Lesions of the caruncle: a description of 42 cases and a review of the literature

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Abstract

Lesions of the caruncle are uncommon. On account of the histological composition of the caruncle, which includes, in addition to conjunctiva, hair follicles, sebaceous glands, sweat glands, and accessory lacrimal tissue, the caruncle may develop lesions that may be similar to those found in the skin, conjunctiva, or lacrimal gland. Clinical preoperative diagnosis is very difficult and reached only in about half of the cases. The vast majority of lesions of the caruncle are benign, mainly nevi. Reported malignant lesions are very rare but can be potentially fatal. Although malignancy is clinically overestimated, any suspected malignant lesion should be excised and examined histopathologically by an experienced pathologist. This study presents the clinical and histological data of 42 consecutive caruncular lesions processed at our laboratory and reviews previously reported cases of caruncular lesions.

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Introduction

The caruncle (from Latin *caro* = flesh) is a soft, pink, ovoid body, about 5 mm high and 3 mm broad, situated in the lacus lacrimalis medial to the plica semilunaris.¹ It is more prominent on lateral gaze and is retracted on medial gaze.

Lesions of the caruncle are uncommon. On account of the fact that the caruncle harbours skin elements, such as hair follicles, sebaceous glands, sweat glands, and accessory lacrimal tissue, the lesions developing from the caruncle

are very diverse, making their clinical diagnosis very difficult. The vast majority of lesions of the caruncle is benign, although rare malignant lesions have been also reported.

This study aims to present the clinical and histological data of 42 consecutive caruncular lesions processed at our laboratory and to review the relevant literature of caruncular lesions.

Materials and methods

Records from the Ophthalmic Pathology Laboratory at the Hadassah-Hebrew University Medical Centre, Jerusalem, Israel, between the years 1990 and 2007 were retrospectively reviewed. The following data were extracted from patients' files: age at the time of excision, gender, affected eye, suspected clinical diagnosis, gross appearance and tumour dimensions, light microscopic findings, and postoperative complications. Forty-two cases of caruncular lesions were found.

Paraffin sections stained with haematoxylin and eosin were extracted and examined in all cases.

Results

A total of 11 104 records from the Ophthalmic Pathology Laboratory, Hadassah-Hebrew University Medical Centre, Jerusalem, Israel, between the years 1990 and 2007 were reviewed. Forty-two cases of caruncular lesions were found (frequency of 1:264, 0.4%).

Age at the time of excision ranged from 13 to 93 years (mean 39.3 years, median 35.5 years). There were 21 male patients and 21 female patients. The left eye was involved in 27 cases (64%).

Most patients presented with a slowly growing caruncular lesion. In three cases, a

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history of rapid growth was referred. Clinically, pigmented lesions were observed in 29 cases (69%). All cases presented with solitary lesions. No concurrent disorders were observed.

Clinical suspected diagnosis included pigmented lesion (20 cases, 48%), naevus (10 cases), caruncular tumour (three cases), caruncular lesion (two cases), basal cell carcinoma (two cases), granuloma (two cases), papilloma (one case), cyst (one case), and malignant lesion (one case).

All the lesions were completely removed. There were no intraoperative or postoperative complications. The largest dimensions of the lesion varied from $12 \times 8 \times 8$ mm to $2.5 \times 1 \times 1$ mm. Histological findings allowed definitive diagnosis in all cases. There were 40 benign lesions (95%). Clinical suspected diagnosis was correct in 20 cases (48%).

Nevi were the most frequent encountered group (25 cases, 60%). Ten of them (40%) were accurately diagnosed before biopsy. Incorrect or non-specific diagnoses included pigmented lesion (13 cases, 52%), caruncular lesion (one case), and basal cell carcinoma (one case). The mean age of the patients with nevi was 36.6 years (median of 35 years; range between 13–84 years) with a slightly male preponderance (15 cases, 60%). The left eye was affected in 18 cases (72%). The caruncular naevus characteristically appeared as a brown-pigmented mass (Figure 1a). Sometimes the lesion is non-pigmented (Figure 1b). Histopathologically, nests of benign melanocytic cells were found within the epithelium and substantia propria (compound naevus, 22 of 25 cases), or totally in the substantia propria (subepithelial naevus, 3 of 25 cases, Figure 1c). Other histological features included epithelial cyst formation (four cases), focal chronic inflammation (one case), marked chronic inflammation (one case), focal parakeratosis (one case), and focal area of primary acquired melanosis (PAM) with atypia (one case).

In two cases, pigmentation of the basal layer of the epithelium without melanocytic hyperplasia or atypia, consistent with PAM without atypia, was detected (Figures 2a, b). In both cases, the suspected clinical diagnosis was a pigmented caruncular lesion. No cases of melanoma of the caruncle were detected in our laboratory.

