CASE REPORT

Chronic red eye: a masquerade of advanced neoplastic disease

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SUMMARY

A 42-year-old woman presented with chronic history of left red eye for more than 12 months, treated with difference topical medication but without response. Ocular external examination demonstrated a firm palpable mass in the medial portion of the lower eyelid and slit-lamp evaluation of the lesion showed an ulcerated conjunctival nodule, keratin secretor. CT of the orbits revealed left-sided orbital mass located anteriorly, inferiorly and medially in the orbit, adjacent to the globe and orbit walls. Incisional biopsy of the lesion was consistent with invasive squamous cell carcinoma of the conjunctiva. As the tumour had no response to initial adjuvant systemic chemotherapy, exenteration of left orbit was performed due to advanced disease.

BACKGROUND

Squamous cell carcinoma (SCC) is the most common malignancy of the ocular surface.¹ It is part of a pathological *continuum* called ocular surface squamous neoplasia (OSSN) that includes localised lesions confined to the surface epithelium (dysplasia and intraepithelial neoplasia) and invasive SCC that invades the underlying stroma.¹ Conjunctival SCC clinical presentation extends across a wide spectrum, making its diagnose hard to perform. More commonly, the lesions have a leukoplakic or gelatinous appearance, starting in bulbar conjunctiva near the limbus and extending across it to involve the cornea. However, they can also present with a diffuse involvement of the conjunctiva that appears persistently red, masquerading a chronic conjunctivitis.² Therefore, a high degree of suspicious is mandatory in every atypical red eye or lesions that must always be promptly biopsied.

Although uncommonly, these tumours can have a potentially very aggressive behaviour and may penetrate the anterior chamber of the eye, the soft tissues of the orbit, the nasal sinuses and the brain. The lesions can also metastasise through conjunctival lymphatics and regional lymph nodes, having an important impact on sight and survival. Therefore, an aggressive therapeutic strategy is sometimes inevitable to ensure a long-term survival.

In this case report, we describe an atypical clinical presentation of squamous cell carcinoma in a young female, involving not only bulbar but also tarsal conjunctiva and skin with extension to the orbit that lead to a delayed diagnosis of advanced disease.

CASE PRESENTATION

A 42-year-old woman presented with a chronic ocular history of left red eye for more than 12 months. The patient had underwent, in other centres, multiple treatment regimens of topical antibiotics, antihistaminics and anti-inflammatories, without improvement of the symptoms. The initial examination demonstrated a best-corrected visual acuity of 20/20 bilaterally. Ocular external examination was significant for a firm mass palpable in the region of medial lower eyelid. Slit-lamp evaluation showed an ulcerated tarsal conjunctival nodule on the 2/3 medial portion of the lower eyelid, keratin secretor, with extension to the inferonasal bulbar conjunctiva and eyelid margin ([figure 1](#)). Apparent posterior extension deeply into the orbit soft tissues was suspected. Superficial vessel tufts were present around the lesion. No other alterations were detected, namely, evidence of invasion of the anterior segment of the eye and funduscopy was normal. Medical history including ophthalmological history and family history were negative.

INVESTIGATIONS

CT was immediately requested and the scans showed extension to the orbit with a mass located anteriorly, inferiorly and medially on the left orbit, adjacent to the globe and to the medial and inferior orbit walls, without apparent invasion of these structures ([figure 2](#)). An incisional biopsy of the nodule and bulbar conjunctiva was performed and was consistent with invasive squamous cell carcinoma of the conjunctiva, involving the tarsal and bulbar conjunctiva. Thereafter, the patient underwent metastatic workup consisting of CT of the brain and positron emission tomography (PET), both negative for the presence of local and distant metastasis. The lesion was staged T4aN0M0 (tumour invasion of orbit soft tissues, without bone invasion), according to the American Joint Committee Cancer (AJCC) classification.³

TREATMENT

An initial adjuvant approach with systemic chemotherapy with cisplatin, docetaxel and 5-fluorouracil was performed in order to achieve chemoreduction of the lesion and attempt full local excision of the tumour. However, after three cycles of chemotherapy, there was no clinical ([figure 3](#)) or imagological evidence of regression, and the multi-disciplinary tumour committee decided to proceed with an orbital exenteration, due to the aggressive

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Figure 1 Ulcerated lesion of the inferior eyelid keratin secretor.

behaviour of the lesion and the risk of further extension of the tumour. A partial left orbit exenteration was performed, preserving the superior eyelid.

