turned out to be malignant, out of which five (62.5%) were diagnosed accurately as sebaceous gland carcinoma.

Mean follow-up duration of patients was 13 ± 16.5 months (Range: 1 month–5 years). Recurrence after excision was noted in five patients. Among the patients having recurrences, four had sebaceous gland carcinoma while one had epithelial inclusion cyst. Three patients having sebaceous gland carcinoma needed re-excision while one patient had to undergo exenteration owing to the extensive pagetoid spread. The patient with epithelial inclusion cyst was also managed by re-excision and had no further recurrence at the final follow-up.

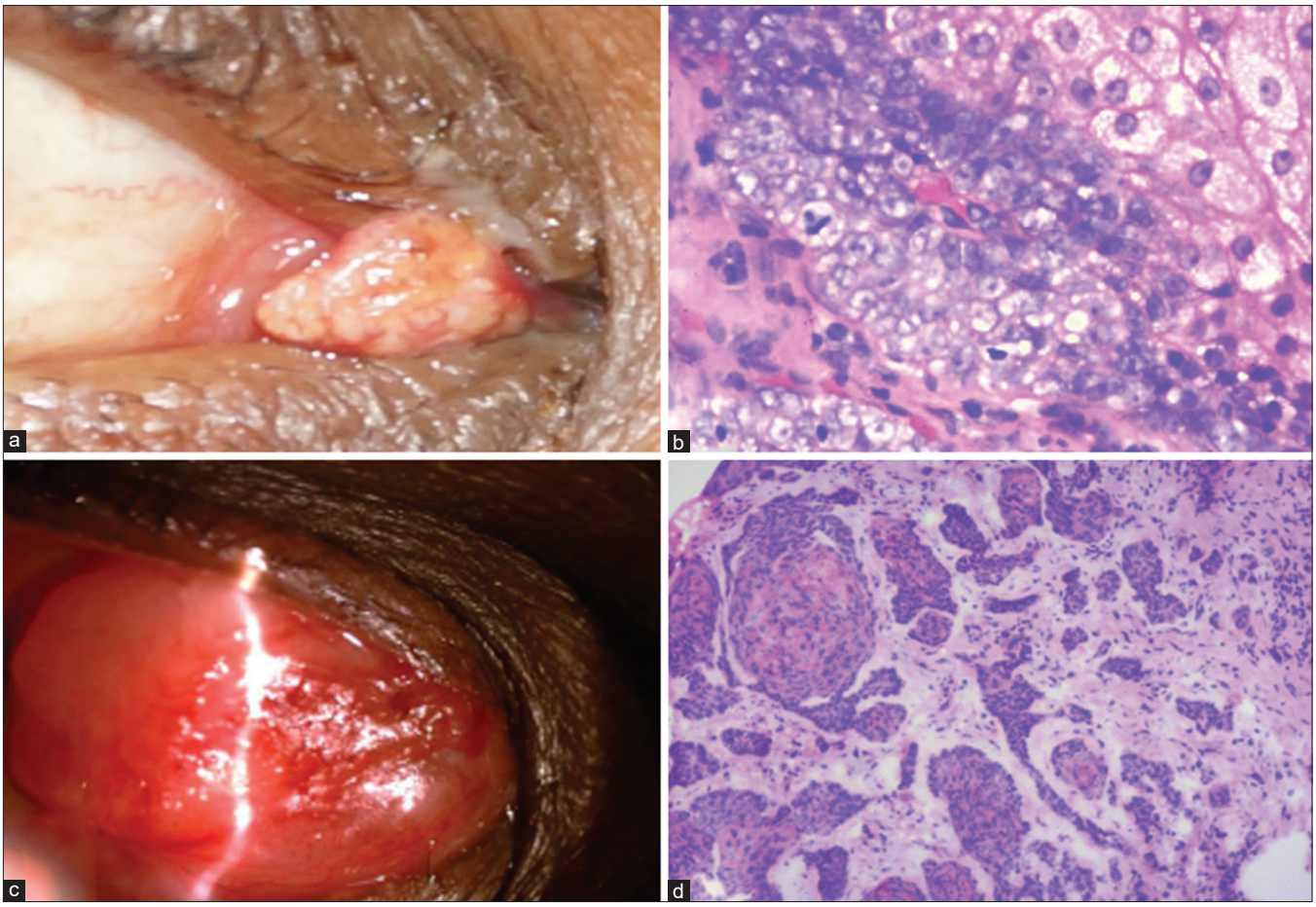

Figure 3: (a) Slit-lamp photograph showing a solid yellowish coloured mass arising from the caruncle; (b) Microphotograph showing multiple tumor cells arranged in lobular pattern. The tumors have high nucleocytoplasmic ration and display mitoses and stained positive for adipophilin, suggestive of sebaceous gland carcinoma; (c) Slit-lamp photograph showing an ill-defined, diffused solid mass arising from the caruncle. The lesion is found extending to medial canthus; (d) Microphotograph showing tumor cells having basaloid and squamous differentiation suggestive of basosquamous cell carcinoma

Table 2: Clinicopathological correlation of the excised lesions

Pathological diagnosis	Clinical diagnosis		Total (*n*=36)
	Correct	Incorrect	
Reactive lymphoid hyperplasia	2	3	5
Epidermoid cyst	1	1	2
Epithelial inclusion cyst	3	3	6
