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REVIEW ARTICLE

Malignant lesions of the caruncle

Pav Gounder[1]✉, Dinesh Selva[2] and Saul N. Rajak[1]

Caruncle malignancy is rare, but signs of disease can be easily missed by both patients and clinicians. There is significant potential for significant morbidity and even mortality from delayed diagnosis and treatment. Clinical features of primary malignant cancer include rapid growth, pigment deposition, ulcerated surface and bleeding. Malignant diagnoses include lymphoproliferative disease, basal cell carcinoma, squamous cell carcinoma, sebaceous carcinoma and malignant melanoma. Increased pigmentation is associated with melanoma, yellow coloured deposition with sebaceous carcinoma and a salmon-pink hue with lymphoproliferative disease. Treatment involves excision with margin control which may necessitate exenteration. Metastases to cervical and preauricular lymph nodes has been reported.

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INTRODUCTION

Caruncle malignancy is rare, but signs of disease can be easily missed by both patients and clinicians. There is significant potential for significant morbidity and even mortality from delayed diagnosis and treatment.

ANATOMY

The caruncle (*caruncula lacrimalis*) is a pink, fleshy nodule, located in the most medial aspect of the palpebral fissure within the lacrimal lake (*lacus lacrimalis*). It measures 4–5 mm horizontally and 3–4 mm vertically [1, 2]. It contains accessory lacrimal glands, hair follicles, goblet cells, sweat glands, smooth muscle fibres and sebaceous glandular tissue [1, 3–5]. It develops embryologically as a separation from the lower eyelid and is not formed from the conjunctiva [1].

EPIDEMIOLOGY

The prevalence and incidence of caruncular lesions are unknown. However, tissue biopsy of the caruncle comprise 1% or less of all ophthalmic specimens, indicating them to be rare [4, 6, 7]. Malignant lesions of the caruncle are even rarer, comprising 2.5–5% of all biopsied caruncular lesions [4, 6, 8, 9]. In our multicentre series 10/281 (3.56%) caruncular biopsies in Australia and the United Kingdom from 2000 to 2022, were found to be malignant (unpublished). Reported malignancies of the caruncle include lymphoma, basal cell carcinoma, squamous cell carcinoma, sebaceous carcinoma, and melanoma.

CLINICAL PRESENTATION

Although the caruncle lies in an exposed position, subtle changes may go unnoticed as the caruncle is not typically examined in eye or even oculoplastic examinations. Patients generally notice growth over a period of months and may describe increase in pigmentation or redness. Lesions of the caruncle may interfere with tear drainage and cause epiphora given its proximity to the lacrimal puncta [10]. Discomfort and pain is rarely reported although may be more likely if lesions involve neighbouring tissue. Growth of lesions can extend to cutaneous structures in the medial canthus, surrounding conjunctiva and deep to the medial orbit. Irregular or ulcerated surfaces to caruncular lesions have been described as well as bleeding.

Rapid growth over a period of weeks may alert the clinician to a potential malignant lesion. Other features of malignant lesions include pigment deposition, ulceration or an irregular surface and bleeding. Malignant lesions tend to present in patients older than 50 years but can present as young as 4 years [11].

MANAGEMENT

Examination of patients should include checking for local and regional spread. The upper and lower eyelids should be everted, and conjunctiva examined for local extension of disease. Prognosis is poorer for both conjunctival and cutaneous malignancy that involves the caruncle secondarily with higher rates of recurrence and metastasis [12, 13]. Regionally, lymph nodes should be palpated in the preauricular, submandibular, and cervical regions.

If there is suspicion of deeper extension a T1 weighted orbital MRI with fat suppression should be requested. Circulating blasts in the peripheral blood film may raise the suspicion of a lymphoproliferative disorder.

Given the potential diagnoses and location of the caruncle, lying in front of the medial orbit, clinicians should have a low threshold for biopsy when any changes have been noticed in the caruncle. Once malignancy is confirmed, appropriate systemic imaging should be requested as well as discussion at the relevant cancer multidisciplinary meeting.

