

**Lacrimal sac primary squamous cell carcinoma with synchronous tonsillar primary squamous cell carcinoma**

Zhiheng Lin, Southend University Hospital, corresponding author (zlin@doctors.org.uk)

Carl Philpott, University of East Anglia

Katherine Sisson, Norfolk and Norwich University Hospital

Bridget Hemmant, James Paget University Hospital

Primary lacrimal sac malignancies are rare and are either epithelial or non-epithelial. Epithelial tumours are more common, with squamous cell carcinoma (SCC) being the most common epithelial tumour.<sup>1</sup> SCC classically presents with the non-specific symptom of tearing plus the clinical sign of lacrimal swelling, and is often initially misdiagnosed as chronic dacryocystitis.<sup>2</sup> Suspicion should arise if there are bloody tears or discharge, with or without epistaxis, or swelling that extends above the medial canthal tendon.

Lacrimal sac SCCs can be primary and spread directly with invasion of the orbit and paranasal sinuses or in later stages indirectly via the lymphatic system, metastasizing most frequently to lungs.<sup>3</sup> They can also originate elsewhere with secondary spread to the sac.

We present a case where lymph node involvement with histological inconsistency in an atypical location prompted further investigation, which subsequently led to the finding of an additional primary SCC.

### **Case Report**

A 61 year old man presented with left epiphora that had not resolved following 2 previous endonasal dacryocystorhinostomies (DCR) 9 and 3 years ago respectively. His symptoms were thought to be secondary to previous sinusitis. He had a history of ocular hypertension treated with timolol, but no past medical history of note.

On initial examination there was no palpable mass over the medial canthus. Probing the left side came to a soft stop at common canaliculus, with reflux on syringing. The right side was normal. He was listed routinely for DCR via an external approach given his previous unsuccessful endonasal operations.

During the procedure (which took place 3 months after listing), the lacrimal sac was found to be thickened and fleshy. Histopathology showed a focally-keratinising SCC, positive for human papilloma virus (HPV) and p16 expression. Subsequently, a CT orbits with contrast showed an enhancing left anterior nasal soft tissue mass with extension into the left eyelids, nasolacrimal duct, periorbital fat, anterior ethmoid sinus and nasal cavity (figure 1, figure 2). Destruction of the left frontal process of the maxilla was noted. A level 2 lymph node was enlarged but on the contralateral side. A CT chest showed non-specific ground glass nodules in the left lower lung lobe, with no mediastinal lymphadenopathy. On further discussion with radiology, destruction of the frontal process was attributed to previous surgery, and the tumour was therefore downgraded from T4a to T1.

A rhinologist opinion was sought which found a large nasal mass laterally displacing the left middle turbinate. A biopsy was taken which was reported as chronic non-specific inflammation. The head and neck team agreed on exenteration with bilateral neck dissection, with removal of the lids, nasal cartilage along with parts of the maxilla, nasal septum and middle turbinate. Reconstruction was performed with an anterolateral thigh free flap.

Further histopathology showed a grade 2 SCC arising from the lacrimal duct mucosa, with lymphatic but not perineural invasion. There was involvement of the medial canthus to the skin of nose, medial periorbital fat and possibly extraocular muscle. The bony destruction was confirmed to be secondary to the previous DCR surgery and not tumour extension. Neck dissection showed a single contralateral node with a 16mm non-keratinising SCC, again positive for HPV and p16 expression, with no extracapsular spread.

The node was not focally-keratinising unlike the lacrimal primary SCC, and an additional primary lesion in oropharynx was suspected based on lymph drainage. Examination of the throat was normal, however a PET-CT showed increase uptake in the right oropharynx at the palatine tonsil. This was

excised and histopathology confirmed a non-keratinising SCC also positive for HPV and p16, thought to be another primary tumour. The patient was offered radiotherapy.

### **Comment**

To the best of our knowledge, this case reports the first case of an inconsistency in histology and atypical location of lymph node involvement leading to the discovery of a second primary SCC.

Most cases of lacrimal sac malignancy are picked up incidentally during DCR, when the appearance of the mucosa appears abnormal. As in this case, the external approach allows better visualisation of the lacrimal sac. Biopsies are usually performed in cases of abnormal tissue, clinical suspicion or known systemic disease.<sup>4,5</sup> Deeper tissue should be taken as superficial tissues often only shows chronic inflammation as with the second biopsy in this case.<sup>6</sup>

The presence of HPV and p16 expression impact on the management and prognosis. The association between HPV and carcinoma is well established, with a nationwide programme of vaccination for adolescent girls and more recently boys. HPV 16 has the strongest association in head and neck SCCs and ophthalmic SCCs.<sup>7</sup> In the absence of HPV, SCCs are less responsive to chemotherapy with lower survival.<sup>7</sup> p16 is a tumour suppressor gene and inactivation by HPV leads to a poorer prognosis.<sup>8</sup> Our case was positive for both for all biopsies.