Three cases (7%) of squamous papilloma were found. From these three cases, a correct clinical diagnosis before the biopsy was made in one case; in the other two cases, a tumour and a pigmented lesion were suspected clinically. Patients' age was 17, 29, and 54 years, respectively. Histopathologically, typical fibrovascular fronds with acanthotic epithelium were detected (Figure 3).

Oncocytoma was detected in three cases (7%). Patients were older than the average age in the entire group

Figure 1 (a) Clinical appearance of a compound naevus in an 18-year-old patient with small surface cysts. (b) Clinical appearance of a non-pigmented large protruding naevus with overlying clear cysts in a 51-year-old patient. (c) Subepithelial naevus shown in Figure 1b. Nests of benign melanocytic cells (arrow), and cystic epithelial inclusions (asterisk) are detected at the substantia propria (haematoxylin and eosin, original magnification $\times 4$).

(57, 58, and 93 years, respectively). There were two female patients and one male patient. Suspected clinical diagnosis before biopsy was pigmented lesion in two cases and caruncular tumour growing steadily in one

Figure 2 Primary acquired melanosis without atypia. (a) Clinical appearance of the lesion in a 14-year-old patient. (b) Microscopic appearance of the same lesion. Increased number of melanocytes without melanocytic hyperplasia or atypia is detected at the basal layer of the epithelium (asterisk). Some melanophages (arrow) and chronic inflammation are found at the substantia propria (haematoxylin and eosin, original magnification $\times 20$).

Figure 3 Squamous papilloma. The tumour is composed of acanthotic epithelium wrapped around fibrovascular cores (arrow; haematoxylin and eosin, original magnification $\times 4$). It is usually described as a frond-like mass with fine vascular tufts visible clinically in the central core of each frond.

case. Microscopically, oncocytomas were composed of benign epithelial cells with abundant eosinophilic granular cytoplasm (Figure 4a and b).

Figure 4 Oncocytoma. (a) A cystic structure lined by several layers of eosinophilic cells with granular cytoplasm is identified at the substantia propria (arrow). The cyst is filled with seromucinous material (asterisk; haematoxylin and eosin, original magnification $\times 4$). (b) The tumour is composed of columnar cells with eosinophilic cytoplasm and benign nuclei. No mitotic figures are observed. The central lumen shows an eosinophilic acellular material (asterisk; haematoxylin and eosin, original magnification $\times 40$).

Non-specific chronic inflammation was observed in two cases (Figure 5a and b). Patients were older than the average age group (55 and 63 years, respectively). Preoperatively, these lesions were diagnosed as naevus and pigmented lesion, respectively.

One case of sebaceous gland hyperplasia and one case of sebaceous adenoma were observed (Figures 6 and 7). The suspected clinical diagnosis before the biopsy was granuloma and caruncular lesion, respectively. There were no cases of sebaceous gland carcinoma in our series.

One case of moderate epithelial dysplasia was found in our series. Clinically, a caruncular tumour was suspected in a 46-year-old female patient. Dysplastic changes were observed in the lower and middle thirds of the conjunctival epithelial thickness (Figure 8a and b).

Figure 5 Chronic inflammation. (a) Clinical appearance of a caruncular lesion in a 55-year-old patient. (b) Microscopic appearance of the same lesion composed of chronic inflammatory cells (white arrow) around epithelial islands (asterisk; haematoxylin and eosin, original magnification $\times 4$).

Figure 6 Sebaceous gland hyperplasia. The lesion is composed by hyperplastic lobules (asterisk) situated around a single duct (arrow); a normal cellular maturation sequence is observed (haematoxylin and eosin, original magnification $\times 4$).

Figure 7 Sebaceous gland adenoma. The sebaceous lobules have lost the normal cellular maturation sequence. There is a peripheral layer (arrow) of small basaloid cells, with mature sebaceous cells centrally and transitional forms in between (haematoxylin and eosin, original magnification $\times 4$).

Figure 8 Moderate epithelial dysplasia. (a) Sharp demarcation (arrow) between normal (black asterisk) and acanthotic dysplastic epithelium (white asterisk; haematoxylin and eosin, original magnification $\times 10$). (b) Dysplastic changes are observed in the lower and middle thirds of the conjunctival epithelial thickness (double arrow; haematoxylin and eosin, original magnification $\times 20$).

There was one case of solitary fibrous tumour. This case was previously reported in a 29-year-old patient.² The lesion existed for at least 1 year. On examination, an elliptical pink mobile mass was detected at the lower fornix and caruncle (Figure 9a). It was composed mostly of spindle cells arranged randomly in a 'patternless pattern' (Figure 9b and c). Tumour cells were stained positively with CD34, O13 (CD99), BCL2, and vimentin, and negatively with S100 and α -actin.