[1]The Sussex Eye Hospital, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK. [2]South Australian Institute of Ophthalmology, Royal Adelaide Hospital, Adelaide, SA, Australia. ✉email: pav.gounder@gmail.com

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Table 1. Reported cases of caruncular lymphoma.

Case, ref.	Age, gender	Lymphoma type	Symptoms	Appearance	Treatment
Ash [36]	42	B-Cell Lymphocytic	Growth for 6 months	–	Excision
Fradkin et al. [37]	42, F	T-Cell Cutaneous	Epiphora	Enlarged, pale	Radiotherapy
Santos and Gomez-Leal et al. [17]	75, M	B-Cell Lymphocytic	–	Salmon coloured	–
Minasian et al. 1999 [38]	79, M	B-Cell NHL MALT	Red eye	Enlarged, salmon-pink swelling	Chemotherapy (chlorambucil)
Shields et al. [39]	72, F	T-Cell	Growth for 3 weeks	Pink, multinodular mass	Radiotherapy
Kaeser et al. [6]	48, M	B-Cell MALT	Growth for 24 months	–	Excision
Østergaard et al. 2005 [18]	F	B-Cell MALT	Growth	Salmon coloured, vascularised	–
Østergaard et al. [18]	–	B-Cell MALT	–	–	–
Østergaard et al. [18]	–	B-Cell Mantle cell	–	–	–
Østergaard et al. [18]	–	B-Cell MALT	–	–	–
Ting et al. [40]	85, F	T-Cell Anaplastic large cell	Growth for 3 months	Irregular surface, pink nodule	Palliative due to systemic disease
Gounder et al. 2022	80, F	B-Cell High Grade	Growth for 6 weeks	Pink, vascularised	Excision
Gounder et al. 2022	61, F	B-Cell Marginal zone	Growth for 5 months	Firm, vascularised	Chemotherapy
Gounder et al. 2022	71, F	B-Cell Lymphocytic	–	Cystic	–
Gounder et al. 2022	75, F	B-Cell MALT	–	–	–

– No information available.

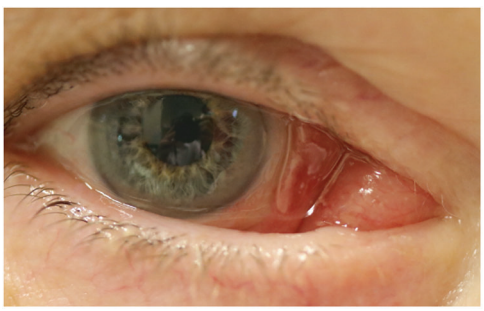

Fig. 1 High grade B-cell lymphoma. An 80 year old female with an enlarged, vascularised caruncle.

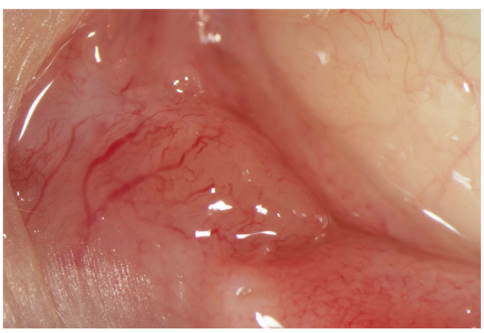

Fig. 2 Marginal zone lymphoma. A 61 year old female with an enlarged, vascularized caruncle.

MALIGNANT LESIONS

A literature review of malignant caruncular lesions was conducted with results described below. Reports without any clinical information provided were not included in this review.

LYMPHOPROLIFERATIVE LESIONS

Fifteen cases (11 reported, and four from our unpublished series) of caruncular lymphoma are summarised in Table 1. The demographics and diagnosis are consistent with other lymphomas of the ocular adnexa with 12/15 (80%) being B-cell lymphomas with an average age of 64 years (range 35–85), and a slight female preponderance (9/15, 60%) [14–16].

At least 13 cases of reactive lymphoid hyperplasia of the caruncle have been reported [8, 17–19]. Patients with lymphoid hyperplasia tend to present at a younger age (average 38 years) [8, 17, 18].

