

Malignant Melanoma of the Lacrimal Sac: Case Report and Major Review with Treatment Update

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Abstract

Purpose: To present a rare case of Primary Lacrimal Sac Melanoma, and review all reports of this condition in the literature to date.

Methods: In this review the clinical characteristics, presenting symptoms, treatment and morbidity of all patients with lacrimal sac melanoma reported in the literature from 1926 to the present. We have also discussed new approaches available for adjuvant radiotherapy in the context of this frequently recurrent tumour.

Results: Primary Melanoma of the Lacrimal Sac is a rare disease which is frequently diagnosed late. Common presenting symptoms include epiphora, blood-stained tears and painless swelling. Intensity modulated radiation therapy appears to hold promise in the adjuvant treatment of this disease, to reduce morbidity and mortality from recurrence and/or metastasis.

Conclusions: Existing case series and reports of Lacrimal Sac Melanoma describe a variety of treatment regimens and poor follow-up - highlighting the lack of a widely accepted strategy to prevent recurrence of disease. This case and review reminds practitioners of presenting signs and symptoms that should raise suspicion of Lacrimal Sac Melanoma, and a contemporary approach to adjuvant radiation therapy.

Keywords: Lacrimal sac, Melanoma

Introduction

Chronic dacryocystitis is often the only presenting symptom in lacrimal sac tumours. Lacrimal sac melanomas form an extremely rare subgroup of these tumours, with less than 50 documented in the literature. Although they are rare, the life threatening nature of these tumours due to propensity for local recurrence and metastasis makes their early diagnosis and management paramount for the improved survival of patients. A case of primary lacrimal sac melanoma is presented, with a contemporary approach to radiation therapy in this disease.

Case

A 65-year-old Caucasian woman was referred to the Ophthalmology Department at Cairns Base Hospital (Queensland, Australia) with an 8-month history of chronic dacryocystitis, and painful mass over the left medial canthus, not responding to oral antibiotics. Examination revealed a firm swelling over the left medial canthus extending above the medial canthal tendon. The remainder of the eye examination was unremarkable. She received 4 days of intravenous antibiotic therapy without significant improvement. Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain and orbits during her admission showed a soft tissue mass of 21x14mm in the region of the lacrimal sac, with invasion through the lateral wall of upper nasal canal and anterior ethmoidal air cells (Figure 1). Probing and syringing of the canaliculi showed obstruction and 2 weeks later she underwent a left dacryocystorhinostomy (DCR). Within the lacrimal sac, an irregular dark brown mass was found fully adherent to the sac wall (Figure 2). Histologic examination showed a malignant tumor consisting of ovoid to spindle-shaped cells with moderately frequent mitotic figures and deposits of melanin on high power view (40x) (Figure 3). Immunohistochemistry staining was strongly positive against S100, and melanoma markers HMB45 and Melan-A, confirming the diagnosis of malignant melanoma.

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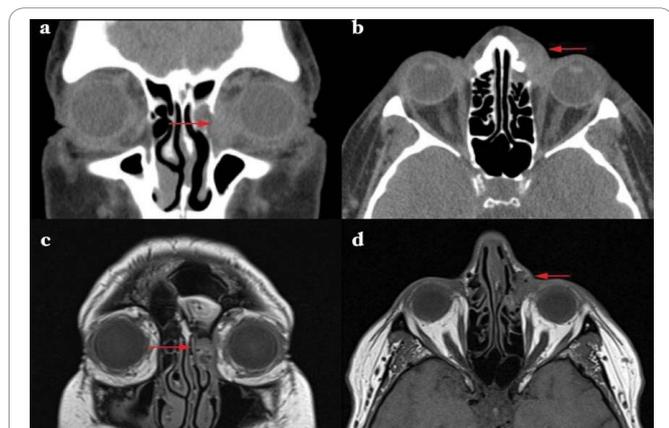


Figure 1: Imaging demonstrating mass in the lacrimal sac and nasolacrimal duct, with invasion into the anterior ethmoidal air cells: CT a) coronal and b) transverse images; MRI T2 c) coronal and d) transverse images.



Figure 2: a) and b) Opened lacrimal sac revealing melanoma during DCR; c) dark pigmented melanoma after excision.