Pyogenic granuloma	1	-	1
Nevus	2	1	3
Pterygium	-	1	1
TB	-	1	1
Sebaceous hyperplasia	1	3	4
Papilloma	1	-	1
Sebaceous adenoma	2	-	2
Dermoid	-	1	1
Oncocytoma	1	-	1
Sebaceous gland carcinoma	5	1	6
Squamous cell carcinoma	-	1	1
Basosquamous cell carcinoma	-	1	1
Total	19 (53%)	17 (47%)	

One patient was found to have caruncular tuberculosis on histopathology. The patient underwent systemic investigations to rule out systemic tuberculosis and was treated with a course of antitubercular treatment and was completely cured.

Discussion

Fifteen different histopathological lesions were identified in the present series. This diversity is explainable based on the multitude of tissues forming the caruncle. There was a slight male preponderance as opposed to female preponderance noted in the previous studies.[1–4] A total of four pediatric cases were operated out of which two had reactive lymphoid hyperplasia, one was dermoid cyst and one was epithelial inclusion cyst. In the majority of studies, melanocytic lesions in the form of nevi constituted the largest group of caruncular lesions (average of 45.8%, range: 33.7–59.5% of lesions).[1,3,5] However, in our study, epithelial inclusion cyst and sebaceous gland carcinoma were the most common lesion (6 each, 16.6%) followed closely by reactive lymphoid hyperplasia (5, 13.8%) [Fig. 4d]. Although 22 and 20 lesions were clinically diagnosed as epidermoid cyst and nevus, respectively, since most of them did not undergo surgery, we cannot comment upon their exact histopathological types.