Caruncular lymphoproliferative lesions are typically pink or salmon coloured fleshy lesions (Figs. 1, 2). They should be managed by a multidisciplinary haematology-oncology team, Radiotherapy and chemotherapy are the mainstay of treatment and sometimes surgical debulking is undertaken.

BASAL CELL CARCINOMA

To date, 14 cases of primary basal cell carcinoma (BCC) of the caruncle have been reported (Table 2). The mean age of these patients is 62 years (Range of 24–82) and is consistent with an the average age of diagnosis of eyelid BCC (60) [20]. As with eyelid and other cutaneous involvement, cases of caruncular BCC tend to disproportionately affect males (M:F 10:4) [20, 21].

Of patients with clinical descriptions provided, all reported a period of growth of the lesion over 2–12 months. One patient

Table 2. Reported cases of caruncular BCC.

Case, ref.	Age, gender	Symptoms	Appearance	Treatment	Recurrence/Follow up
Shields et al. [41]	61, F	–	–	Excision	–
Poon [42]	74, M	Growth for 6 months	Multilobulated, vascularised, pink	Excision	–
Hirsch et al. [34]	72, M	–	–	Excision	–
Meier [43]	24, M	Growth for 3 months	Nodule, vascularised, white, red centre	Excision	No 14 months
Mencia-Guitierrez et al. 2005 [44]	80, M	Growth for 5 months	Irregular, brown-black, vascularised	Excision	No 7 years
Østergaard et al. [22]	60, F	Growth Discomfort	Lobulated, cystic, vascularised, pale	Excision	Orbital recurrence
Rossman et al. [45]	82, M	Growth for 2–3 months	Firm, pale, whitish-yellow	Excision-Adjuvant radiotherapy	No 6 months
Kaeser et al. [6]	72, F	–	Cystic	Excision	No
Kaeser et al. [6]	52, M	–	Solid, black	Excision	No
Levy et al. [4]	67, M	–	–	Excision	–
Lee et al. [16]	73, M	–	Lobulated, brown-black, telangiectatic, irregular surface	Excision Intraarterial chemotherapy	Yes following intraarterial chemotherapy
Fino et al. [46]	24, F	Growth for 6 months	Lobulated, brown	Excision	No 12 months
Ugurlu et al. [47]	67, M	Growth for 12 months	Fragile, nodular, whitish-pink, vascularised	Excision	No 33 months
Mihailovic et al. [48]	58, M	–	Brown pigment	Excision	No 6 months

Table 3. Reported cases of primary SCC of the caruncle.

Case, ref.	Age, gender	Symptoms	Appearance	Treatment	Recurrence/Follow up
Nylander and Atta [49]	76, F	Growth for several months	Firm, ulcerated surface	Excision	No
Hirsch et al. [34]	46, F	Growth	Pink, vascularised	–	–
Dithmar et al. [50]	48, –	Growth for 3 months	Flesh coloured, papillary tumour	Excision	–
Van de Put et al. [25]	38, M	Painful growth for 3 weeks Epiphora	Red, vascularised, white yellow discharge, brown-black pigmentation	Excision Radiotherapy	No
Van de Put et al. [25]	72, F	Painful growth	White discharge	Excision Radiotherapy	Yes, orbital
Sagili et al. [26]	54, M	Growth for 3 months	–	Excision Adjuvant topical MMC 0.04%	Metastasis to submandibular region
Sagili et al. [26]	60, F	Growth	Leukoplakic, telangiectasia	Excision Adjuvant topical 5-FU	Yes 2 months after excision treated by orbital exenteration
Sagili et al. [26]	69, F	Growth	–	Excision	No
Gounder et al. 2022	70, F	–	Pink nodule with bleeding	Excision	No—despite involved margins 16 years

Table 4. Reported cases of caruncular sebaceous carcinoma.