One lesion was diagnosed as reactive lymphoid hyperplasia. Clinically, a cyst was suspected in a 19-year-old female patient. Histopathologically, the lesion was composed of a mixture of mature lymphocytes, plasma cells, and eosinophils (Figure 10).

In three cases, a malignancy was suspected clinically but confirmed histologically in two cases. In the two cases with malignant histological lesion ('so-called' malignant fibrous histiocytoma and basosquamous carcinoma), a malignancy was suspected clinically (basal cell carcinoma and 'malignant lesion,' respectively). The third case, an intradermal naevus, was incorrectly clinically diagnosed as basal cell carcinoma. The 'so-called' malignant fibrous histiocytoma was composed of round and spindle cells, showing a storiform pattern, marked cellular pleiomorphism, and mitotic figures (Figure 11). Numerous foamy macrophages were detected. The atypical cells stained positively for vimentin and negatively for HMB-45, α -actin, and LCA. The patient with basosquamous carcinoma was 67-year old. The tumour presented histopathological features of both basal cell and squamous cell carcinomas (Figure 12).

Discussion

The caruncle is modified skin, bearing goblet cells, and lacrimal tissue, in addition to hairs, sebaceous, and sweat glands.¹ The epithelium is non-keratinized, stratified squamous similar to the conjunctival epithelium, and the sebaceous glands are like those of the lids and the hairs. Modified lacrimal glands (of Krause), surrounded by a thin layer of fat, are often conspicuous in the centre of the caruncle. 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.¹ The function of the caruncle is poorly understood.³ All mammals possess a caruncle, and it is usually larger than that found in humans. In the camel, the caruncle may occupy the entire medial canthus, and in the dog, the caruncle is large and contains numerous accessory lacrimal glands.³ The embryology of the caruncle also is not well understood.³ It is formed at the end of the third month of gestation after the eyelids have fused. It is believed to develop either secondary to cutting off of a portion of the lower

Figure 9 Solitary fibrous tumour. (a) A large pink elliptical lesion is observed at the lower fornix and caruncle. (b) The tumour is covered by conjunctival epithelium (arrow) and composed of spindle cells and collagen fibres (haematoxylin and eosin, original magnification $\times 4$). (c) Higher magnification shows spindle cells arranged randomly in a 'patternless pattern' with collagen fibres between them (haematoxylin and eosin, original magnification $\times 20$).

eyelid with its appendages by the ingrowth of the lower canaliculus, or it is formed independently of the canaliculus by a cellular proliferation of the epithelium

Figure 10 Benign reactive lymphoid hyperplasia. A lymphoid follicle with germinal centre (asterisk) is observed (haematoxylin and eosin, original magnification $\times 4$).

Figure 12 Basosquamous carcinoma. Multiple islands of neoplastic cells displaying both basaloid (arrow) and squamous (asterisk) differentiation are detected (haematoxylin and eosin, original magnification $\times 4$).

Figure 11 'So-called' malignant fibrous histiocytoma. The tumour is composed of round and spindle cells, showing a storiform pattern, marked cellular pleiomorphism, and mitotic figures (black arrow). Numerous foamy macrophages (white arrow) are also present (haematoxylin and eosin, original magnification $\times 40$).

on the posterior surface of the nasal lower eyelid. The average distance between the external surface of the caruncle and the common canaliculus has been reported to be 0.85 mm, whereas the shortest distance measured is of 0.50 mm.⁴ Consequently, caution should be exercised when operations are performed on or near the caruncle to avoid inadvertent damage to the canalicular system.

The caruncle may develop a tumour or cyst that may be similar to one found in the skin, conjunctiva, or lacrimal gland. Lesions of the caruncle are reported to be uncommon. Since 1854, when von Graefe⁵ reported the first series of lesions of the caruncle, only a few reviews have been published, the majority of them reported more

than 15 years ago.^{3,6-13} In our series, caruncular lesions represented only 0.4% of all surgical specimens submitted to our Ophthalmic Pathology Laboratory during the 18 years of the study. This incidence is in agreement with the incidences previously reported (0.3–1.1%).^{9-11,13}

Thirteen different histopathological types of lesions were identified in our series. This diversity is explained based on all the different tissues forming the caruncle. Table 1 shows the relative frequency of caruncular lesions in this study and in previously reported large series. In the majority of studies,^{9,11,13} as in this study, nevi constituted the largest group of caruncular lesions (average of 45.8%, range: 33.7–59.5% of lesions). However, other authors found a preponderance of papillomas^{6,7,10} or epithelial cysts⁸ in lesions removed from the caruncle. The majority of the lesions is benign. Except for the studies published before 1940, where a very high frequency of malignant lesions of up to 27% was found,^{6,7} the rest of studies show that malignant caruncular lesions are very rare (average of 4.15% of total lesions; range: 2.7–5.4%). Preoperative clinical diagnosis is reported to be correct in only about half of cases (range: 37–52%),^{10,11,13} which is in concordance with our figures (48%). Coming up next, we present a detailed description of the reported lesions of the caruncle.

