Sebaceous cell carcinoma presenting as ocular Marjolin ulcer following immunosuppression for a chemical burn

Marjolin ulcer is a term used to describe malignancy that originates from chronically inflamed, ulcerated, or scarred tissue.[1] The potential for malignant transformation of ocular surface chemical injuries to a Marjolin ulcer is not well recognized.[2] In fact, this progression may be accelerated by the immunosuppressive treatments often used to control the postburn cicatrizing process. This report presents an ocular Marjolin ulcer following an alkali burn that was diagnosed histopathologically as sebaceous carcinoma.

A 67-year-old otherwise healthy and nonsmoking White female presented with a 2-year history of gradual onset of pain, redness, tearing, and blurred vision in her right eye. Four years previously, she had suffered an alkaline burn of the right eye from a common household cleaning agent, Windex Glass Cleaner (SC Johnson, Racine, Wisc.). Although eye irrigation was performed, the duration and extent were unclear. At presentation, right visual acuity was 20/1200 and near vision was <20/200. Intraocular pressure was 15 mm Hg. The examination demonstrated marked ocular surface disease and cicatrizing conjunctivitis (Fig. 1; Supplementary Fig. 1, available online). The left eye was normal. The patient was referred to a subspecialty dermatologist who performed conjunctival and oral mucosal biopsies. However, investigations for malignancy and other causes of cicatrizing conjunctivitis such as mucous membrane pemphigoid returned negative.

The patient was subsequently started on topical and systemic immunosuppression and underwent symblephara excision and staged simple limbal epithelial and amniotic membrane transplantation. Although there was initial improvement, the cicatricial disease progressed. She developed intractable pain, her visual acuity decreased to hand movements, and examination was notable for increased corneal neovascularization, recurrence of symblephara, and restriction of extraocular movements. She eventually developed microbial keratitis complicated by corneal perforation and underwent an evisceration. She also had biopsies of the right upper and lower eyelids taken to investigate abnormal periocular tissue. Histopathologic analysis revealed high-grade, poorly differentiated sebaceous cell carcinoma with intraepithelial pagetoid spread. To achieve tumour extirpation, an anterior exenteration with 5 mm margins and a skin graft was performed (Supplementary Fig. 2, available online). The sebaceous cell carcinoma was confirmed to involve the skin, palpebral conjunctiva of the right upper and lower eyelids, superior and medial fornices, and bulbar conjunctiva (Fig. 2; Supplementary Figs. 3 and 4, available online). The corneal epithelium was denuded but not involved. The skin margins were free of tumour. No lymphatic, vascular, or perineural infiltration was demonstrated on staging investigations. The patient underwent adjuvant radiotherapy to the socket and periocular tissues. No evidence of recurrence or metastasis was seen 36 months after these interventions.

In the 2002 biopic *My Big Fat Greek Wedding*, the larger-than-life Gus Portokalos states that all maladies from "psoriasis to poison ivy" can be cured just by "put[ting] some Windex on it" and is depicted applying the product liberally onto himself and others. However, perusal of the 2016 Australian Material Safety Data Sheet prepared by SC Johnson reveals that Windex Glass Cleaner is distinctly alkaline with a pH of 10.7 and contains ammonium hydroxide. Alkaline chemicals are recognized to be devastating to the integrity of the ocular surface because of their lipophilic nature, which leads to liquefactive necrosis and deeper penetration into intraocular structures compared with acidic substances.[3] Of note, ammonium hydroxide (ammonia) has been demonstrated previously to have the fastest penetration rate into the ocular surface of all alkaline substances.[3] This report serves as cautionary reminder of the dangers of all common cleaning agents that include alkaline substances.

Marjolin ulcers represent a neoplastic transformation arising from an area of chronic inflammation and scarring.[1] The development of a Marjolin ulcer in the periocular and ocular region is rare, but the propensity for its development should be recognized. The most common histologic subtype of Marjolin ulcer is squamous cell carcinoma, but basal cell carcinoma, melanoma, and sarcoma all have been reported.[1] This is the second case of a sebaceous cell carcinoma Marjolin ulcer in the literature. In 2014, Nayak et al.[2] reported the first patient who developed a periocular Marjolin ulcer 16 years after sustaining a lye chemical burn while working as a medical laboratory technician. The authors postulated that the low incidence of sebaceous cell carcinoma Marjolin ulcers was due to the limited distribution of sebaceous glands in the eyelid.[2]