Case	Age, gender	Symptoms	Appearance	Treatment	Recurrence/Follow up
Kielar [51]	77, M	Growth for 1 year	Bleeding, umbilicated, vascular	Excision	No 29 months
Luthra et al. [19]	54, M	Growth	–	Excision	Yes—treated with orbital exenteration
Folberg et al. [52]	34, M	Growth for 1 month	–	Excision (Mohs)	Yes—exenteration Submandibular metastasis
Debnath et al. [53]	77, F	Growth for 3 months	Brown mass	Excision	–
Santos and Gomez-Leal [17]	75, F	Rapid growth	–	–	–
Yen et al. [54]	34, M	Growth for 6 months	Yellowish nodule, vascular	Excision (exenteration)	Preauricular metastasis 1 year later
Shields et al. [55]	68, M	Growth	Multinodular, yellow mass, vascularised	Excision	–
Kaeser et al. [6]	60, F	Growth	Non pigmented	Excision	No 17 years
Østergaard et al. [18]	62, M	–	–	–	–
Østergaard et al. [18]	81, M	–	–	–	–
Song et al. [28]	35, M	Growth	Vascularised, firm	Excision	Yes, exenteration. Metastasis to regional lymph nodes
Rudkin and Muecke [57]	83, M	Growth	Polypoid mass	Excision and cryotherapy Adjuvant topical MMC 0.04%	No 29 months
Pfeiffer et al. [58]	69, M	–	–	Excision	Submandibular spread after 11 years
Zhang and Sun [56]	63, M	Growth for 3 years	Bleeding, irregular surface	Excision + MMC 0.04%	No 12 months
Eneh et al. [59]	49, M	–	–	Excision	Preauricular lymph node involvement and parotid gland
Salazar-Villegas et al. [60]	74, F	Growth for 1 year	Irregular surface, vascularised and yellow deposits	Excision	No 3 years
Boccalatte et al. [61]	63, M	–	Erythematous, lobulated, tortuous vessels	Excision and sentinel lymph node biopsy	–

Table 5. Reported cases of melanoma of the caruncle.

Case	Age, gender	Symptoms	Appearance	Treatment	Recurrence/Follow up
Ash [36]	38, M	Growth for 6 years	Pigmented	Excision	No 15 years
Luthra et al. [19]	56, M	Increased pigmentation	Pigmented	Excision	Yes and died from metastatic disease
Luthra et al. [19]	62, M	Growth for 2 years	Pigmented	Excision	Yes 12 months
Santos and Gomez-Leal [17]	15, M	Growth, increased pigmentation	Pigmented lesion at the site of previous biopsied compound naevus	–	–
Santos and Gomez-Leal [17]	66, M	Growth	Pigmented	–	–
Santos and Gomez-Leal [17]	M	Growth	Pigmented	–	–
Santos and Gomez-Leal [17]	M	Growth	Pigmented	–	–
Kalski et al. [62]	84, F	Growth for 3 months	Multilobulated, excoriated, pink, irregular foci of pigmentation	Excision and cryotherapy	–
Esmaeli et al. [63]	49, M	–	Pigmented	Excision and sentinel lymph node biopsy	–
Østergaard et al. [18]	70, F	Growth from PAM lesion	–	–	–
Østergaard et al. [18]	82, M	–	–	–	–
Kikuchi et al. [64]	84, F	Growth for 2 years and pigmentation	Pigmented nodule	Excision Topical IFN alpha-2b	No 78 months
Maeda et al. [65]	72, M	Growth for 3 years	Black spot	Excision and sentinel lymph node biopsy	No 10 years
Gounder et al. 2022	65, M	–	Pigmented, lobulated	Excision	No
Gounder et al. 2022	66, M	–	Mildly pigmented	Excision	–
Gounder et al. 2022	91, F	Growth, discomfort	Pedunculated, vascular lesion	Exenteration	No 5 months

described discomfort from the lesion [18]. The lesions have been described as vascularised (4), lobulated (4), cystic (2) and with widely varied colouration, including white, red, pink, brown and black.

Surgical excision with a margin was undertaken for all reported caruncular BCCs. Two recurrences have been reported, with orbital invasion in one and recurrence at the initial resection margin on the conjunctiva in the other, following 3 months of adjuvant intraarterial chemotherapy [16, 22].

