Case Presentation

Severe exposure keratopathy secondary to oncologic surgery in a patient with epidermodysplasia verruciformis

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Abstract

A 43-year-old woman presented with multiple exophytic lesions on both eyelids of the left eye. The patient underwent excisional biopsy of the lesions, and later 2 more interventions were necessary for the excision of the affected margins. She was followed by dermatology and medical oncology specialists, as she presented several skin tumors in other locations. Two years after the intervention, she developed a lower corneal abscess in the left eye, with cultures positive for *Candida* spp. Approximately 12 months later, the infection had completely resolved, leaving a leukoma with both superficial and deep vascularization in the lower cornea. Lagophthalmos was observed along with a predominantly lateral cicatricial ectropion of the lower eyelid, accompanied by increased corneal vascularization, lipoid degeneration, and greater central opacity. The patient underwent cauterization of the superficial vessels and intrastromal bevacizumab injection into the deep vessels and has now been offered penetrating keratoplasty. Epidermodysplasia verruciformis is a rare skin condition characterized by the development of squamous cell carcinomas and flat warts. When these lesions involve the eyelid, close communication between dermatologists, corneologists, and oculoplastic surgeons is essential for optimal management of these patients.

Introduction

Epidermodysplasia verruciformis (EV) is a rare genetic disease within the genodermatoses group. It is characterized by the development of flat warts and lesions associated with human papillomavirus (HPV) infection that can undergo malignant transformation in approximately 50% of cases, most commonly into squamous cell carcinomas (SCC), basal cell carcinomas, or actinic keratosis.[1, 2] This disease is thought to result from a defect in cellular immunity, which is unable to recognize and reject antigen-presenting keratinocytes.[3,4] The most common inheritance pattern is autosomal recessive. Mutations have been identified on chromosome 17 that, together with cocarcinogenic factors such as ultraviolet light or gamma radiation, predispose affected individuals to the development of these skin tumors.[5]

Verrucous lesions in EV are usually resistant to standard treatments such as electrosurgery, cryotherapy or topical therapies. Secondary SCC typically present similarly to the classic form, although they are associated with greater local aggressiveness and higher recurrence rates.[6] Ocular and orbital involvement of EV and its secondary tumors has been reported only in a limited number of studies.[7,8] In these situations, ophthalmologists must aim to achieve optimal tumor resection and reconstruction to preserve effective eyelid function and maintain ocular surface protection. Achieving adequate safety margins may be particularly challenging and can result in corneal complications that require careful evaluation. Exposure keratopathy is a potential consequence of extensive eyelid resections that impair eyelid protection. The development of corneal scars or leukomas and neovascularization are secondary complications that can significantly impact visual acuity in these patients.[9]

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Case Synopsis

A 43-year-old woman presented with multiple exophytic lesions on both eyelids of the left eye. She reported progressive enlargement and increased number of lesions, with occasional bleeding.

Her medical history included dermatitis on the back, neck, and face consisting of hypochromic and hyperchromic macules and papules. She had previously been diagnosed with pityriasis versicolor, although the condition was resistant to standard antifungal therapy. She also reported numerous warts in the axillary region and on both feet. Physical examination revealed 3 lesions—2 on the upper eyelid and 1 on the lower eyelid—with ulceration and superficial keratinization (**Figure 1A–C**). The patient was offered excisional biopsy and was referred to dermatology for joint evaluation of the dermatosis.

Surgery was successful, and only a skin graft from the upper eyelid was required for reconstruction. Pathology showed enlarged cells in the granular and spinous layers, koilocytosis, and foci of dysplasia in all lesions, along with a diagnosis of SCC in 1 upper eyelid lesion, with positive margins. The findings were shared with dermatology, who—given the clinical context and distribution of lesions—diagnosed EV. Two additional interventions were required to achieve clear margins on the upper eyelid, including intraoperative biopsies on both occasions. Reconstruction was performed using multiple eyelid-sharing techniques. Local radiotherapy was subsequently indicated by the hospital skin tumor committee (50 Gy in fractionated doses).

The patient was followed by dermatology and medical oncology owing to the presence of multiple skin tumors elsewhere. Ophthalmologic follow-up was irregular until 2 years after the initial intervention (1.5 years after radiotherapy), when she presented with a lower corneal abscess in the left eye (**Figure 1D**). Cultures grew *Candida* spp., prompting initiation of antifungal therapy with weekly follow-up. Approximately 12 months later, the infection had fully resolved, leaving a leukoma with both superficial and deep vascularization in the inferior cornea. The best-corrected visual acuity (BCVA) at that time was 0.5.