OUTCOME AND FOLLOW-UP

Pathological evaluation of the exenteration specimen demonstrated a complete excision of the lesion with orbital periosteum free from tumour invasion. The patient will start aesthetical rehabilitation with external prosthesis after complete secondary healing of the bony socket. A strict follow-up is being performed every 3 months for the first year and then every 6 months for at least 5 years, in order to detect eventual local or regional recurrences.

DISCUSSION

OSSC occurs more frequently in fair skin man with an incidence average age of 56 years. There are several described risk factors associated with malignant SCC, including ultraviolet radiation exposition, human papilloma virus infection, immunodeficiency

Figure 2 CT coronal scan of the orbits showing a left orbital mass adjacent to the globe and the inferior and medial orbital walls.

Figure 3 Photography of the same lesion after three cycles of systemic chemotherapy.

virus infection, cigarette smoking, fair skin and dysfunctional DNA repair.² However, in this case report, the patient presented the disease at a younger age and apparently does not present any of the risk factors described.

The management of SCC of the conjunctiva varies with the extent of the lesion. Although there are different treatment modalities available, complete excision of the lesions ensuring tumour-free margins remains the most accepted treatment strategy. However, when complete excision is not possible due to the size and extension of the lesion, the use of adjuvant treatment modalities is accepted. The role of intravenous neoadjuvant chemotherapy was not established in any study, as SCC with orbital invasion requiring exenteration is relatively rare. However, systemic chemotherapy with cisplatin and 5-fluorouracil has been used successfully in conjunctival SCC, resulting in significant reduction in the tumour volume.⁴ Furthermore, cisplatin, 5-fluorouracil and docetaxel have been used in advanced SCC of the skin and other malignancies of head and neck. Combination of cisplatin, 5-fluorouracil and docetaxel has been described as a first-line treatment in patients with recurrent or advanced squamous cell carcinoma of the head and neck.⁵ Other adjuvant treatment modalities have also been tried in some clinical series, namely, topical mitomycin, 5-fluorouracil and interferon (IFN). Topical and perilesional IFN α -2b is gaining importance and some groups report good outcomes even for advanced stage disease. In a series of 81 OSSN cases managed with IFN α -2b, used as immunotherapy, immunoreduction and immunoprevention, Shields *et al* verified a high control rate of the disease with minor side effects.⁶

However, if the tumour does not respond to adjuvant treatments and total excision is still not possible, orbital exenteration is the only option to prevent aggressive local recurrences and metastasis. In cases of advanced disease in which exenteration is declined a high mortality must be expected. In 38 case series of advanced SCC (grade T3 and T4 AJCC), Miller *et al* described a mortality of 100% after a meantime of 13 months in patients with late-stage disease that refused further treatment.⁷ The authors also described a recurrence of 52% in patients with primary local excision of advanced tumour versus recurrence of 20% following orbital exenteration.

Desai *et al* described two cases related to regional spread of primary conjunctival SCC.⁸ A 65-year-old woman, with history of excision of a conjunctival SCC of the left eye, presented with

a mass with direct extension into the lacrimal gland. The tumour board recommended orbital exenteration, which the patient only accepted after 12 months, due to increasing pain of the left eye. On 6-month follow-up examination after exenteration, a nodal metastasis of the neck was detected. A 79-year-old man presented with local recurrence of conjunctival SCC, 3 months after incomplete local excision. MRI revealed regional spread to the parotid gland. The patient underwent orbital exenteration and parotidectomy but died 3 months later, after severe functional decline.⁸

Despite successful complete excision of the lesions, local recurrence is common, with reported rates ranging from 5% to 53%.⁹ Areas of apparently normal conjunctiva can in fact represent small tumour islands, making complete excision difficult to ensure. Therefore, adjunctive treatment has been used even after complete excision. Recurrences usually occur within 2 years after removal and tend to be more aggressive than the primary lesion.² Tarsal involvement and positive pathological margins have been described as the main clinical predictors of recurrence in a large series of 389 excised OSSN lesions.¹⁰ According to this case series, higher grade lesions and recurrent disease are also

associated with increased risk of recurrence. Therefore, most authors advocate adjuvant interferon therapy in patients at high risk for recurrence.

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Learning points

- Squamous cell carcinoma of the conjunctiva has a wide clinical presentation spectrum and the diagnose can be very challenging.
- An orbital exenteration is sometimes inevitable to control advanced disease.
- Strict follow-up is mandatory due to frequent recurrences that can occur even after 5 years of excision of the tumour.

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