SQUAMOUS CELL CARCINOMA (SCC)

To date, 8 cases of primary SCC of the caruncle have been reported and a further case from our unpublished series is summarised in Table 3. The mean age at the time of diagnosis is 59 years (range of 38–76). This is comparable to the average age of diagnosis of SCC in the eyelid [23]. Despite cutaneous SCC being more twice frequently more prevalent in males, caruncular SCC has been reported more often in females (M:F 2:6) [21].

Caruncular SCCs have a varied appearance, with vascularisation, ulceration, bleeding and discharge reported. Excision and radiotherapy have been utilised in treatment of caruncular SCC. One centre utilised topical adjuvant antimetabolites following excision, a practice used in the treatment of conjunctival SCC [24].

Two cases of caruncular SCC have recurred following excision. One case recurred in the orbit 2 years after excision and radiotherapy [25]. This was treated with orbital exenteration but unfortunately further recurrence occurred in the socket, ethmoid sinus and palate which led to the patient's death. In the other case, orbital recurrence occurred 2 months after excision and topical 5-Fluorouracil which was treated with exenteration [26].

SEBACEOUS CARCINOMA

To date, 17 cases of sebaceous carcinoma (SC) of the caruncle have been reported with clinical information available. The mean age of patients is 62 years (range of 34–83) (Table 4). This is younger than the median age of sebaceous carcinoma of the eyelid (73 years) [27, 28]. It may occur more frequently in men (13/17 (76%) cases), in contrast to eyelid sebaceous carcinoma which is probably more common in women (although this remains an area of uncertainty).

Two cases of caruncular SC were described as being 'yellow' similarly to the description of some cases of eyelid sebaceous carcinoma [27–29]. Caruncular bleeding occurred in two other cases. All reported cases were treated with excision. Orbital recurrence or metastasis (typically to submandibular, preauricular and parotid glands) occurred in 6/15 (40%) cases.

MELANOMA

To date, 13 cases of primary malignant melanoma of the caruncle have been described and an additional three cases are summarised in Table 5. The average age at the time of diagnosis is 62 years (Range 10 to 91 years. This is consistent with the age of diagnosis of conjunctival melanoma(62 years) and the peak incidence of cutaneous melanoma of the head and neck (50–80 years) [30, 31]. It occurs in men in 12/16 (75%) of cases in contrast to cutaneous, eyelid and conjunctival melanoma in which the incidence is balanced between males and females [21, 31, 32].

Growth and increased pigmentation are common signs of disease (Fig. 3). Excision with wide margins is the mainstay of treatment. Sentinel lymph node biopsy and adjuvant treatments such as interferon may improve prognosis.

Although follow-up data is sparse, there has been two reported cases of recurrence following excision [19]. A 56-year-old male developed local recurrence as well as preauricular and parotid gland metastasis 3 years following excision of the recurrence. He died 7 years after initial diagnosis of caruncular melanoma with generalised metastasis of disease. The other case of recurrence required orbital exenteration and was reported disease free at 12 months. Caruncular involvement in conjunctival melanoma is associated with worse outcomes. In a series of 40 patients with previously untreated conjunctival melanoma, all four patients with caruncular involvement died from metastatic disease [33]. Primary melanoma of the caruncle should be treated similarly with close follow-up and surveillance for metastatic disease.

Fig. 3 Melanoma. A 91 year old with an enlarged caruncle.

RARER LESIONS

There have been four reports of Kaposi's sarcoma of the caruncle from two separate series in 1997 and 2006 (Table 6) [18, 34]. There were clinical descriptions of two of these lesions, one as a red nodule the other as a haemorrhagic cyst. All patients have been aged in their forties and all four patients were HIV positive. Treatment and recurrence data is not available. With the introduction of highly active antiretroviral therapy, the incidence of Kaposi's sarcoma in general has decreased significantly and it would be expected that caruncular involvement in the future will be rarer still [35].

Metastatic spread of malignancy to the caruncle is very rare with only two reported cases in the literature. One patient developed a large cell neuroendocrine carcinoma, metastatic lung cancer prior to diagnosis of their lungs, liver and bones. The other, developed a metastatic carcinoid lesion of the caruncle that appeared to erythematous and had associated bleeding. The primary lesion was believed to originate in the small intestine.

