Bilateral primary squamous cell carcinoma of the conjunctiva

Squamous cell carcinomas (SCCs) of the conjunctiva are rare, with an estimated incidence of 1–2.8 per 100 000 people per year. SCC is the most frequently occurring malignant epithelial tumour of the conjunctiva. Here we present a case of a patient presenting with 2 distinct primary carcinomas of the conjunctivae over a 3-year period.

In September 2018, a 57-year-old female presented to the emergency room (ER) complaining of a pruritic lesion in the left medial canthus that began to swell after scratching. It was first noticed approximately 1 month prior to presentation and had been growing since then. The lesion was tender, firm, and fungating from the left conjunctival fornix with extension over the left lower lid margin and onto the globe of the left eye. The body of the lesion contained streaks of heme and pigment and caused a mechanical ectropion.

The best-corrected visual acuity was 20/20-2 OD and 20/25-2 OS without complaints of blurry vision, photophobia, ocular pain, or bodily symptoms. The patient was born in Ghana, was of a dark complexion (Fitzpatrick VI), and had no remarkable ocular or dermatologic history. The patient was known only for hypertension at the time of presentation and was HIV negative.

Arsenic can be a risk factor for SCC and is present in high concentrations in some regions of Ghana. However, based on the town and region the patient was from, significant arsenic exposure was unlikely. Similarly, no arsenic level was determined for this patient because she had been living in Canada for >30 years.

Following an incisional biopsy, the histopathologic review showed an invasive neoplastic process of the left lower eyelid with large pleomorphic cells and numerous mitotic figures. The diagnosis was consistent with a poorly differentiated carcinoma with areas of squamous differentiation and areas of sebaceous differentiation, as confirmed by immunohistochemical analysis. Staging of the carcinoma was T3N0M0 with no lymphatic or metastatic spread. Clinical examination showed no spread to the nose or other mucus membranes, and no evidence of spread was seen on imaging. For this reason, otolaryngology was not consulted on this case.

The patient shortly thereafter underwent exenteration of the left orbit with a split-thickness skin graft harvested from the right thigh. The exenteration margins were confirmed as free of neoplastic involvement. The anophthalmic socket then healed with the formation of a small pyogenic abscess.

![Figure 1](image-url)

Fig. 1—(A) The patient’s right eye showing the sebaceous conjunctival carcinoma before treatment and the left anophthalmic socket status after exenteration. (B) The patient’s right eye and conjunctiva after 9 cycles of cemiplimab treatment.
granuloma and bloody discharge that cultured positively for *Staphylococcus aureus* that was treated with amoxicillin–clavulanic acid for 10 days twice daily per OS. The patient was asked to wear sunglasses after exenteration. The socket healed, and the patient had no ocular issues during more than 12 months of follow-up.

Approximately 30 months after the initial presentation, the patient presented to the emergency room with a mass in the right inferior conjunctiva. The lesion measured 3 cm in size and was centred in the lower fornix, extending over the eyelid margin and partially covering the pupil (Fig. 1A).

Histopathologic analysis of the lesion revealed an invasive neoplastic process with large pleomorphic cells and numerous mitotic figures. There were areas of squamous differentiation and areas with foamy cytoplasm, suggesting sebaceous differentiation, both of which were confirmed by immunohistochemistry. The histopathologic diagnosis was consistent with a poorly differentiated carcinoma with areas of squamous and sebaceous differentiation (Fig. 2A). The patient was immediately started on a course of 5-fluorouracil drops 4 times a day for 4 days, followed by 10 days off treatment. Magnetic resonance imaging of the orbits showed a

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Fig. 2—(A) Hematoxylin and eosin staining of the patient’s right conjunctiva prior to cemiplimab treatment. High-magnification histopathologic imaging shows large pleomorphic cells with vacuolated cytoplasm, numerous mitotic figures, and areas of poorly differentiated carcinoma with mixed sebaceous and squamous features. (B) Hematoxylin and eosin staining after 3 cycles of cemiplimab treatment shows noncancerous conjunctival tissue with mild acanthosis of the epithelium with nonspecific chronic conjunctivitis.
palpebral bulbar conjunctival lesion with possible extension into the inferior eyelid, approaching the insertion of the extraocular muscles. A computed tomography scan of the neck and full-body fluorodeoxyglucose-positron-emission tomography (FDG-PET) scan showed no evidence of metastasis. For this reason, this lesion was similarly staged T3N0M0.

Considering the known side effects of topical chemotherapy and the monocular status of this patient, the oncology service was consulted to initiate systemic immunotherapy. Topical 5-fluorouracil treatment was stopped, and the patient was started on intravenous cemiplimab (Libtayo, Regeneron Pharmaceuticals, Westchester County, NY) 350 mg every 3 weeks. Cemiplimab is a human monoclonal antibody that blocks T-cell programmed death 1 (PD-1) receptors, therefore blocking the binding of the PD-L1 and PD-L2 ligands of malignant cells and their evasion of T-cell-mediated apoptosis.7 The treatment was well tolerated, and after completing 9 cycles, the size of the lesion was greatly reduced (Fig. 1B). A tissue sample was obtained from the right conjunctiva after 3 cycles of cemiplimab and revealed mild acanthosis of the conjunctival epithelium and chronic inflammation. There were no signs of malignancy in the post-treatment specimen submitted for pathology (Fig. 2B).

In 2018, the only Health Canada–approved treatment option for this patient’s left conjunctival carcinoma was exenteration. In March 2019, cemiplimab was approved by Health Canada for the treatment of adults with metastatic or locally advanced cutaneous SCC who are not candidates for surgery or radiotherapy.5 Immunotherapy, specifically the use of cemiplimab, has been used in the treatment of conjunctival SCC in previous case reports.5 In 2021, with the approval and use of cemiplimab, this monocular patient was spared from exenteration of her right eye.

It has been noted that cemiplimab is more effective and more affordable than pembrolizumab, another immunotherapy, in the treatment of advanced cutaneous SSC.6 An analysis from the U.S. Food and Drug Administration’s Adverse Events Reporting System similarly showed no adverse ocular events reported for the use of cemiplimab, but adverse events were reports for the use of pembrolizumab.7 For this reason, it is therefore likely that cemiplimab is both more cost-effective and has a lower side effect risk, supporting its use in this patient.

First, it is important to appreciate that having the same type of malignancy present in the contralateral eye does not necessarily indicate a metastasis but can be rather a second primary malignancy. Second, prior to determining the therapeutic approach, it is important to stage the disease because 9% of conjunctival carcinomas may have nodal metastases.2 Finally, this particular case demonstrates the direct impact of medical innovations, clinical access, and timely medical approval on the life of this unique patient who presented before and after Health Canada approval of cemiplimab.

In this report, we review the case of a woman with invasive carcinoma of the conjunctiva of the left eye followed by a similar invasive carcinoma of the conjunctiva of the right eye 30 months later. Cemiplimab was not available in Canada when the patient presented with the initial cancer but was approved prior to her developing the second tumour. Had it been approved in Canada when it was approved in the United States,8 we have to wonder if the patient would have the benefit of binocular vision today.

### References


### Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.