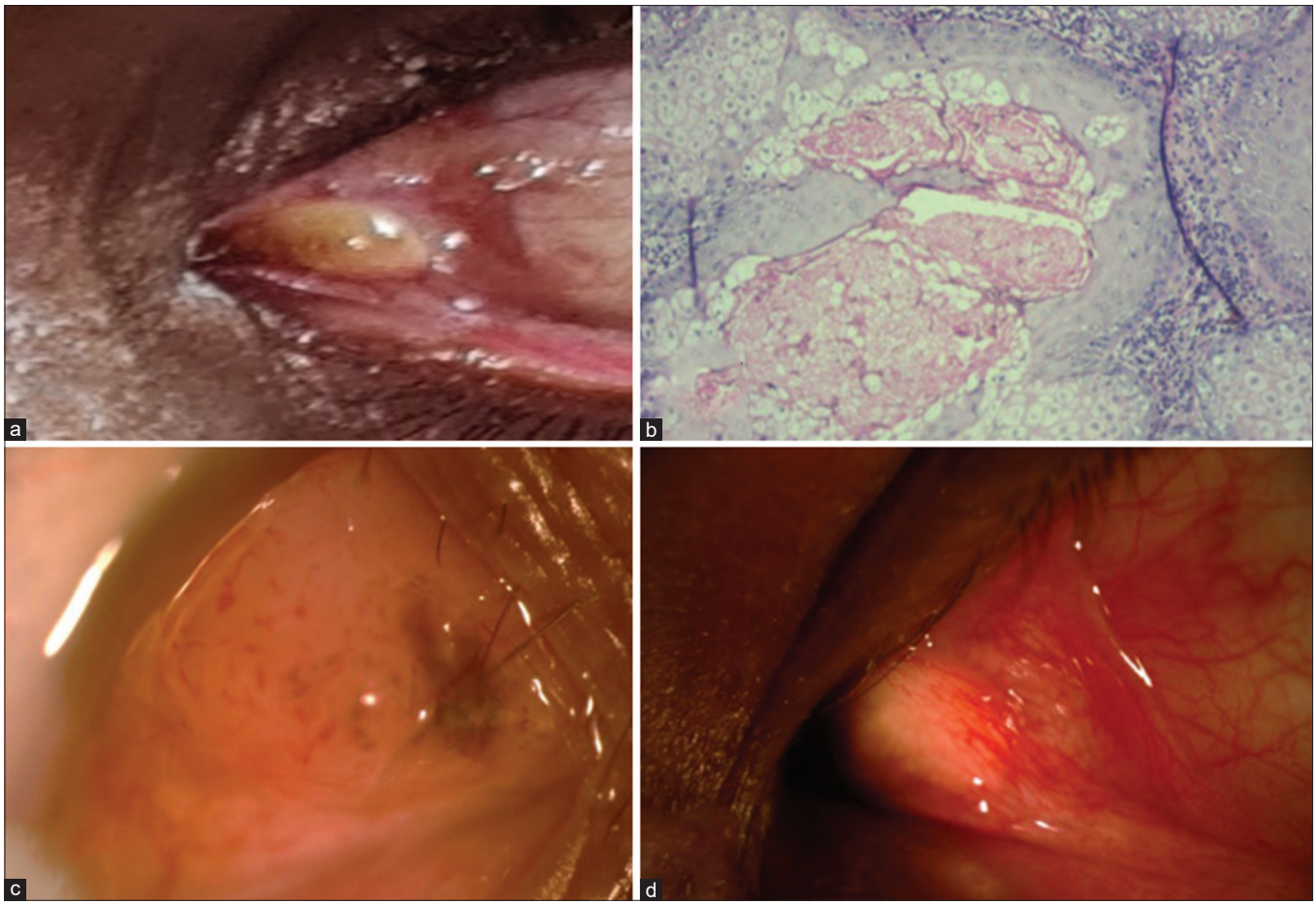

Figure 4: (a) Slit-lamp photograph showing a greasy yellowish caruncular mass. (b) Microphotograph showing portions of epidermis and dermis. In the dermis lobules of sebaceous glands are seen some of which are draining in to the pilosebaceous unit, suggestive of sebaceous gland hyperplasia; (c) Slit-lamp photograph showing a caruncular mass with patchy pigmentation and hair follicles protruding from it. The findings suggest a caruncular nevus; (d) Slit-lamp photograph showing a smooth yellowish caruncular mass suggesting an epidermoid cyst

Table 3: Correct pathological diagnosis of the clinically misdiagnosed lesions

Clinical diagnosis	Pathological diagnosis	Number
Pyogenic granuloma	Reactive lymphoid hyperplasia	2
Not specified	Reactive lymphoid hyperplasia	1
Epidermoid cyst	Pterygium	1
Epidermoid cyst	Sebaceous hyperplasia	1
Papilloma	Inclusion cyst	1
Papilloma	Melanocytic nevus	1
Papilloma	Sebaceous hyperplasia	1
Not specified	TB	1
Not specified	Inclusion cyst	2
Not specified	Dermoid	1
Not specified	Sebaceous gland carcinoma	1
Not specified	Squamous cell carcinoma	1
Not specified	Basosquamous cell carcinoma	1
Not specified	Nevus	1
Not specified	Sebaceous Hyperplasia	1