A 2 mm lagophthalmos was noted, along with predominantly lateral cicatricial ectropion of the lower eyelid and medial thickening. The patient was referred for partial tarsorrhaphy and a lateral tarsal strip to protect the ocular surface and to evaluate the possibility of a future Deep Anterior Lamellar Keratoplasty. Despite partial invasion of the visual axis by the leukoma, the patient maintained a BCVA of 0.5 and declined corneal transplantation.

Autologous serum eye drops and moisturizing ointment were prescribed. Over 5 years of follow-up, clinical stability of the leukoma and BCVA was observed. After the SARS-CoV-2 pandemic, however, the patient reported significant foreign body sensation. Examination revealed irregular epithelium, increased corneal vascularization, lipoid degeneration, and greater central opacity. The upper eyelid showed an irregular margin, retraction of the subtarsal conjunctiva, and trichiatic eyelashes, which were removed (**Figure 2A–B**). At that time, BCVA had decreased to 0.2, so cauterization of superficial vessels and intrastromal bevacizumab injection into deep vessels were performed (**Figure 2C–D**).

At 2-month follow-up, the patient showed near-complete remission of corneal vascularization, decreased exudation, and improvement of BCVA to 0.4. However, at 6 months, central corneal thinning was observed, and BCVA had declined again to 0.2. The patient has now been offered penetrating keratoplasty in the left eye but has had to postpone surgery owing to the need for further treatment of cutaneous carcinomas in multiple other locations (**Figure 3**).

Case Discussion

EV is a rare skin condition that is frequently misdiagnosed owing to the similarity of its lesions to pityriasis versicolor and common warts. However, the carcinogenic potential of HPV and chronic sun exposure typically lead to malignant transformation in approximately 50% of lesions over a patient's lifetime. Various locations for SCC-type skin tumors have been described in the literature, predominantly in photoexposed areas.[10] The skin of the eyelids and periocular region is no exception, and tumors in this area may compromise the normal function of critical periocular structures. Therapeutic approaches to SCC may include adjuvant intralesional or systemic agents such as alpha interferon or anti–PD-1 monoclonal antibodies, including cemiplimab.

Oncologic resections with wide margins often require reconstruction using multiple techniques depending on the anatomical region involved. Skin grafts are usually the first choice for repairing the anterior lamella, whereas more complex grafts and flaps are needed to address full-thickness defects.[11] Although preservation of eyelid protective function is the primary goal, the involvement of the facial region necessitates attention to cosmetic outcomes as well. The most limiting factors include the width of the required resection margins and the involvement of complex structures such as the eyelid margin or the medial and lateral canthi. Eyelid malpositions, ectropion, and lagophthalmos are potential sequelae that must be carefully evaluated and treated.

Exposure keratopathy can result from impaired eyelid protection owing to a variety of conditions. In the present case, both the extensive tumor resections and subsequent radiotherapy led to eyelid margin irregularity, incomplete closure, and subtarsal conjunctival retraction, ultimately causing significant complications. Although radiotherapy was performed with strict shielding of the globe, minimizing direct ocular damage, the combined effects of eyelid tissue resection and irradiation contributed to the development of exposure keratopathy.

A corneal abscess is a serious, though not uncommon, complication of exposure keratopathy. Although bacteria are typically implicated, fungi can also be responsible,