Congenital and developmental lesions

A number of developmental anomalies of the caruncle can seldom occur. Absence or hypoplasia and cleavage of the caruncle are almost always associated with other congenital anomalies.¹⁴ Hyperplasia of the caruncle is frequently associated with hyperplasia of the plica

Table 1 Relative frequency of lesions of the lacrimal caruncle: comparison of surveys

Pathologic diagnosis	Frequency (%) ^a			
	Serra ⁶ (n = 136) ^b	Evans ⁷ (n = 200) ^c	Wilson ⁸ (n = 107) ^d	Luthra et al ⁹ (n = 112)
<i>Congenital tumours</i>				
Epidermoid cyst	7.4			
Dermoid	5.1	4		0.9
<i>Inflammatory process</i>			28	
Chronic inflammation				4.4
Lipogranuloma	5.9	1.5		
Foreign body granuloma				2.7
Non-specific changes				
Secondary caruncular pigmentation				0.9
Normal tissue				
<i>Epithelial lesions</i>				
Seborrhoeic keratosis				0.9
Actinic keratosis				0.9
Papilloma	16.2	21.5	4.7	13.4
Keratocanthoma				
Conjunctival intraepithelial dysplasia				
Carcinoma <i>in situ</i>				
Basal cell carcinoma	14.7	9.5	2.8	
Squamous cell carcinoma				
<i>Cysts</i>	8.1	6.5	34.6	
Epithelial inclusion cyst				3.6
Hidrocystoma				0.9
Steatocystoma				0.9
<i>Melanocytic tumours</i>	9.6			
Freckle				0.9
Naevus		19.5	16.8	42.9
Dysplastic naevus				
PAM without atypia				
PAM with atypia				
Malignant melanoma		17.5	0.9	1.8
<i>Sebaceous tumours</i>				
Sebaceous hyperplasia	6.6	2		8
Sebaceous adenoma	6.6		2.8	
Sebaceous carcinoma				0.9
<i>Other adnexal tumours</i>				
Oncocytoma				3.6
<i>Myeloproliferative disorders</i>				
Benign lymphoid hyperplasia				3.6
Lymphoma	0.7	0.5		
Extramedullary plasmacytoma				0.9
<i>Vascular lesions</i>	7	2	5.6	
Pyogenic granuloma				2.7
Capillary hemangioma				1.8
Cavernous hemangioma				0.9
Lymphangiectasia				
<i>Neural tumours</i>				
Neurofibroma		1.5		
Granular cell tumour				0.9

Table 1 (Continued)

Pathologic diagnosis	Frequency (%) ^a			
	Serra ⁶ (n = 136) ^b	Evans ⁷ (n = 200) ^c	Wilson ⁸ (n = 107) ^d	Luthra et al ⁹ (n = 112)
<i>Fibrous and fibrohistiocytic proliferations and tumours</i>				
Fibroma	7.4	2.5	0.9	
Fibrolipoma			1.9	
Solitary fibrous tumour				
'So-called' malignant fibrous histiocytoma				
Pathologic diagnosis	Frequency (%) ^e			
	Shields et al ¹⁰ (n = 57)	Santos et al ¹¹ (n = 113)	Kaeser et al ¹³ (n = 195)	Current study (n = 42)
<i>Congenital tumours</i>				
Epidermoid cyst		2.7		
Dermoid		3.5		
<i>Inflammatory process</i>				
Chronic inflammation	7	0.9	6.7	4.8
Lipogranuloma	1.8			
Foreign body granuloma				
Non-specific changes			2.6	
Secondary caruncular pigmentation				
Normal tissue	3.5		1	
<i>Epithelial lesions</i>				
Seborrhoeic keratosis	1.8			
Actinic keratosis				
Papilloma	31.6	25.7	14.9	7.1
Keratocanthoma			0.5	
Conjunctival intraepithelial dysplasia			1	2.4
Carcinoma <i>in situ</i>			0.5	
Basal cell carcinoma	1.8		1	2.4
Squamous cell carcinoma	1.8			
<i>Cysts</i>				
Epithelial inclusion cyst	7	12.4	5.1	
Hidrocystoma			0.5	
Steatocystoma			0.5	
<i>Melanocytic tumours</i>				
Freckle				
Naevus	24.6	33.7	47.2	59.5
Dysplastic naevus			1	
PAM without atypia				4.8
PAM with atypia			0.5	
Malignant melanoma		3.5	0.5	
<i>Sebaceous tumours</i>				
Sebaceous hyperplasia	1.8	4.4	7.7	2.4
Sebaceous adenoma	1.8	1.8	1	2.4
Sebaceous carcinoma		0.9	0.5	
<i>Other adnexal tumours</i>				
Oncocytoma	3.5		3.6	7.1
<i>Myeloproliferative disorders</i>				
Benign lymphoid hyperplasia		2.7		2.4
Lymphoma	1.8	0.9	0.5	
Extramedullary plasmacytoma				