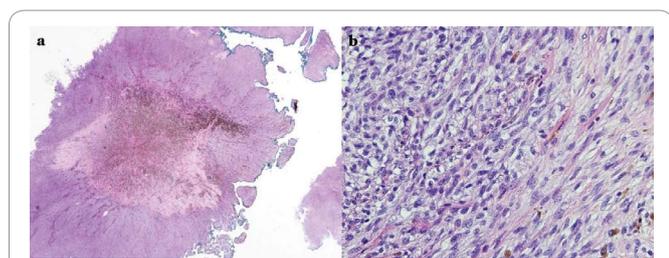


Figure 3: Hematoxylin and Eosin staining showing: a) Malignant melanoma deep to surface epithelium; b) higher magnification showing spindle and ovoid shaped tumor cells with moderately frequent mitotic figures and deposition of melanin.

No regional lymphadenopathy was present and further staging CT and positron emission tomography (PET) scans excluded distant metastases. Two months after her DCR, the patient underwent left medial maxillectomy, ethmoidectomy and medial orbital wall resection at another institution (Royal Prince Alfred Hospital, Sydney, Australia). Histology of the excised tissue revealed malignant melanoma ulcerating the lacrimal duct mucosa, with infiltration into the adjacent maxillary bone and skeletal muscle.

The patient returned to Cairns Base Hospital and received adjuvant radiotherapy with volumetric modulated arc therapy (VMAT). Traditionally, intensity modulated radiation therapy (IMRT) is used in these cases. As well as VMA T, IMRT and 3-dimensional conformational radiotherapy (3DCRT) were planned for comparison. These plans were optimized to best spare critical structures whilst achieving acceptable target coverage to limit local recurrence and distant spread. The patient received 30 sessions of radiotherapy (54 Gy) over 6 weeks to the entire operative bed.

Six years after completion of radiotherapy there was no local recurrence of the tumor or evidence of metastasis.

Discussion

Primary malignant melanoma of the lacrimal sac is extremely rare, with fewer than 50 reported in the literature to the best of our knowledge [1-30]. It represented only 3.5% of all lacrimal sac tumors in a review by Stefanyshyn and coworkers [15]. The average age at diagnosis in this review was 59 (range 27-81) with no sex predilection (Table 1). Lacrimal sac melanomas present insidiously and masquerade as chronic dacryocystitis, with early symptoms such as epiphora (38%), blood-stained tears (44%) and painless swelling (42%) most frequently reported (Table 2). Dacryocystorhinostomy is not usually performed for many months or until development of later signs such as blood-stained tears and epistaxis [15]. Flanagan & Stokes proposed that the triad of chronic dacryocystitis, blood reflux and a mass above the medial canthal tendon should alert the clinician to the presence of a lacrimal sac malignancy [31].

Diagnostic delay is likely the overwhelming cause for the poor survival outcomes in this disease. Even when presenting for specialist review, patients with lacrimal sac malignancy are diagnosed late due to the overlap with chronic dacryocystitis in the presenting symptoms of chronic watering and limited early visibility of the lacrimal sac [32]. The low index of suspicion, insidious onset and diagnostic delay mentioned, contribute to the spread of the tumor through vascular and nasolacrimal routes [33-34]. Of the 44 cases of lacrimal sac melanoma in the literature, only 25 have reported follow up times (mean 14 months). Thirty-two of the reported cases mentioned monitoring for relapse, and 20 of these (45%) did have tumour recurrences (Table 3). Of these, there were only five reported deaths - implying a survival of 89%. This again is likely due to poor longterm data in this disease, rather than treatment success. A retrospective case series of mucosal melanomas of the head and neck reported a 2- and 5- year overall survival of only 64% and 38%, respectively [35].

	Age (years)			Sex		Total
	Range	Mean	Median	Male	Female	
Melanoma	27-81	59	61	30	25	45

Table 1: Characteristics of Patients with Lacrimal Sac Melanoma.

Symptom/s at Presentation	Number of patients
Epiphora	17 (38%)
Palpable mass	19 (42%)
Bloody discharge / tears	20 (44%)
Epistaxis	4 (9%)
Motility Restriction	1 (2%)

Table 2: Clinical Presentation of lacrimal sac melanomas.

Treatment	Number	Number Followed Up	Recurrence Number (Rate, %)
Removal of tumour at time of DCR	17	9	8 (89)
Removal of tumour at time of DCR + radiation	3	2	2 (100)
Removal of tumour at time of DCR + radiation + chemotherapy	1 (+1 planned, refused)	1	1 (100)
En bloc excision + wide excision bony wall	7	6	2 (33)
En bloc excision + wide excision bony wall + radiation	10	10	4 (40)
En bloc excision + wide excision bony wall + radiation + chemotherapy	1	1	1 (100)
En bloc excision + wide excision bony wall + chemotherapy	2	2	2 (100)
Exenteration + wide excision bony wall + radiation	1	1	0 (0)

Table 3: Modalities of treatment for lacrimal sac melanomas.