Keratinizing SCCs as with the lacrimal sac lesion have a much lower incidence of lymph node metastasis compared to non-keratinizing SCCs, although poorer survival.<sup>9,10</sup> The difference in histology and prompted further investigation leading to the discovery of a second primary not found on initial examination, although metastases can be histologically different from the primary. Metastases are late occurrences, and whilst the level of node involved is typical, the contralateral site is not.<sup>11</sup> The contralateral tonsillar SCC could also have been a metastasis, however this has never been previously published and the location makes this improbable. It is also possible that the multiple previous DCR operations seeded the primary sac tumour.<sup>12</sup> One other mode of spread is lacrimal oncorrhoea, referring to free tumour cells in the tear film shed from a conjunctival primary, which then settles along the lacrimal duct system.<sup>13,14</sup>

This case highlights that lymph node involvement with histological inconsistency or atypical location should prompt further investigation. It also reemphasises the importance of nasoendoscopy before external DCR. We suggest having a low threshold for biopsy in DCRs especially for repeat surgery, and to obtain tissue from as deep as possible.

### **Word Count 979**

### **Disclosure statement**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

### **References**

1. Stefanyszyn MA, Hidayat AA, Pe'er J, Flanagan JC. Lacrimal sac tumors. *Ophthalm Plast Reconstr Surg*. 1994;10:169–84.
2. Yasemin A, Katircioglu, U, Emrah Altiparmak, et al. Squamous cell carcinoma of the lacrimal sac. *Orbit*. 2003;22(3):151-153. doi:10.1076/orbi.22.3.151.15616
3. Ni C, D'Amico DJ, Fan CQ, et al. Tumors of the lacrimal sac: A clinicopathological analysis of 82 cases. *Int Ophthalmol Clin*. 1982;1:121-40.

4. Bernardini FP, Moin M, Kersten RC, Reeves D, Kulwin DR. Routine histopathologic evaluation of the lacrimal sac during dacryocystorhinostomy. How useful is it? *Ophthalmology*. 2002;109:1214–8.
5. Merkonidis C, Brewis C, Yung M, Nussbaumer M. Is routine biopsy of the lacrimal sac wall indicated at dacryocystorhinostomy? A prospective study and literature review. *Br J Ophthalmol*. 2005;89:1589–91.
6. Krishna Y, Coupland SE. Lacrimal Sac Tumors - A Review. *Asia Pac J Ophthalmol (Phila)*. 2017;6(2):173-178. doi:10.22608/APO.201713.
7. Stephen JK, Divine G, Chen KM, Chitale D, Havard S, Worsham MJ. Significance of p16 in site-specific HPV positive and HPV negative head and neck squamous cell carcinoma. *Cancer Clin Oncol*. 2013;2(1):51-61. doi:10.5539/cco.v2n1p51
8. Ajila V, Shetty H, Babu S, Shetty V, Hegde S. Human Papilloma virus associated squamous cell carcinoma of the head and neck. *J Sex Transm Dis*. 2015;791024. doi:10.1155/2015/791024
9. Reddy SP, Raslan WF, Gooneratne S, Kathuria S, Marks JE. Prognostic significance of keratinization in nasopharyngeal carcinoma. *Am J Otolaryngol*. 1995;16(2):103-8
10. Vazquez A, Khan MN, Govindaraj S, Baredes S, Eloy JA. Nasopharyngeal squamous cell carcinoma: a comparative analysis of keratinizing and nonkeratinizing subtypes. *Int Forum Allergy Rhinol*. 2014;4:675–683.
11. Rahmi D, Ceyda B, Mehmet B, Sibel O, Ismail A. Squamous cell carcinoma of the lacrimal sac: a case and literature Review. *Ophthalmology Research*. 2014;2(6): 431-439.
12. Clayman G, Cohen JL, Adams GL. Neoplastic seeding of squamous cell carcinoma of the oropharynx. *Head Neck*. 1993 May-Jun;15(3):245-8.
13. Karcioğlu ZA, Carroll W: Conjunctival Tumors. In, Karcioğlu ZA (Ed) *Orbital Tumors: Diagnosis and Treatment*. New York, Springer 2015, pp 277-292
14. Rao R, Honavar SG, De Padua M, Mulay K, Reddy VP. Melanorrhea: Noncontiguous spread of palpebral conjunctival melanoma to the nasolacrimal duct. *Indian J Ophthalmol*. 2018 Feb; 66(2): 302–303.