Table 1 (Continued)

Pathologic diagnosis	Frequency (%) ^c			
	Shields et al ¹⁰ (n = 57)	Santos et al ¹¹ (n = 113)	Kaeser et al ¹³ (n = 195)	Current study (n = 42)
<i>Vascular lesions</i>				
Pyogenic granuloma	8.8	2.7	1.5	
Capillary haemangioma			1	
Cavernous haemangioma		0.9	0.5	
Lymphangiectasia	1.8			
<i>Neural tumours</i>				
Neurofibroma				
Granular cell tumour				
<i>Fibrous and fibrohistiocytic proliferations and tumours</i>				
Fibroma		1.8		
Fibrolipoma		1.8		
Solitary fibrous tumour				2.4
'So-called' malignant fibrous histiocytoma				2.4

^aTotal percentage is not exactly 100 because of rounding. In each series, the type of lesion with the highest frequency is highlighted in bold.

^bTumours classified as 'sarcomas' were not included in the table.

^cTumours classified as 'sarcomas' or 'benign tumours' were not included in the table.

^dOne tumour classified as 'benign round-cell tumour' was not included in the table.

^eTotal percentage is not exactly 100 because of rounding.

semilunaris, but a supernumerary caruncle seems to be invariably an isolated developmental anomaly, with only a few reports in the literature.¹⁴ It may be found in the lower or upper eyelid, and may be singular or multiple.^{15,16} Supernumerary lacrimal punctum on the caruncle has also been reported.¹⁷ A supernumerary punctum connected to a supernumerary canaliculus and ending in a blind supernumerary sac is extremely rare.¹⁸ Caruncular abnormalities, including bilobed caruncles and ectopic caruncles, have been described in patients with Goldenhar syndrome,¹⁹ which is a congenital disorder believed to be caused by the defective development of the first and second brachial arches and the first brachial cleft during the fourth through eighth weeks of embryologic development.

Dermoid and epidermoid cysts can occur in the caruncle.²⁰ Dermoid cysts are usually ovoid and yellowish.¹¹ Both cysts are lined by squamous stratified epithelium, with skin appendages (sebaceous glands and hair follicles) in the case of dermoid cysts. Histopathologically, epidermoid cysts are indistinguishable from the epithelial inclusion cysts of squamous origin.

Inflammatory process

Several types of inflammatory processes have been described in the caruncle. Among them, the most frequent reported in the large series of caruncle lesions

are chronic non-granulomatous inflammation, lipogranulomatous inflammation, and foreign body granuloma.^{6,7,9-11} Other exceptional inflammatory process described are methicillin-resistant *Staphylococcus aureus* caruncle abscess,²¹ inflammatory pseudotumor,²² involvement of the caruncle in ocular cicatricial pemphigoid,²³ cytomegalovirus infection,²⁴ molluscum contagiosum,²⁵ spherulocystosis,²⁶ and Armillifer armillatus infection.²⁷

Secondary caruncular pigmentation

Silver deposits (argyrosis) on the eyelids, conjunctiva, and caruncle have been described after long-term application of readily available cosmetic eyelash tints.²⁸ Similarly, patients receiving long-term topical eyedrops containing epinephrine compounds can develop pigmented deposits on the conjunctiva and caruncle.²⁹

Epithelial lesions

Frequent benign skin lesions, such as seborrhoeic keratosis and actinic keratosis have been also reported in the caruncle.^{9,10} A squamous caruncular horn with gradual enlargement in a 3-month infant has been described.³⁰ On the basis of the similarities between this case and the tusks of elephants, the authors suggested that the caruncle can be a vestigial remnant of the upper incisor of lower animals.