The pathogenesis of lacrimal sac melanomas is not well understood as melanocytes are not normally present in the lacrimal sac, but are routinely seen in the adjoining conjunctiva. It has been postulated that lacrimal sac melanoma may originate from primitive melanosomes, either laid down beneath the epithelium during ectodermal downgrowth, or migrating from the conjunctival sac within the epithelial mucosa into the lacrimal apparatus during embryologic development [12]. Histologically they may difficult to differentiate from carcinomas, sarcomas and lymphomas, and requires special immunohistochemical staining with melanoma-specific markers such as S-100 and HMB-45 to confirm diagnosis [19].

Malignant melanoma of the lacrimal drainage apparatus can also be secondary, from spread of conjunctival tumours [36]. Recently, 5 cases of lacrimal drainage apparatus melanomas have been reported in patients who initially presented with conjunctival melanoma [36]. Satchi and coworkers report a much higher rate of lacrimal drainage apparatus involvement in conjunctival melanoma (9.6%), than previously described [36]. The authors hypothesize that melanosis may spread from the conjunctiva to the lacrimal sac intraepithelially, or via exfoliation of cells into tears.

Lacrimal sac melanomas share many features with other mucosal melanomas of the head and neck, which are generally far more aggressive than their cutaneous counterparts, and carry a much higher rate of local recurrence and metastasis. Malignant melanomas in this region are highly invasive with involvement of the nasolacrimal ducts and in some cases, the medial orbital wall [12,32,34]. A review of 15 cases of mucosal melanomas of the head and neck by Hoyt and coworkers revealed an average survival after treatment of 1.8 years, and 5-year survival rate of only 10% [33]. A further study by Gleizal and colleagues found that 73% (15 /21) of lacrimal sac tumors recurred.²⁴ Prognostic predictors for melanomas of the head and neck have yet been elucidated [37,38].

Histologic cell type is a significant predictor of prognosis in uveal melanomas. Spindle A type is associated with the best 5-year survival (90-100%), followed by spindle-B (66-75%), mixed (spindle B and epitheloid - 50%) and epitheloid (25-33%) [39,40]. Prognostic factors have not been elucidated for head and neck melanomas, nor the role of histologic predictor. The main cell types described are spindle, epitheloid, mixed, and undifferentiated (small blue round cell or larger pleomorphic cells). The undifferentiated cell type has been suggested to be poor prognostic predictor, but this was not consistently found in other studies [37,38]. The rarity of malignant lacrimal sac melanoma means that a clear consensus on prognostic factors and treatment of this disease is lacking.

Traditionally, suspected lacrimal sac tumors are treated with incisional biopsy of the sac under frozen section, followed by dacryocystectomy once diagnostic confirmation is achieved [41]. This is followed by definitive therapy including resection and adjuvant chemo- or radiotherapy. This strategy has lost favour in recent years, as it can lead to inadequate initial clearance of extensive lesions [41]. Currently, wide-field en block resection of the entire nasolacrimal system, with medial maxillectomy, total ethmoidectomy and medial orbital floor resection appears to be the most favoured surgical management in preventing local recurrences [16,17,31]. The benefit of adjuvant radiotherapy and chemotherapy remains unclear. Melanoma is known to be relatively radiotherapy-resistant and in a large series of postoperative radiotherapy in head and neck mucosal melanoma over 28 years radiotherapy was found to offer a significant benefit on local control, but not on survival [42].

Radiotherapy of the lacrimal region is often complicated by the proximity of critical structures, namely the intra-orbital and intra-cranial contents. Volumetric modulated arc therapy uses the same hardware (linear accelerator) as IMRT, but delivers radiation treatment in rotational or arc geometry rather than several static beams. It gained popularity in the United States in 2004, although there remains limited evidence of its use in lacrimal sac tumours [43-45]. In our case, IMRT was compared to VMAT for the radiation of the field of interest. VMAT was found to be clearly superior to 3DCRT in all respects, and was comparable to IMRT in terms of target coverage. Overall, VMAT resulted in lower doses to organs at risk (orbit, lens, optic chiasm, brainstem and optic nerves), and the dose fall off and conformality were also better in this modality [46].

Lacrimal sac melanomas are infinitely rare, with only 44 cases previously reported in the literature in almost 90 years. However, experience with other mucosal melanomas of the head and neck suggests that tumors of this cell line are very difficult to control and carry poor prognosis - even in the current era of advanced chemo- and radiation therapy. Early diagnosis is the key to improving prognosis, and clinicians need to have a high index of suspicion when atypical symptoms such as bloody discharge, and mass above medial canthal tendon are seen.

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