The majority of the lesions of caruncle are usually benign, as was noted in our study (78%). Except for the few studies published before 1940, where a very high frequency of malignancy of up to 27% was noted,[5,6] the rest of the studies show that malignant caruncular lesions are very rare accounting to just 2.7%–5.4% of the total.[5,7] In our study too the percentage of malignant lesions was slightly higher (22%). Majority of the patients having malignant lesions opted for surgery and that too can be a cause for the high percentage of malignant lesions. Correct clinicopathological correlation has been noted in 37%–52% of the cases in the literature, which is very similar to our study (52.7%). The possible explanation lies in the variety of tissues present in the caruncle, giving rise to a wide spectrum of pathologies.

Among the benign epithelial lesions, epidermoid cyst constituted 5% of the total lesions similar to the reports in several other literature (2%–7%);[1,3,4] however, we believe this to be an underrepresentation since majority of these cases did not undergo surgery.

Papillomas form the most frequent lesions of the caruncle in some series.[5–7] Only one case (2.78%) of papilloma was noted in our study.

We had just one case of caruncular oncocytoma in the present series and this particular case has already been published previously.[8] Although caruncular oncocytoma has been reported more frequently in the western literature,[1–6] it is not

Table 4: Review of literature

Diagnosis	Solari *et al.* (1993-2008) (*n*=42)	Shields *et al.* (1977-1985) (*n*=57)	Santos *et al.* (1957-1990) (*n*=113)	Levy *et al.* (1990-2007) (*n*=42)	Kaeser *et al.* (1979-2005) (*n*=192)	Present study (2000-2020) (*n*=36)
Nevus	9 (21.42%)	14 (24%)	34 (33.63%)	25 (59.5%)	92 (48.21%)	3 (8.33%)
Primary acquired melanosis	-	-	-	2 (4.8%)	1 (0.51%)	-
Malignant melanoma	-	-	4 (3.54%)	-	1 (0.51%)	-
Papilloma	4 (9.52%)	18 (32%)	26 (25.66%)	3 (7.1%)	29 (14.87%)	1 (2.78%)
Sebaceous gland hyperplasia	-	1 (2%)	4 (3.54%)	1 (2.4%)	15 (7.69%)	4 (11.11%)
Sebaceous gland adenoma	1 (2.38%)	1 (2%)	2 (1.77%)	1 (2.4%)	2 (1.03%)	2 (5.56%)
Epidermoid cyst	3 (7.14%)	-	3 (2.65%)	-	10 (5.13%)	2 (5.56%)
Epithelial inclusion cyst	3 (7.14%)	4 (7%)	12 (12.39%)	-	2 (1.02%)	6 (16.67%)
Dermoid cyst	-	-	4 (3.54%)	-	-	1 (2.78%)
Oncocytoma	3 (7.14%)	2 (4%)	-	3 (7.1%)	7 (3.59%)	1 (2.78%)
Keratoacanthoma	-	-	-	-	1 (0.51%)	-
Carcinoma in situ	2 (4.76%)	-	-	-	2 (1.03%)	-
Intraepithelial dysplasia	-	-	-	1 (2.4%)	1 (0.51%)	-
Primary basal cell carcinoma	1 (2.38%)	1 (2%)	-	1 (2.4%)	2 (1.03%)	-
Squamous cell carcinoma	-	1 (2%)	-	-	-	1 (2.78%)
Basosquamous cell carcinoma	-	-	-	-	-	1 (2.78%)
Sebaceous gland carcinoma	-	-	1 (0.88%)	-	1 (0.51%)	6 (16.67%)
Inflammatory lesions	14 (33.33%)	4 (7%)	1 (0.88%)	2 (4.8%)	13 (6.67%)	-
Nonspecific changes	-	-	-	-	5 (2.57%)	-
Pterygium	-	-	-	-	-	1 (2.78%)
Caruncular TB	-	-	-	-	-	1 (2.78%)
Inflammatory tumorlike lesion (Pyogenic granuloma)	-	5 (9%)	3 (2.65%)		3 (1.54%)	1 (2.78%)
Lipogranuloma	-	1 (2%)	-	-	-	-
Fibroma/Fibrolipoma	-	-	4 (3.54%)	-	-	-
Solitary fibrous tumor	-	-	-	1 (2.4%)	-	-
Malignant fibrous histiocytoma	-	-	-	1 (2.4%)	-	-
Seborrheic keratosis	-	1 (2%)	-	-	-	-
Cavernous hemangioma	-	-	1 (0.88%)	-	1 (0.51%)	-
Capillary hemangioma	-	-	-	-	2 (1.03%)	-
Lymphoid tissue hyperplasia	1 (2.38%)	1 (2%)	3 (2.65%)	1 (2.4%)	-	5 (13.9%)
Lymphoma	1 (2.38%)	1 (2%)	1 (0.88%)		1 (0.51%)	-