Other rare carcinomas have been reported in the caruncle and include apocrine adenocarcinoma, rhabdomyosarcoma and plasmacytoma.

CONCLUSION

Malignant lesions of the caruncle are rare but are very high risk, especially for SC and melanoma. An assessment of the caruncle should be incorporated as part of the eyelid examination and clinicians should have a low threshold for biopsy given the potential for significant morbidity and mortality. Suspicions for malignancy should be raised in older patients and those who present with lesions that bleed or lesions that have an irregular surface. A clinical appearance of increased pigmentation, yellow deposition, salmon-pink hue correlate with melanoma, SC and lymphoma respectively.

Table 6. Rarer malignancies of the caruncle.

Case, ref.	Diagnosis	Age, gender	Symptoms	Appearance	Treatment	Recurrence/Follow up
Hirsch et al. [34]	Kaposi sarcoma	41, M	–	Red nodule	–	–
Hirsch et al. [34]	Kaposi sarcoma	43, M	–	–	–	–
Ostergaard et al. 2006 [18]	Kaposi sarcoma	36	–	Cyst with haemorrhage	–	–
Ostergaard er al. 2006 [18]	Kaposi sarcoma	45	–	–	–	–
Lie et al. [66]	Metastatic lung carcinoma	76, F	Growth for 3 months	White-yellowish, glassy, round	Chemotherapy	–
Gritz and Rao [67]	Metastatic carcinoid tumour	70, F	Growth for 3 weeks with bleeding	Nodular, erythematous mass	Excision, oncologist referral	–
Duke et al. [68]	Apocrine adenocarcinoma	34, M	Growth for 18 months	–	Orbital exenteration	No, 21 month follow-up
Shashni et al. [69]	Apocrine adenocarcinoma	60, M	Growth for 3 months	Firm, pink, lobulated surface with orbital extension	Orbital exenteration Adjuvant radiotherapy	No, 4 month follow-up
Mendez et al. [11]	Rhabdomyosarcoma (embryonal)	4, M	Growth for 1 month	Vascularised, nodular	Excision	–
Ramstead et al. [70]	Rhabdomyosarcoma (alveolar)	54, F	Growth for 1 week	Pink, multilobulated	Excision Chemotherapy	Yes, 9 months later treated with exenteration and then further recurrence to abdomen, ispilateral parotid gland and contralateral orbit
Cooper et al. [71]	Plasmacytoma	81, M	Epiphora Growth for 4 weeks	Friable, bleeding, salmon flesh colour	Excision	No, 18 months
Kremer et al. [72]	Plasmacytoma	70, M	Growth for 6 months	Salmon-pink	Excision	No
Bonaffini et al. [73]	Solitary fibrous tumour	78, M	Growth for 3 months Diplopia Decreased vision	Fleshy, vascularised	Excision	No
Rodman et al. [74]	Mucoepidermoid carcinoma	57, M	Epiphora	Vascular fleshy	Excision	No, 16 month follow-up
Harbiyeli et al. [75]	Pilomatrix carcinoma	45, M	Growth for 3 months	Pink, smooth, non vascular	Excision and cryotherapy Topical bevacizumab for 3 months	No, 12 month follow-up
Lam [76]	Undifferentiated carcinoma	66, M	Growth for 3 months	Firm, erythematous	Excision	No, 24 month follow-up

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AUTHOR CONTRIBUTIONS

PG was responsible for designing the review protocol, writing the protocol and report, conducting the search, screening for potentially eligible studies, extracting and analysing data, interpreting results, updating reference lists. DS was responsible for designing the review protocol and screening potentially eligible studies. He provided feedback on the report. SNR was responsible for designing the review protocol and providing feedback on the report.

COMPETING INTERESTS

The authors declare no competing interests.

CONSENT TO PARTICIPATE

Patient consent was received for the use of Figs. 1, 2, 3 in published media.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Pav Gounder.