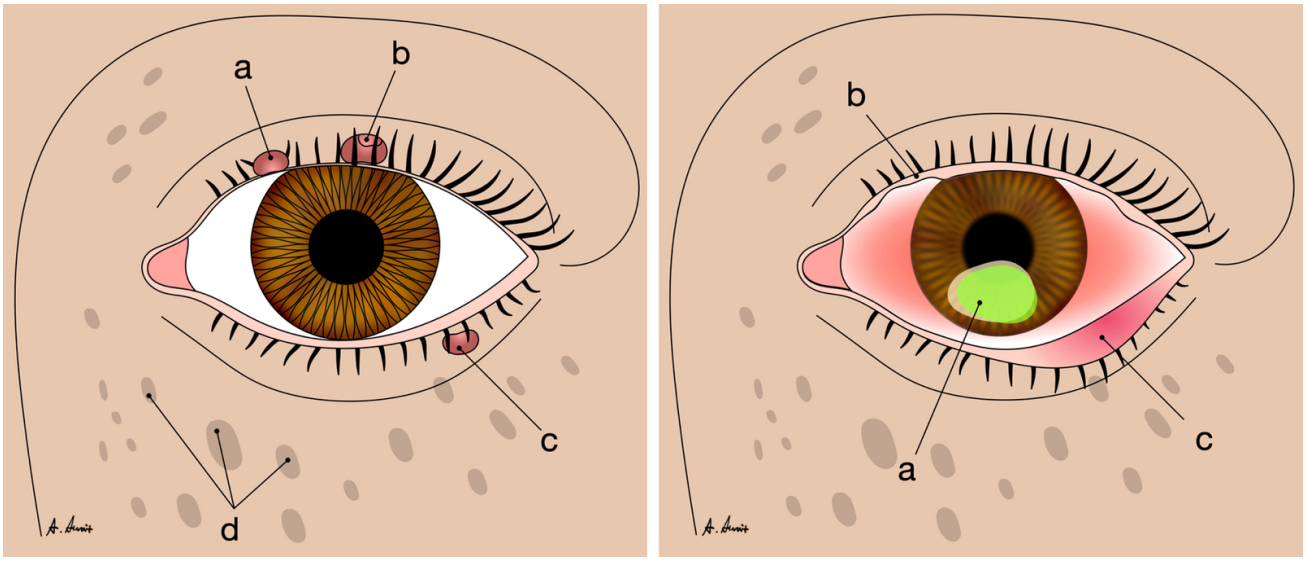

Figure 1. ***(A)*** *Illustration of the location of the different periocular lesions the patient presented.* ***(A–C)*** *Exophytic lesions with ulceration and keratinization.* ***(D)*** *Hyperchromic/hypochromic macular lesions.* ***(A, B)*** *Illustration of the status of the eyelids and cornea at presentation with an abscess.* ***(B)*** *Irregularity of the eyelid margin and* ***(C)*** *predominantly lateral ectropion can be observed. Source: Own elaboration.*

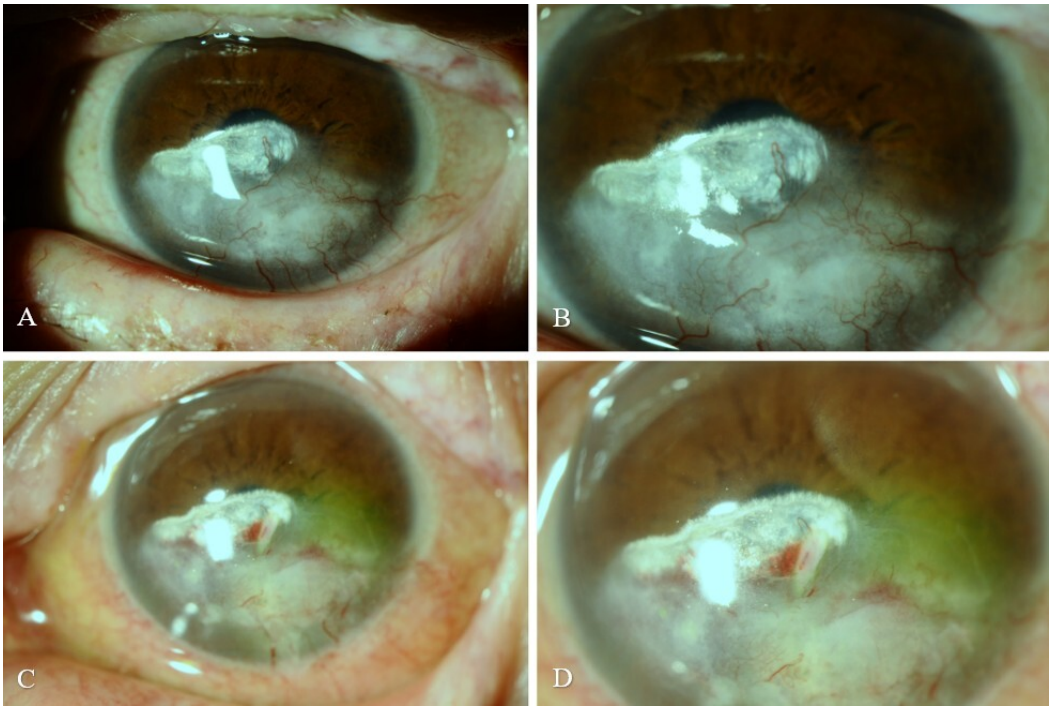

Figure 2. ***(A)*** *Photograph of the left eye before surgery.* ***(B)*** *Detail of the corneal vascularization within the leukoma.* ***(C)*** *Photograph of the left eye 1 week after cauterization of the superficial vessels and intrastromal bevacizumab injection.* ***(D)*** *Detail of the corneal leukoma. Superficial residual hemorrhage and peripheral vascular stops can be observed.*

particularly in subacute cases, and may lead to dense, heavily vascularized leukomas as part of a chronic disease course.