Several hypotheses have been proposed to explain the pathophysiology underlying Marjolin ulcer development. We believe that the theory most pertaining to an ocular Marjolin ulcer revolves around a cocarcinogen concept where the initial burn or injury acts to increase tissue susceptibility to other carcinogens such as ultraviolet radiation.[4] The process of chronic irritation and repeated ulceration and healing also likely contributes to continuous mitotic activity and cell atypia. Other potential theories include a poor immunosurveillance response secondary to poor lymphatic flow and loss of normal immune cells in the chronic scar tissue allowing malignant cells to avoid immunologic detection.[1]

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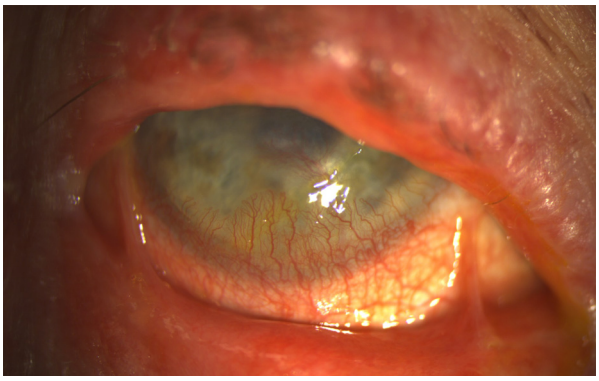

Fig. 1—Slit-lamp photograph of the right eye demonstrating marked postburn ocular surface inflammation consistent with a cicatrizing conjunctivitis with associated severe dry eye disease and both limbal and conjunctival stem cell failure. Signs observed include periocular erythema, chemosis, significant madarosis inferiorly, trichiasis, central corneal scarring, inferior corneal vascularization, evidence of previous corneal melting, temporal and nasal symblephara, and severe foreshortening and scarring of the inferior fornix.

Immunosuppression also likely exacerbates and accelerates the malignant transformation of a Marjolin ulcer. We believe that the intensive topical and systemic immunosuppressive regime in our patient may have contributed to the development of her neoplasm. In a comparable study, an ocular surface squamous neoplasia developed in a patient 3 years following the start of immunosuppressive therapy for a living-related conjunctival limbal allograft.[5] We also postulate this to be the reason for the shorter timeframe of Marjolin ulcer development in our patient when compared with the patient of Nayak et al.[2] Our case also may represent the increasingly recognized "acute" variant of Marjolin ulcer.[1]

As with most malignancies, early detection and treatment of Marjolin ulcers likely will yield more positive outcomes.

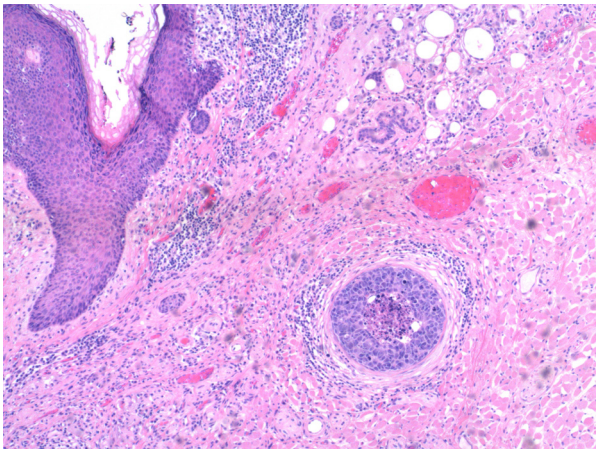

Fig. 2—Multiple foci of high-grade, poorly differentiated sebaceous cell carcinoma demonstrating pagetoid intraepithelial spread (top left). (Haematoxylin & Eosin stain). Note the intradermal nest of invasive sebaceous carcinoma exhibiting central comedo-type necrosis (bottom right).

Factors that may arouse a clinician's suspicion include the presence of an ulcer that persists for more than 3 months, rolled or everted wound margins, a foul-smelling discharge, or an increase in size, pain, or bleeding.[1] Recently, guidelines for the surgical management of Marjolin ulcers have been published.[1]

In conclusion, the potential for malignant transformation of ocular and periocular chemical injuries into Marjolin ulcers needs to be recognized. Sebaceous cell carcinomas should be included in the potential spectrum of histopathologic subtypes. Furthermore, this case raises an important consideration when initiating topical and (or) systemic immunosuppression for severe postburn cicatrizing disease, stem cell failure, and transplantation surgeries. We recommend that patients with previous chemical ocular burns, especially those started on immunosuppressive therapy, should be carefully evaluated, monitored, and counselled for the potential risk of Marjolin ulcer development.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jcjo.2022.02.023.

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Footnotes and Disclosure

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