so common in the Indian subcontinent, as far as the literature is concerned.[9]

Nevus was the only melanocytic lesion noted in the present study (3, 8.3%) and there were no cases of malignant melanoma. Non pigmented amelanotic nevi can mimic other benign lesions and diagnosis can be difficult [Fig. 4c]. A low risk of malignant transformation in a pre-existing caruncular nevus has been reported.[10–12]

Sebaceous hyperplasia can present as a slow-growing, painless, yellow, "greasy," granular, nodular lesion, which is associated with overlying telangiectatic vessels of unknown etiology and diagnosing it clinically can be very difficult [Fig. 4a and b]. It is a relatively uncommon lesion found in only 2%–7% of cases in the previous studies,[1,3,7] similar to the present cohort (11%). There have been some reports of patients experiencing pain in cases of sebaceous gland hyperplasia.[13]

Several types of inflammatory processes have been described in the caruncle. Among them, the most frequently reported are chronic non-granulomatous inflammation, lipogranulomatous inflammation, and foreign body granuloma.[3–7] Inflammatory lesions were seen in eight cases (22.2%) in the present cohort. Other rare inflammatory lesions described in the literature are methicillin-resistant *Staphylococcus aureus* caruncular abscess, inflammatory pseudotumor, cicatricial pemphigoid, cytomegalovirus infection, molluscum contagiosum, spherulocytosis, and *Armillifer armillatus* infection.[14–20] Caruncular tuberculosis is a novel finding of our study which has not been previously reported. This particular case underwent a thorough evaluation to rule out pulmonary tuberculosis and was started on antitubercular treatment. We had a rare case of elastotic degeneration involving the caruncle which was labelled as pterygium histopathologically.

Among malignant tumors, SGC was the most common lesion seen in six cases (6.89%). This was in contrast to previous studies which reported malignant melanoma as the most common malignant lesion of the caruncle.[1,3,5,6] Other malignant lesions noted in the study were a rare basosquamous cell carcinoma and

a squamous cell carcinoma. There was a high accuracy rate in the diagnosis of malignant lesions and five of the eight (62.5%) malignant lesions were diagnosed accurately. We had a rare case of basosquamous cell carcinoma having both basaloid and squamous cell pattern on histopathology. Only one such case has been previously reported.[2] Caruncular malignancies usually have a good prognosis, as has been noted in our series.[1] The exposed location of the caruncle, which allows both the patient and the ophthalmologist to note any early change, leading to early diagnosis, may contribute to the favorable prognosis.

Table 4 presents a literature review of the previous major series reported on caruncular lesion, comparing it with the present study.

The present series reports a large variety of caruncular lesions and their Indian perspective. Retrospective design and nearly half of the patient not opting to get operated precluding a histopathological diagnosis are some of the limitations of the present study.

Conclusion

Caruncular lesions are uncommon and very diverse. Reported clinical diagnosis is correct only in about half of the cases. Benign melanocytic and epithelial lesions constitute a majority of the lesions. Malignant lesions are uncommon and sebaceous gland carcinoma is the most common caruncular malignancy in the Indian subcontinent. As compared to the western literature, caruncular oncocytoma is rarely encountered.

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Conflicts of interest

There are no conflicts of interest.

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