Squamous papillomas are one of the three most frequent lesions of the caruncle and in some series, constitute the largest group of caruncular lesions.^{6,7,10} In our series, papillomas accounted for the second most frequent caruncular lesion, together with oncocytomas. A previous study found a strong association between conjunctival papillomas and certain types of human papilloma virus, mainly types 6 and 11.³¹ Viral aetiology has been proposed as a possible explanation for the variation in frequency between different series.¹² Papillomas are usually described as a frond-like mass with fine vascular tufts visible clinically in the central core of each frond. They can be removed to rule out malignancy.¹⁰ Reported recurrence rates of conjunctival papillomas vary from 6 to 27%.³² Topical α -interferon has been used successfully for some recalcitrant cases.³³ Inverted papillomas have been reported in the caruncular area, and they have a higher incidence of local invasion.³⁴ They consist of fold of papillomatous epithelium that invaginate into the underlying stroma rather than growing in the pure exophytic fashion characteristic of the common squamous papilloma.³⁴

Only one case of caruncular and a few cases of conjunctival keratoacanthoma have been described previously.¹³ Cutaneous keratoacanthoma typically shows rapid growth before undergoing spontaneous regression. The natural history of their conjunctival counterparts is unknown because of early excision.¹³ Some pathologists consider keratoacanthoma as a subtype of squamous cell carcinoma,³⁵ so complete excision of the lesion is recommended.

Epithelial premalignant lesions, such as conjunctival epithelial dysplasia and carcinoma *in situ* in the caruncle are rarer than in the conjunctiva. We found only one case of moderate epithelial dysplasia, in which dysplastic changes were observed in the lower and middle thirds of the conjunctival epithelial thickness.

Basal cell carcinoma has been reported to affect the caruncle.^{13,36–40} About 90% of the eyelid cancers are basal cell carcinomas and the conjunctiva is usually invaded secondarily from an eyelid tumour, with only very few cases of primary developing tumour at the caruncle, as it is a sun-exposed area. In our series, we found one case of basosquamous carcinoma in an old patient; the tumour presented histopathological features of both basal cell and squamous cell carcinomas. Basal cell carcinoma of the caruncle may originate from basal cells of the epithelium or infundibular cells of the hair follicles, or from pluripotent stem cells.³⁷ Surgical removal of caruncular basal cell carcinoma with clear surgical margins can be sometimes difficult. Mohs' micrographic surgery in selected cases may preserve more normal tissue than conventional surgery with less reported rates of recurrence.⁴¹ Radiation can be used as an adjuvant

therapy to help reduce the chance of tumour recurrence or orbital invasion.³⁶ Recurrences have been described even after complete excision, making long-term follow-up mandatory. Rare cases of squamous cell carcinoma,^{10,42} adenosquamous carcinoma,⁴³ mucoepidermoid carcinoma,⁴⁴ and undifferentiated carcinoma⁴⁵ of the caruncle have been also reported.

Cysts

Epithelial cysts are lesions frequently encountered at the caruncle,^{8,11} and in one large series were the most frequent lesion removed from the caruncle.⁸ Other rare epithelial cysts described in the caruncle are apocrine hidrocystoma⁹ and steatocystoma.^{46,47} In the former, the cyst is lined by an inner layer of low cuboidal secretory cells and an outer row of slightly flattened myoepithelial cells. The steatocystoma consists of a cyst lined by stratified squamous epithelium and containing sebaceous glands in its wall. Treatment consists of simple excision with removal of the cyst wall intact to reduce the risk of recurrence.

Melanocytic lesions

The majority of melanocytic lesions encountered at the caruncle are nevi. Nevi are the most frequent reported caruncular lesion in the majority of large series in the literature, as in ours, with frequency rates ranging between 33.7 and 59.5%.^{9,11,13} Classically, nevi appear near puberty and may show slight change in size or colour with time.¹⁰ Preoperative clinical diagnosis was accurate in 40% of our cases, but as suggested by Shields *et al*,¹⁰ in most instances, the lesions are removed for cosmetic reasons or to exclude the possibility of melanoma. If progressive changes in size, colour, or vascularity are noted, excision is recommended to rule out malignant transformation.

Simple caruncular freckles are rarely reported. The freckles are rarely subjected to biopsy because they are not usually confused with melanoma and they are not a cosmetic problem.¹⁰ Complexion-associated pigmentation (a better descriptive term for racial pigmentation) is also reported in the caruncle. Norn⁴⁸ noted pigmentation of the plica semilunaris and/or lacrimal caruncle in 2% of 380 white north Europeans, in 4% of 189 Mongols, and in 45% of 257 Eskimos. In Eskimos, the phenomenon was found to be bilateral in 60% and confluent with pigmentation of the bulbar conjunctiva in 18%. The author concluded that caruncular pigmentation, like other pigmentation, is racially influenced. As in our series, the majority of reported nevi are of the compound type.^{49–51} Other less frequent types are subepithelial, combined, and blue

nevi. At clinical examination, cysts are recognized in up to 65% of conjunctival nevi.⁴⁹ In contrast, conjunctival melanoma rarely, if ever, displays intralesional cysts.⁴⁹