In complex situations such as this, addressing exposure defects should be prioritized before considering corneal transplantation. Only once adequate eyelid closure and blinking function are restored can penetrating or anterior lamellar keratoplasty be safely considered. Additional factors, including the patient's overall condition, quality of life, and daily functional impact, must also be weighed when deciding whether and when to proceed with surgery.

For patients with dermatologic conditions affecting the periocular region, such as EV, preventing severe ocular surface damage following oncologic resection is essential. In the present case, the patient experienced mul-

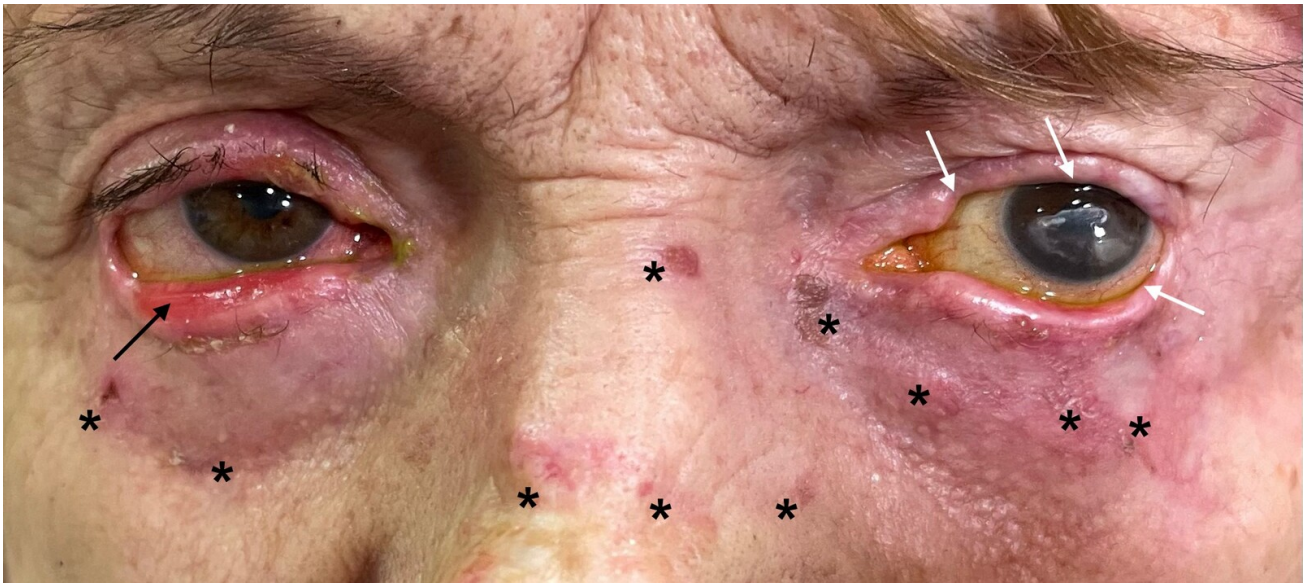

Figure 3. *Photograph showing the periocular skin lesions and involvement of the nasal area characteristic of epidermodysplasia verruciformis (asterisks). Destruction of the upper and lower eyelid margins of the left eye and a non-vascularized corneal leukoma can be observed (white arrows). Ectropion of the lower eyelid of the right eye can also be observed (black arrow).*

tiple complications, including persistent epithelial defects, secondary keratitis, and dense scarring with corneal vascularization, which ultimately compromised vision. This case underscores the importance of careful preoperative planning and individualized postoperative care for EV patients to prevent serious ocular injury. The particular vulnerability of the periocular area in EV highlights the necessity of coordinated management among dermatologists, oncologists, and ophthalmologists.

Conclusion

The present case illustrates how dermatologic conditions can significantly affect the ocular surface, underscoring the close relationship between the protective function of the eyelids and the integrity of the globe, as well as the functionality of the cornea and other anterior segment structures. The clinical context, thorough history-taking, and careful physical examination are essential to differentiate common isolated eyelid malignancies from more complex systemic causes. Furthermore, this case highlights the importance of maintaining effective communication not only among ophthalmologic subspecialties but also with dermatologists and oncologists to ensure an appropriate and coordinated approach. Multidisciplinary care allows for optimal resource utilization and the development of therapeutic strategies focused on preserving visual function and the quality of life of affected patients.

Potential conflicts of interest

The authors declare no conflicts of interest.

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