PAM is less frequent encountered at the caruncle than nevi. In our series, we found two cases of PAM without atypia. PAM without atypia shows no progression to melanoma, whereas PAM with severe atypia shows progression to melanoma in up to 13% of cases.^{52,53} Specifically, PAM recurrence is 3.53 times more frequent to occur in lesions affecting the caruncle than in cases without caruncular involvement.⁵³ Lesions suspected clinically to be PAM at the caruncle should be excised.

Malignant melanoma has been reported to be the most prevalent malignant lesion of the caruncle. However, its occurrence on the caruncle is rare compared with its occurrence in the conjunctiva.¹³ It has been reported to occur in up to 17.5% of caruncular series in Evans' series,⁷ although the majority of series show a rate of less than 4%.^{8,9,11,13} This difference can be explained by the bias in collection of Evans' cases, which came from many sources. Reported treatments for malignant melanoma of the caruncle include wide excision, adjuvant cryotherapy, and radiotherapy, or orbital exenteration for tumours with conjunctival, skin, and orbital extensions.^{13,54} The caruncle is considered an 'unfavourable' location for conjunctival melanoma (together with palpebral, plica, and forniceal involvement, and opposed to 'favourable' location of bulbar conjunctiva and limbus), with an associated higher risk for melanoma recurrence and associated mortality.^{55–58} The conjunctiva at the limbus is constituted of dense collagen preventing the penetration of the tumour. At the caruncle, the melanoma can more easily penetrate in depth and consequently cause lymphatic dissemination.^{59,60}

Sebaceous tumours

Sebaceous gland hyperplasia and adenoma are seldom reported at the caruncle.^{6,7,10,11,13,61} Clinically, both lesions are similar and characterized by their yellow, nodular appearance, but they are distinguishable histopathologically. Sebaceous gland hyperplasia is characterized by hyperplastic lobules situated around a single duct; a normal cellular maturation sequence is observed.¹⁰ In the sebaceous gland adenoma, there is a loss of this maturation sequence.¹⁰

Sebaceous carcinoma rarely arises in the sebaceous glands of the caruncle.^{62,63} It develops most often in the eyelids, usually from the meibomian glands of the tarsus and less often from the Zeis glands of the cilia. A recent study of 60 cases from a tertiary centre revealed a single case arising from the sebaceous glands of the caruncle.⁶³ However, the caruncle may be affected in up to 25% of cases of eyelid sebaceous carcinoma.⁶⁴ The clinical

differential diagnosis of sebaceous carcinoma of the caruncle is different from those of the eyelids and includes sebaceous hyperplasia and adenoma, oncocytoma, squamous cell carcinoma, naevus, and papilloma.⁶³ The tumour should be removed with clear margins as wide as possible. Extensive cryotherapy, conjunctival reconstruction, and map biopsies to rule out subclinical pagetoid spread should be performed.^{63,65}

Oncocytoma

Oncocytoma (oxyphil cell adenoma) is a rare but typical caruncular tumour with a reported frequency of about 3.5% of caruncular lesions.^{9,10,13} In our series, we found three cases of caruncular oncocytoma (7.1% of cases). Benign oncocytomas arising in the ocular adnexa have been described in the lacrimal gland, lacrimal sac, plica semilunaris, bulbar conjunctiva, upper and lower fornices, mucocutaneous junction, and caruncle.^{66–70} Of these, the caruncular oncocytoma is by far the commonest, but it is still a rare lesion. Oncocytomas of the caruncle are more frequent in elderly women, as in our series. Its natural history is of a slowly growing painless mass. In spite of its rarity, the diagnosis should be considered when there is a caruncular swelling, particularly if the lesion appears cystic or has a bright cherry red colour. Microscopically, oncocytomas are composed of benign epithelial cells with abundant eosinophilic granular cytoplasm, which is found on ultrastructural examination to be composed of altered mitochondria. The histogenesis of caruncular oncocytomas has been reviewed by Rennie⁶⁶ who believed that the lesion arises from glands or their secretory ducts. Clinically, aggressive behaviour has not been documented in oncocytomas arising in the caruncle, whereas in other locations have indeed behaved aggressively.⁷⁰

Sweat gland tumours

Benign sweat gland tumours (for example, hidrocystoma) have been already described. A very rare case of malignant apocrine sweat gland carcinoma of the caruncle in a young patient who underwent exenteration has been reported.⁷¹

Myeloproliferative disorders

Myeloproliferative disorders have been extensively described in the ocular adnexa^{72–74} and rarely affect the caruncle. In some series of caruncular lesions, the most common lesion was benign lymphoid hyperplasia,^{9,11} with a reported frequency of about 3% of all caruncular lesions, similar to our experience. However, in large

series of conjunctival lymphoid lesions, lymphoma was detected in 56% of 117 cases and benign lymphoid hyperplasia in 17% of cases. Only 7% of the 117 cases of conjunctival lymphoid lesions occurred at the caruncle.⁷²

Typical clinical presentation is of a slow growing salmon coloured lesion, but definite diagnosis requires always tissue biopsy. Isolated case reports of caruncular myeloproliferative lesions include benign lymphoid hyperplasia,^{75–77} lymphoma,⁷⁸ Langerhans cell histiocytosis,^{79,80} and granulocytic sarcoma.⁸¹

Lymphoid tumours of the conjunctiva are reported to be associated with systemic lymphoma in 31% of patients. Systemic lymphoma is found more often in those patients with forniceal or midbulbar conjunctival involvement, and in those with multiple conjunctival tumours.⁷² The authors advised the long-term systemic follow-up, because related systemic lymphoma can manifest many years later.⁷²

Vascular lesions

Pyogenic granuloma is the most frequent vascular lesion with a reported rate ranging between 1.7 and 8.8% of caruncular lesions.^{8,10,11,13} Pyogenic granuloma of the caruncle appears as a fleshy vascular mass usually after surgical or accidental trauma.¹⁰ It may resolve on its own or after application of steroid drops. Shields *et al*¹⁰ described two cases occurring after medial rectus muscle surgery for strabismus. Medial rectus muscle surgery may lead to granulation tissue in the caruncle because the medial rectus sheath has fibres that penetrate the deep structures of the caruncle.

Other reported vascular lesions at the caruncle are capillary hemangioma,^{9,13} cavernous hemangioma,^{9,11,13} lymphangiectasia,¹⁰ lymphangioma,⁸² and Kaposi sarcoma.⁸³

Neural tumours

Exceptional cases of neurofibroma,^{7,84} neurilemoma (schwannoma), either isolated⁸⁵ or as part as Carney complex⁸⁶ (myxomas, spotty pigmentation, endocrine overactivity, and conjunctival schwannomas), and granular cell tumour^{9,87} have been reported in the literature.

Myogenic tumours

Only one case of primary leiomyoma affecting the caruncle has been reported in the literature.⁸⁸ The authors suggested that the origin of the lesion was either from pericytes or from the medial part of the capsulo-palpebral muscle of Hesser.

Fibrous and fibrohistiocytic tumours

Rare cases of fibroma,^{6,7,8,11} fibrolipoma,^{8,11} solitary fibrous tumour,² and 'so-called' malignant fibrous histiocytoma⁸⁹ have been reported in the caruncle. These lesions are much less frequent than their counterparts affecting the eyelids, orbit, or conjunctiva. Interestingly, and in spite of their rarity, we found one case of solitary fibrous tumour (previously reported),² and one case of 'so-called' malignant fibrous histiocytoma in our series.

Metastatic tumours

Only one case of caruncle tumour as presenting metastatic carcinoid tumour⁹⁰ and other case of caruncle tumour as the first sign of metastatic lung carcinoma⁹¹ have been reported previously. The presence of a conjunctival mass in patients with known prior malignancy and associated ocular and systemic metastases is suggestive of a metastatic lesion.⁹² Conjunctival metastases represent a very bad prognostic sign for the patient; in addition to the high incidence of metastatic disease in other organs, the mean survival time from diagnosis is reported to be only about 9 months.⁹²

Conclusion

Lesions of the caruncle are uncommon and very diverse, which makes clinical diagnosis very difficult. Reported preoperative diagnosis is correct only in about half of the cases, which is explained by the large pathologic variety of lesions encountered at the caruncle. Nevi are the most frequent reported lesions. Malignant lesions are very uncommon. Although there is a reported clinical overestimation of malignancy, malignant lesions can be fatal. Any change in colour, size, or vascularization of a caruncular lesion should be excised. Pathological examination should be mandatory. On account of the enormous variety of reported cases, close collaboration between eye pathologists, dermatopathologists, surgical pathologists, and soft tissue pathologists may be needed in selected difficult cases.

Method of literature search

A search of the PubMed database 1966–2007 was conducted using various combinations of the key words such as caruncle, caruncular, lesion, tumour, and conjunctiva. Articles in all languages were considered, provided that the non-English articles included English abstracts. Relevant articles that were cited in the reference lists of the retrieved articles were also included.

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